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HIGHLIGHT

Homogeneous catalysis using iron complexes: recent developments in selective reductions

Kathrin Junge, Kristin Schröder and Matthias Beller*

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With respect to its availability, low toxicity, and price iron should be one of the most used metals in homogeneous catalysis. Surprisingly, so far the application of iron is underdeveloped in comparison to other transition metals. Herein, we highlight promising attempts obtained in hydrogenation, transfer hydrogenation and hydrosilylation, which nicely illustrate the potential of iron and hopefully initialize a ferric future for catalysis.

Introduction

The development of organometallic catalysis has been a true success story in the past decades and the introduction of molecular-defined organometallic complexes has modernized organic synthesis as well as the industrial production of fine and bulk chemicals. Without doubt the majority of the work in organometallic catalysis has been performed applying noble metals based on palladium, rhodium, iridium, and ruthenium complexes. Due to economic constraints, limited availability, and sometimes sensitivity and toxicity of precious metal complexes, there is an increasing interest to substitute such catalysts by more easily available bio-relevant metals. In this respect homogeneous catalysis with iron complexes offers a highly attractive replacement. Hence, this area has become one of the "hot topics" in catalysis ranging from coupling reactions to oxidations. However, when Bolm[1] reviewed various aspects of iron catalysis in 2004, hydrogenation and reduction played only a negligible role. Since then, more and more research groups have entered the iron age of homogeneous catalysis which is demonstrated by a dramatic increase of research in this area. In this highlight, we report the recent trends of iron-catalysed reduction reactions since the millennium.

Leibniz-Institut für Katalyse e.V. an der Universität Rostock, Albert-Einstein-Str. 29a, 18059 Rostock, Germany.
E-mail: matthias.beller@catalysis.de;
Fax: +49 381-1281-51113

Hydrogenation of C=C bonds

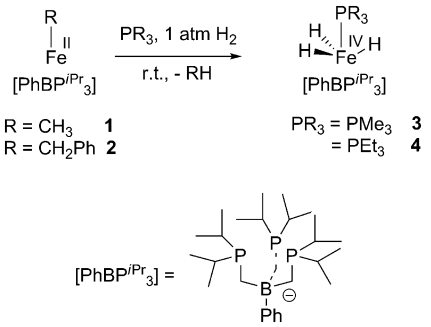
The first iron-catalysed hydrogenations of C=C double bonds reported in the

Kathrin Junge

Kathrin Junge, born in 1967, received her PhD degree in Chemistry from the University of Rostock in 1997 with E. Popowski. After a post-doctoral position in the Max-Planck group of Uwe Rosenthal she joined the group of Matthias Beller in 2000. Since 2008, she is group leader for homogeneous redox catalysis at LIKAT. She has been involved for years in catalysis research and has developed efficient catalytic hydrogenations for ketoesters and other carbonyl compounds. Moreover, new chiral ligands based on the binaphthophosphepine structure were developed by her. Her current main interest is the development of environmentally benign and efficient catalytic reactions based on cheap non-precious metals.

Kristin Schröder

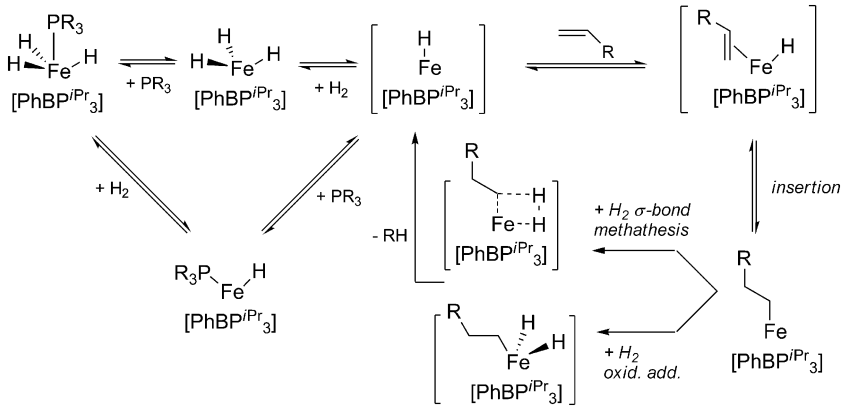
Kristin Schröder was born 1983 near Berlin, Germany. She performed studies in chemistry at the Universities Rostock and La Coruña (Spain). In 2007, she joined the group of Matthias Beller at the Leibniz-Institute for Catalysis (LIKAT) and started her PhD in the field of biomimetic iron catalysis. Her PhD work was supported by the DFG (Deutsche Forschungsgemeinschaft) and a Max-Buchner scholarship, which allowed her also to perform research in Girona (Spain) with Miquel Costas and Xavi Ribas. After finishing her PhD in 2010, she is currently working as scientist in the group of Prof. M. Beller. Her interests include redox reaction, iron catalysis together with bio-inspired complexes.



Scheme 1 Preparation of iron complexes according to Peters and Daida.

1960's led to poor chemoselectivity.[2] Hence, it was interesting to note in 2004 that the groups of Chirik[3] and Peters and Daida[4] independently presented defined iron complexes for the hydrogenation of unsaturated hydrocarbons under mild conditions (room temperature). More specifically, Daida and Peters developed a family of tris-(phosphino)borate-supported iron(II) alkyl **1–2** and iron(IV) trihydride complexes **3–4**, which serve as pre-catalysts for the hydrogenations of simple olefins and alkynes (Scheme 1). While styrene, ethylene, 1-hexene, cyclooctene, and 2-pentyne gave the corresponding alkanes, terminal alkynes led to olefin isomerisation and oligomerisations.

A mechanism was proposed based on NMR studies, whereby [PhBP$^{iPr}_3$]Fe(H)$_3$ was detected. The authors postulated an equilibrium between this trihydride species and [PhBP$^{iPr}_3$]Fe(H)(H$_2$) followed by loss of H$_2$ and concomitant olefin binding *via* the four-coordinated iron(II) hydride [PhBP$^{iPr}_3$]Fe(H) (Scheme 2). The resulting iron alkyl complex should then react with hydrogen to release the alkane and to regenerate the iron hydride source.



Scheme 2 Mechanism of iron-catalysed hydrogenation postulated by Peters.

Matthias Beller

Matthias Beller is director of the Leibniz-Institute for Catalysis in Rostock, Germany. His scientific work has been published in >450 publications and >90 patent applications. He has received several honours such as the Otto-Roelen Medal, the Leibniz-Price of the DFG and the German Federal Cross of Merit. In 2010, he was awarded the first "European price for Sustainable Chemistry" and the "Paul-Rylander Award" of the Organic Reaction Catalysis Society. Matthias Beller is head of the "Sustainable Chemistry" group of the German Chemical Society (GDCH) and a member of several academies including the German National Academia of Science "Leopoldina".

Chirik and co-workers presented a 14-electron [L$_3$Fe(0)] fragment containing a tridentate pyridinediimine ligand as an active hydrogenation catalyst (Fig. 1).[3] The dihalogen complexes **5a–b** are converted to the bis-dinitrogen complexes **6a–b** which are relatively labile compounds. Hence, loss of one equivalent of dinitrogen or an exchange with hydrogen or alkynes occurred in solution at room temperature. Applying low catalyst loadings (0.3 mol% of the low-valent bis(imino)pyridine iron complex **6a**) allowed for the hydrogenation of non-activated alkenes (mono-, di-substituted) with turnover frequencies (TOF) up to 1814 h^{-1} under comparatively mild reaction conditions. Noteworthily, even higher catalyst activities compared to precious-metal catalysts like Pd/C (TOF = 366 h^{-1}), the Wilkinson catalyst RhCl(PPh$_3$)$_3$ (10 h^{-1}), and Crabtree's catalyst [Ir(cod)(PCy$_3$)-(py)]PF$_6$ (75 h^{-1}) are feasible.

The scope and limitation of the catalyst system was demonstrated in the hydrogenation of various olefins including geminal, internal and tri-substituted olefins as well as diolefins. A broad substrate scope was also accessible for the hydrogenation of functionalized olefins bearing unprotected amines, esters, and ethers demonstrating the tolerance of several functional groups of complex **6a**.[5] However, only a diminished activity was observed for dimethyl itaconate, albeit using higher catalyst loadings. In the case of cyclohexene, detailed investigations emphasized a deactivation of the catalyst by arene complexation either from the solvent or the aryl groups in the ligand.[6] Internal alkynes such as diphenylacetylene or 2-butyne are also hydrogenated with **6a** yielding alkanes, but attempts using terminal alkynes as substrates failed. In contrast to α,β-unsaturated esters, α,β-unsaturated ketones induced a rapid decomposition of catalyst **6a**.[7] Although complex **6a** showed improved productivity for hydrogenation in pentane instead of toluene, the phenyl-substituted analogue **6b** bearing a more electrophilic iron center showed higher turnover frequencies for the hydrogenation of 1-hexene. For more hindered substrates such as cyclohexene and (+)-(*R*)-limonene, the opposite trend was observed.[6] This difference in

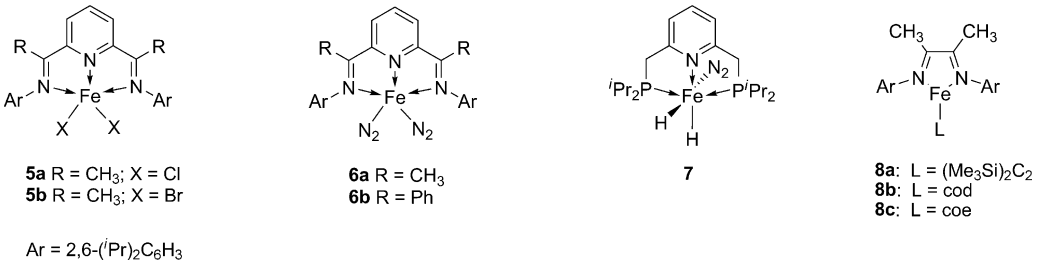
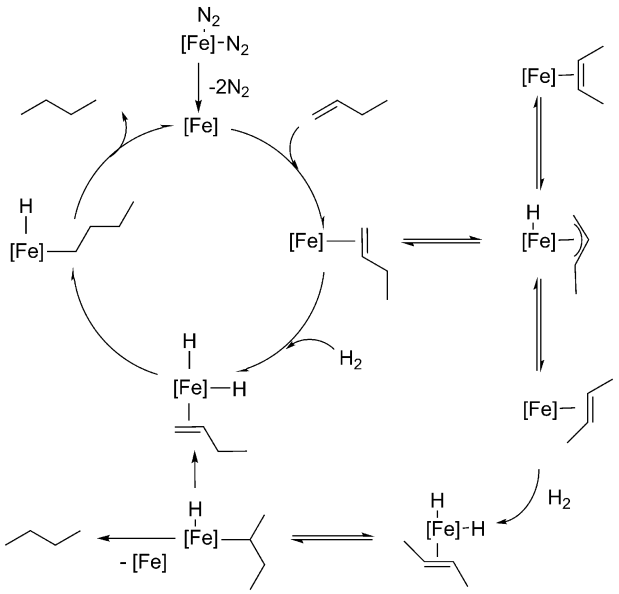


Fig. 1 Iron complexes according to Chirik.

catalytic performance resulted from competitive, irreversible formation of η^6-aryl and η^6-phenyl compounds with the phenyl-substituted complex **6b**. Chirik *et al.* also studied the influence of replacing the imino functionalities by phosphino groups giving ligand system **7** (Fig. 1).[8] Here, a different coordination mode was found since only one nitrogen ligand was replaced by hydrogen. The unstable complex **7** did not show any improvements compared to complex **6a**. Complex **7** was less active for hydrogenation of 1-hexene compared to complex **6a** and not active for more hindered olefins. Also diimine complexes **8** were attainable (Fig. 1)[9] and stabilized by more suitable ligands such as alkynes, olefins or diolefins. However, using **8** in the hydrogenation of 1-hexene only low activities were observed due to rapid formation of bis(chelate) or η^6-arene species leading to catalyst deactivation.

Mechanistic investigations suggested a catalytic cycle in which an unsaturated iron complex is formed by expulsion of both dinitrogen molecules (Scheme 3). Then, coordination of olefin takes place. Subsequently, oxidative addition of hydrogen yields a formally 18-electron complex. Insertion of the olefin formed the corresponding iron alkyl complex, which re-creates the starting complex *via* reductive elimination. Notably, in the absence of dihydrogen the olefin complex also catalyses an isomerisation of the double bond.

More recently, Bhanage and co-workers hydrogenated selectively the C=C double bond of α,β-unsaturated carbonyl compounds in a biphasic medium using water-soluble Fe^{II}/Na_2EDTA as a catalyst which can be easily recycled (Scheme 4).[10] Using citral as a model substrate a catalyst system consisting of $FeSO_4{\cdot}7H_2O$ and $Na_2EDTA{\cdot}2H_2O$ showed the best activity and selectivity towards saturated dihydrocitronellal

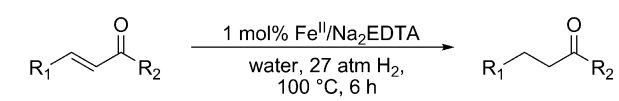


Scheme 3 Catalytic hydrogenation cycle according to Chirik.

(82%). Other α,β-unsaturated carbonyl compounds were hydrogenated with the Fe^{II}/Na_2EDTA catalyst at 100 °C. Cyclohex-2-enone (95%) and 4,4-dimethylcyclohex-2-enone (80%) gave high selectivity and high yield towards saturated cyclic ketones. Also α,β-unsaturated esters were successfully hydrogenated. Selective hydrogenation of crotonaldehyde gave *n*-butanal (68%) when the reaction is performed for 3 h, while a reaction time of 6 h gave *n*-butanol as the only product. Using a biphasic system at 140 °C cinnamic acid resulted in 25% of hydrocinnamic acid under hydrogenation conditions.

Hydrogenation of C=O bonds

Only in recent years, iron complexes have emerged as catalysts for the important hydrogenation of C=O bonds. In 2007, Casey and Guan reported the use of iron catalyst **9** (Knölker complex) in the hydrogenation of carbonyl derivatives under mild conditions (low hydrogen pressure, room temperature, low catalyst loading).[11] A detailed mechanistic study indicated that both the hydride and the hydroxy group contributed in the reduction of ketones, aldehydes, and imines to alcohols and



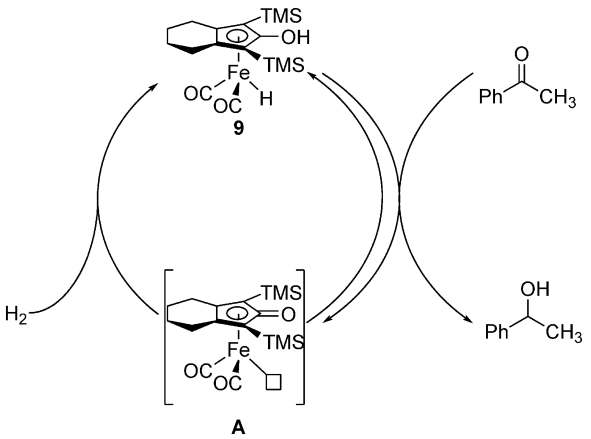
Scheme 4 Hydrogenation of α,β-unsaturated carbonyl compounds in the presence of the Fe/Na_2EDTA catalyst.

amines through an ionic hydrogenation. The catalytic active species was regenerated in the presence of dihydrogen (Scheme 5). Catalyst **9** demonstrated also a broad tolerance of functional groups and displayed good chemoselectivity as alkynes, isolated alkenes, epoxides, and esters were not hydrogenated. However, two limitations still remained: nitrile derivatives, which are potential ligands for unsaturated complexes or intermediates, inhibited the reaction, and the hydrogenation of α,β-unsaturated ketones gave rise to a mixture of unsaturated and saturated alcohols. Intramolecular trapping experiments support a mechanism involving a concerted transfer of a proton from OH and hydride from Fe of **9** to aldehydes.[12] DFT calculations of the mechanism of the carbonyl hydrogenation by the bifunctional iron catalyst **9** underlined that the catalytic reaction consists of two parts, *viz*., hydrogen transfer and dihydrogen activation.[13]

In 2008, Morris and co-workers reported for the first time the enantioselective hydrogenation of acetophenone in the presence of iron complexes. Using moderate hydrogen pressure and an iron(II) complex containing a tetradentate PNNP ligand **10a** led to modest conversion and enantioselectivity (40% conversion, 27% ee) (Fig. 2).[14] Recently, the range of well-defined iron complexes available for carbonyl hydrogenation was enlarged by Milstein's pincer complex **11** (Fig. 2).[15] Iron hydride complex **11** in the presence of 0.1 mol% KO*t*Bu allowed for efficient hydrogenation of ketones under mild reaction conditions (26–28 °C, 4.1 atm H_2). NMR spectroscopic investigations suggested that the reaction proceeds through a dearomatized intermediate.

Nishiyama and Furuta showed that an iron(II) complex containing sodium thiophene-2-carboxylate **12a** catalysed the reduction of 4-phenylphenyl methylketone (Scheme 6) to form the corresponding alcohol in 30% yield. On the other hand high yields with high selectivities were observed under hydrosilylation conditions.[16]

An appealing method for the synthesis of amines is the direct reductive amination (DRA) of carbonyl compounds with an amine in the presence of hydrogen. In this respect, Bhanage and co-workers described the first reductive amination



Scheme 5 Catalytic hydrogenation of ketones according to Casey.

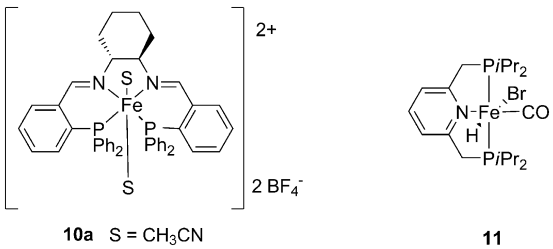
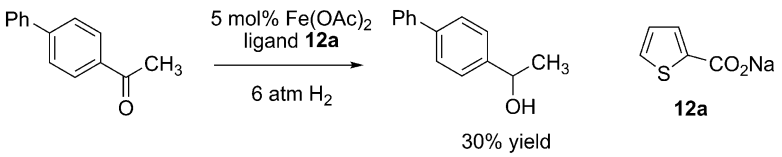


Fig. 2 Iron complexes for hydrogenation of ketones according to Morris and Milstein.

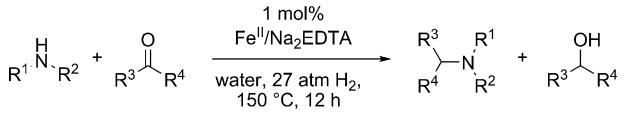


Scheme 6 Hydrogenation of 4-phenylphenyl methylketone according to Nishiyama and Furuta.

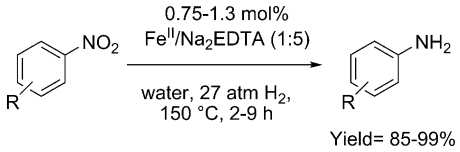
using a water-soluble Fe^{II}/Na_2EDTA complex as the catalyst under low hydrogen pressure (Scheme 7).[17] Even if the reaction conditions remained quite harsh, this simple catalyst appeared to be efficient for the DRA of aliphatic, aromatic and heterocyclic carbonyl compounds with primary/secondary amines. Recently, Enthaler presented an iron-based catalyst for the reductive amination of aldehydes with amines to produce secondary amines.[18] The generality of this method is outlined by application of $FeCl_3$ and PMHS as cheap hydride sources under non-inert conditions with excellent yields and a broad functional group tolerance.

Homogeneous hydrogenation of nitroaromatics and aryl azides

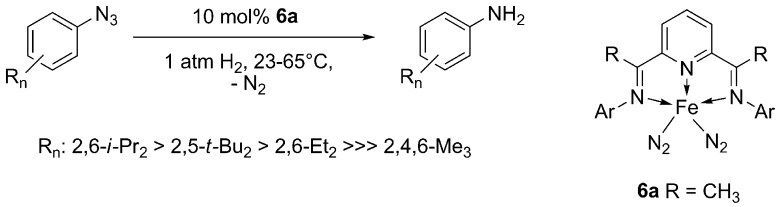
In 2004, Chaudhari and co-workers reported an Fe^{II}/Na_2EDTA complex for catalytic hydrogenation of nitroarenes (Scheme 8). Applying a biphasic system, the catalyst stays in the aqueous phase and allows for catalyst recycling.[19] With this catalyst, a TOF of 136 h^{-1} and a turnover number (TON) of 1333 for nitrobenzene were achieved with complete conversion of nitrobenzene and a selectivity to aniline greater than 98%. Although the activity of the Fe^{II}-system is reduced in the presence of Na_2EDTA



Scheme 7 Reductive amination of carbonyl compounds with amines by Bhanage.



Scheme 8 Hydrogenation of nitroarenes in the presence of Fe^{II}/Na_2EDTA.



Scheme 9 Iron-catalysed hydrogenation of aryl azides.

due to coordination, addition is necessary for keeping the catalyst in the aqueous phase. The aqueous phase was recycled 5 times and used with the fresh organic phase without any relevant loss of activity obtaining a cumulative TON of 6665.

Despite the high reaction temperature different substituted nitrobenzenes were selectively reduced in the absence of organic solvents. However, a reduced selectivity is observed in the case of *p*-nitrobenzoic acid, 4-nitrobenzyl nitrile and 4-nitroanisole due to the formation of azo and diazo derivatives. A more special method for the synthesis of aromatic amines represents the catalytic reduction of aryl azides reported by Chirik *et al.*[20] In the presence of 10 mol% of **6a** using 1 atm of hydrogen a series of aryl azides yielded the desired anilines (Scheme 9). Notably, the rate of catalytic hydrogenation increases with growing size of the aryl group showing fast reaction for 2,6-*i*-Pr_2-$C_6H_3N_3$ (6 h, 23 °C), slower for 2,5-*t*-Bu_2-$C_6H_3N_3$ (16 h, 65 °C) and 2,6-Et_2-$C_6H_3N_3$ (96 h, 65 °C) and finally giving no conversion in the case of 2,4,6-Me_3-$C_6H_2N_3$.

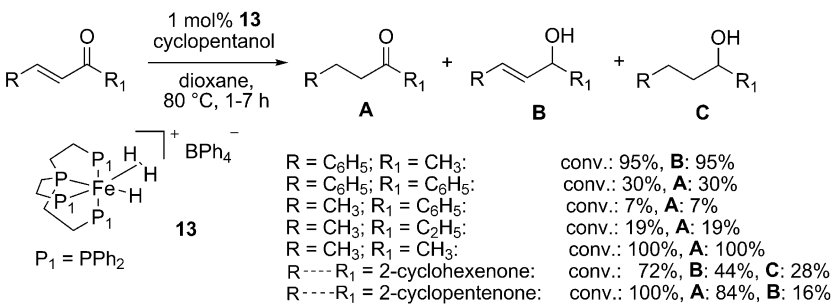
Catalytic transfer hydrogenations

In addition to hydrogenations with molecular hydrogen, transfer hydrogenations using alcohols or formic acid constitute valuable reduction procedures for different functional groups, especially carbonyl compounds. Thus, at the beginning of the 1990's Bianchini and co-workers investigated the transfer hydrogenation of α,β-unsaturated ketones by a non-classical trihydride iron complex $[(PP_3)FeH(H_2)]BPh_4$ (PP_3=P($CH_2CH_2PPh_2$)$_3$) (Scheme 10).[21,22]

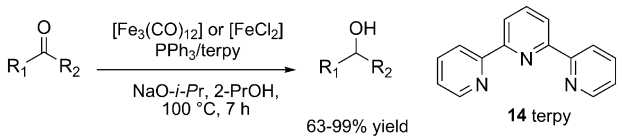
In the presence of 2-propanol or cyclopentanol as a hydrogen donor α,β-unsaturated ketones were hydrogenated to the corresponding saturated ketones with good to excellent selectivity under mild reaction conditions. In some cases, *e.g.* benzylideneacetone or 2-cyclohexenone, the unsaturated or saturated alcohols were formed in the presence of catalyst **13**, thereby also good selectivity was noticed. Noteworthily, no co-catalyst, *e.g.* base, is necessary to activate the catalyst or the hydrogen donor, which is needed for most other catalyst systems. However, for carbonyl hydrogenation, *e.g.* acetophenone and 3-pentanone, the Fe catalyst displayed only low activity and no reaction was observed for aldehydes or non-activated C=C double bonds.

In 2006, our group reported the application of three-component iron catalysts prepared *in situ* from $FeCl_2$ or $Fe_3(CO)_{12}$, 2,2′ : 6′,2″-terpyridine (terpy) **14** and PPh_3 for the transfer hydrogenation of aliphatic and aromatic ketones using 2-propanol as the hydrogen source (Scheme 11).[23] While studying the influence of different reaction parameters on the reduction of acetophenone a crucial influence of base and base concentration was observed. Good yields of the reduced product were obtained with NaO-*i*Pr or NaO-*t*Bu at temperatures which are higher compared to ruthenium-catalysed transfer hydrogenations. It should be noted that at high reaction temperatures (>100 °C) also simple base-catalysed reductions of carbonyl compounds might occur.[24]

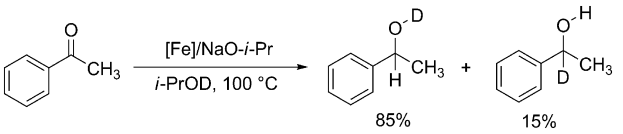
Spectroscopic investigations showed no clear picture of the active Fe–H species, although a radical-type reduction was excluded by using a "radical clock" substrate like cyclopropyl phenyl ketone. Application of 2-propanol-d_1 as a solvent/donor for transfer hydrogenation of acetophenone produced a mixture of two deuterated 1-phenylethanols (Scheme 12) in a ratio of 85 : 15. This incorporation of deuterium is in agreement with the so-called monohydride mechanism, implying a major formation of metal monohydride species in the catalytic cycle.



Scheme 10 Application of a non-classical iron trihydride complex in transfer hydrogenation according to Bianchini and co-workers.



Scheme 11 *In situ* catalyst based on [Fe]/terpy/PPh_3 in the transfer hydrogenation of ketones.



Scheme 12 Incorporation of deuterium into acetophenone.

Parallel to the work on *in situ* three component catalysts we also developed a biomimetic iron porphyrin system for ketone reductions (Scheme 13).[25] The porphyrin complexes (Fig. 3) which are known for high stability and inertness against oxygen and moisture achieved higher activities than the [Fe]/PPh_3/terpy system.

Under optimised reaction parameters turnover frequencies up to 642 h^{-1} were attained at low catalyst loadings (0.01 mol%). A ligand screening including naturally occurring ligands **16** and **17** emphasised porphyrins **15b** and **15e** as most active ligands for further investigations on substrate variation. In addition to aryl alkyl ketones also different dialkyl ketones were reduced.

Using Fe porphyrin systems transfer hydrogenations of more challenging α-hydroxyl-protected ketones were reported, too (Scheme 14). Here, the corresponding mono-protected 1,2-diols are obtained in good yields and TOF.[26] Remarkably, addition of small amounts of water (5–10 mol%) improved the catalyst activity up to 2500 h^{-1} at low catalyst loadings (0.01 mol%).

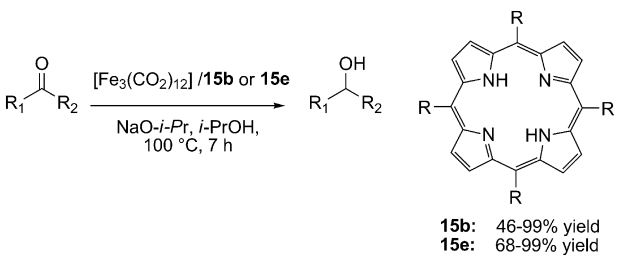
Nishiyama and Furuta reported another *in situ* Fe-based system composed of iron acetate and sodium thiophene-2-carboxylate **12a** that showed some activity for the reduction of 4-phenylphenyl methylketone (Scheme 6) in the presence of NaO*t*Bu/*i*-PrOH.[16]

Important developments were also reported by Casey and Morris. Both prepared well-defined iron complexes **9** and **10a–c** which catalysed the transfer hydrogenation of acetophenone.[11,14] While investigating this model reaction in detail, an asymmetric reaction proceeding at room temperature in the presence of **10b–c** was developed (Fig. 4).[14] Notably, already in 2004 Gao and co-workers reported the application of this ligand type in combination with $[Et_3NH][HFe_3(CO)_{11}]$ for the transfer hydrogenation of ketones to obtain enantioselectivities up to 98% ee although in moderate yields.[27]

Complexes **10b–c**, which were found to be inactive for hydrogenations with molecular hydrogen, are on the other hand efficient catalysts for transfer hydrogenation of ketones, aldehydes, and imines. Here, a variety of substrates was investigated. Noteworthily, the electronic properties of substituents on the phenyl ring of aryl ketones influenced the reduction rate but had less effect on the enantioselectivity. The highest enantioselectivities obtained with **10b** and **10c** were 61% ee and 76% ee respectively; however in the latter case only moderate conversion (34%) was achieved. The more difficult ketimine (Ph–CMe=N–Ph) was only reduced to a minor extent (<5%), while cyclohexanone showed no reactivity at all. Later on, Morris and co-workers presented the improved catalyst precursor **18** which compared to **10b** showed significantly higher activity and selectivity.[28] Here, the reduction of more hindered aromatic ketones proceeded with excellent enantioselectivities up to 99% ee, although a decrease in conversion for the more bulky *t*-butyl substituent was observed. On testing challenging substrates like non-aromatic ketones or imines only moderate ee and low activities were detected.

Related iron complexes with tetradentate ligands **19–21** were applied by the group of Le Floch (Fig. 5).[29] They studied the coordination of these ligands to iron(II) metal centres and synthesized the corresponding complexes starting from $[FeCl_2(THF)_{1.5}]$. The different neutral and cationic complexes showed catalytic activity in the transfer hydrogenation of acetophenone at temperatures above 80 °C, while no reaction took place at room temperature.

Morris *et al.* enlarged the range of iron complexes containing tetradentate P_2N_2-ligands to probe the effect of substitutions at the diamine backbone



Scheme 13 Bio-inspired transfer hydrogenation of ketones with iron porphyrin catalysts.

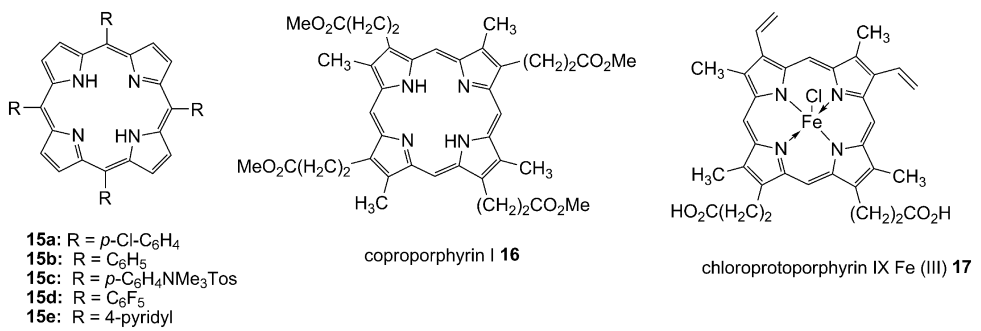
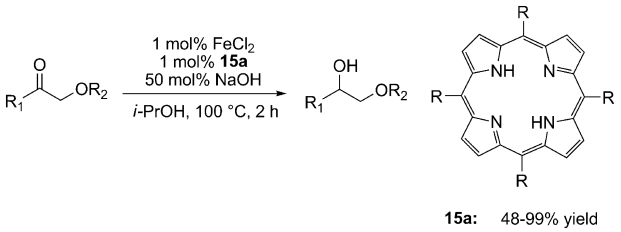


Fig. 3 Selection of porphyrin ligands and catalysts.



Scheme 14 Reduction of α-substituted ketones in the presence of iron porphyrin catalysts.

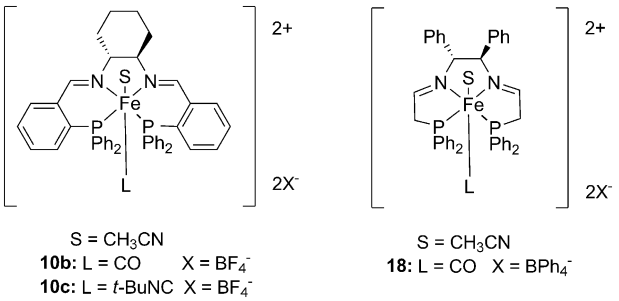


Fig. 4 Defined Fe-complexes for asymmetric transfer hydrogenations according to Morris.

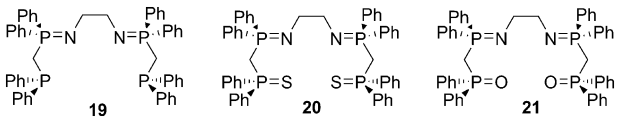


Fig. 5 Tetradentate ligands according to Le Floch.

on the catalyst activity and enantioselectivity in the hydrogenation of acetophenone in basic 2-propanol (Fig. 6).[30] Using optimised conditions (50 °C, 25 bar H_2) complexes **22b**, **25** and **26** proved to be moderately active pre-catalysts with activities comparable to that of **10a**.[14] Even though the two chiral complexes **23** and **24a** displayed poor reactivity referred to the bulky axial substituents blocking the access to the iron centre, complex **24a** gave (*S*)-1-phenylethanol with 61% ee. Applying complex **24b** an improvement of catalytic activity was also observed.[31] With a catalyst/base/substrate ratio of 1 : 8 : 600 almost complete conversion has been achieved for all substrates after 1 h. Alcohols with ee of up to 96% and catalyst turnover frequencies of up to 2600 h^{-1} were obtained. Most recently, another series of related iron complexes was presented by varying the phenyl substituents at both phosphorous atoms of ligand **18** (into Cy, *i*-Pr, Et) concomitant with a change of the ligand's linker backbone (Ph or H).[32] However, none of these complexes led to similar or higher yields in comparison with the original ligand **18**. Additionally, studies on the variation of the ligand diamine backbone were recently published.[33] Besides the coordinated acetonitrile was exchanged by a bromide ligand, however, no significant enhancement of TOF or ee could be achieved.

In 2010, also novel iron bis(isonitrile) complexes **27a–e** were applied in the asymmetric transfer hydrogenation of aromatic and heteroaromatic ketones by Reiser and co-workers (Fig. 7).[34] Applying a combination of complex **27c** (5 mol%), KO-*t*Bu and *i*-PrOH at 22–24 °C acetophenones were converted into the corresponding alcohols with ee's ranging from 52% to 67% and provided up to 91% ee for pyridyl ketones. Furthermore, Peris and Royo reported cyclopentadienyl-functionalized NHC Fe(II) complexes **28** and **29** for the transfer hydrogenation of aromatic ketones and cyclohexanone.[35] In the latter case reactions were carried out at 80 °C with 1 mol% of catalyst loading utilizing KOH as a base and *i*-PrOH as a hydrogen source. Good reactivities

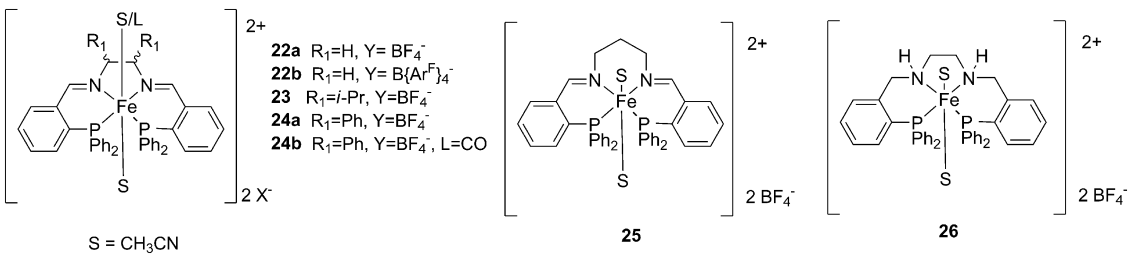


Fig. 6 Iron complexes containing P_2N_2-ligands.

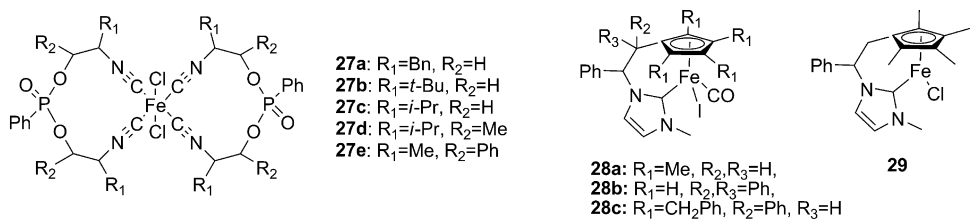
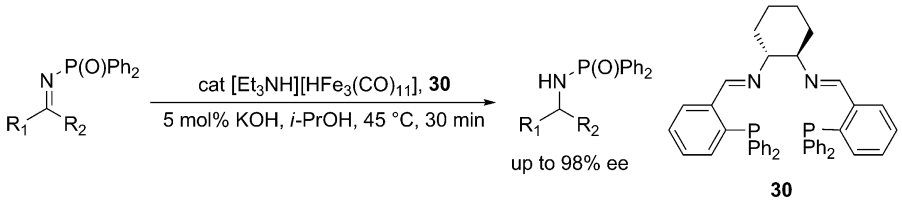


Fig. 7 Iron complexes synthesized by Reiser and Peris and Royo.



Scheme 15 Asymmetric transfer hydrogenation of imines.

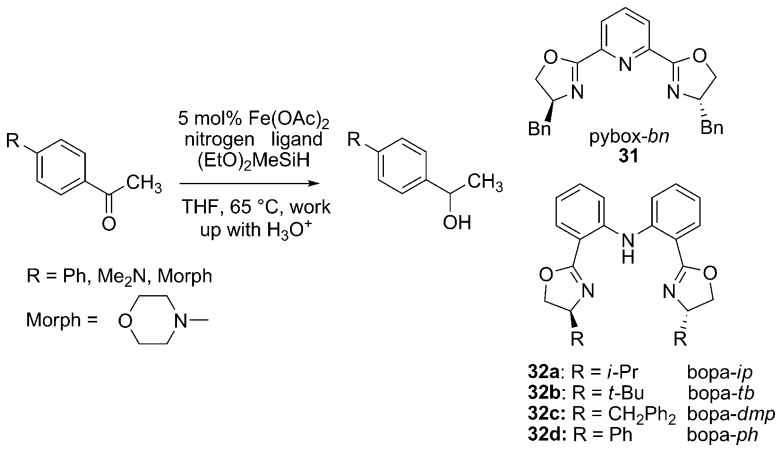
(up to >99% yield for cyclohexanol) were achieved and catalyst **28** was also active in hydrosilylation reactions.

Very recently, our group reported on the first iron-catalysed transfer hydrogenation of ketimines.[36] Facile *in situ* generation of the active catalyst took place from ligand **30** and an iron carbonyl hydride cluster (Scheme 15). Up to 99% yield and 98% ee were obtained with 0.33 mol% of the iron precursor utilizing *i*-PrOH as the hydrogen source. Catalyst loadings could even be decreased to 0.17 mol% and still demonstrated 95% yield and 96% ee for the substrate *N*-(diphenylphosphinyl)-(1-phenylethylidene)imine. A variety of chiral amines is accessible including aromatic, heteroaromatic and cyclic amines from the corresponding *N*-(diphenylphosphinyl) ketimines through this novel protocol.

Catalytic hydrosilylations

In addition to catalytic reductions with molecular hydrogen or transfer hydrogen reagents also hydrosilanes represent useful reducing agents.[37] The first example of the enantioselective iron-catalysed hydrosilylation of acetophenone has been reported as early as 1990 by Brunner *et al.* investigating the photo-induced activation of [Fe(Cp)(CO)] complexes.[38,39] Then, it took several years before Nishiyama and Furuta presented an efficient catalytic system based on $Fe(OAc)_2$ and multi-nitrogen-based ligand (Scheme 16).[40] The hydrosilylation of ketones was carried out under mild conditions (THF at 65 °C) producing yields up to 95%. Using tmeda as a nitrogen ligand Fe-catalysed hydrosilylation works also with a number of aromatic ketones.

Replacing tmeda by chiral tridentate bisoxazoline ligands an enantioselective reduction is possible. While pybox-*bn* **31** gave 37% ee, bopa-*ip* **32a** and *tb* **32b**



Scheme 16 Asymmetric hydrosilylation of ketones with iron catalysts according to Nishiyama and Furuta.

increased the enantioselectivity up to 57% ee and 79% ee, respectively. In a further study Nishiyama and co-workers were able to improve the asymmetric hydrosilylation of ketones by ligand design. More bulky substituents on the oxazoline ring in **32c** led to higher enantioselectivity (up to 88% ee).[41] To elucidate the mechanism the differences of well-defined complexes and *in situ* catalyst systems were investigated, too.[42] Interestingly the phenyl-substituted (*S*,*S*)-bopa/iron catalyst can access both enantiomers from a single chiral source depending on the use of either the well-defined iron complex ($FeCl_2$/bopa) and zinc or the *in situ* system ($Fe(OAc)_2$/bopa). Very recently Nishiyama and co-workers reported achiral and chiral iron complexes with bis(oxazolinyl)phenyl (phebox) ligands.[43] Interestingly, the alkyl Fe(II) complexes showed up to 66% ee with full conversion of methyl(4-phenylphenyl)ketone.

While Nishiyama focussed mainly on *in situ* catalyst systems, Chirik and co-workers investigated defined iron dialkyl complexes of pybox ligands **33** and bisoxazoline **34** in the hydrosilylation of carbonyl compounds (Fig. 8).[44] Moderate enantioselectivities (up to 49% ee) could be increased to 93% ee for catalyst **34a** by treatment of the pre-catalyst with ($B(C_6F_5)_3$). Our group reported a general asymmetric hydrosilylation of acetophenone in the presence

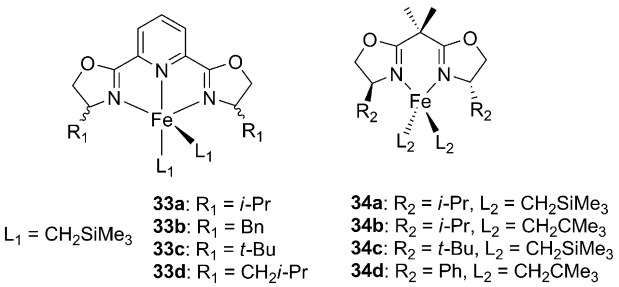
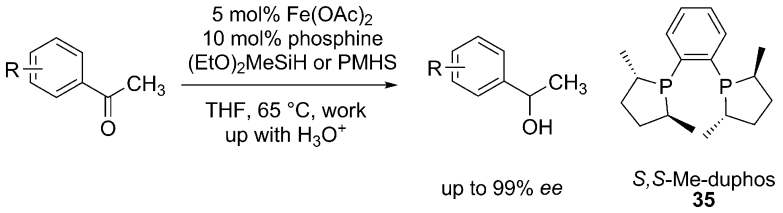


Fig. 8 Pyridine bisoxazoline and bisoxazoline iron dialkyl complexes studied in the asymmetric catalytic hydrosilylation.



Scheme 17 Asymmetric hydrosilylation of ketones with iron catalysts according to Beller.

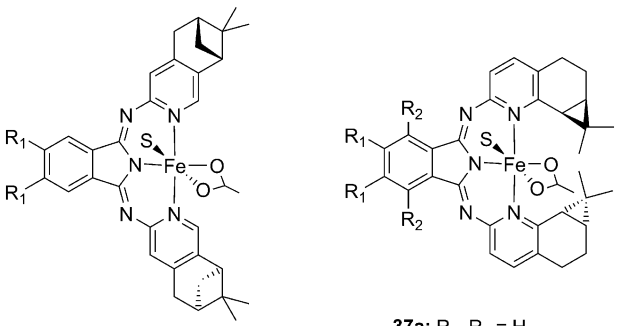


Fig. 9 Chiral Fe-complexes developed by Gade *et al.*

of electron-rich chiral phosphines (Scheme 17). Combining $Fe(OAc)_2$ and ligands like (*S*,*S*-Me-Duphos) enantioselectivities up to 99% ee are achieved for several aryl ketones.[45]

Parallel to the enantioselective version, we also described a chemoselective iron-catalysed hydrosilylation of aldehydes and later on for ketones in the presence of $Fe(OAc)_2$ and basic phosphines like PCy_3 showing broad functional group tolerance.[46,47] Here, inexpensive PMHS (polymethylhydrosiloxane) is used as a hydride source to react with various aryl, heteroaryl, alkyl, and α,β-unsaturated aldehydes. Simple hydrolysis led directly to the corresponding alcohols. In addition, Nikonov *et al.* investigated well-defined iron pre-catalysts like $[Cp(R'_3P)Fe(CH_3CN)_2]^{2+}$ which catalysed hydrosilylation of benzaldehyde efficiently at ambient temperature.[48]

Recently, Gade and co-workers showed that iron complexes of chiral bis(pyridylimino)iso-indoles **36** and **37** also worked as efficient catalysts for the asymmetric hydrosilylation of ketones under mild conditions (Fig. 9).[49] By using the optimised iron-based system **37c** enantiomeric excesses up to 93% were achieved.

On the basis of their preceding work applying molecular hydrogen, Nishiyama and Furuta used thiophene derivatives as ligands in iron-catalysed hydrosilylations (Scheme 18).[16] Thus, they found complete reduction of ketones with a catalyst derived from ferrous acetate and sodium thiophene-2-carboxylate **12a** and diethoxymethylsilane as hydrogen source. Comparing the results to the $Fe(OAc)_2$/tmeda system, yields and selectivities were significantly improved.

Iron-catalysed hydrosilylations of olefins in the presence of nitrogen ligands were first realised by Chirik *et al.*[3] Reactions of 1-hexene, cyclohexene, and (*R*)-(+)-limonene with $PhSiH_3$ in the presence of iron catalyst **38b** (Fig. 10) proceeded at ambient temperature.[6] Both aldehyde and ketone reductions occurred in the presence of bis(imino)pyridine iron pre-catalysts **38a**, **39** and **40** without the need for an activator.[50] In 2009, Campagne and co-workers reported hydrosilylative deoxygenations of ketones and aldehydes under simple conditions.[51] In the presence of 10 mol% $FeCl_3$ and PMHS several aromatic ketones are reduced under microwave irradiation at 120 °C in good yields (81–98%). However, no reaction was observed for esters, anhydrides, and β-ketoesters. Yang and Tilley investigated the silylamide $[Fe\{N(SiMe_3)_2\}_2]$ as a simple and active catalyst for the hydrosilylation of carbonyl functionalities.[52] Using $PhSiH_3$ as a reductant a number of aldehydes and ketones afforded the corresponding silylethers at room temperature. Independently at the same time our group[53] and Nagashima *et al.*[54] reported the reduction of carboxamides to amines with iron carbonyl complexes as pre-catalysts. Selective reduction of tertiary amides including aromatic, aliphatic, heteroaromatic and heterocyclic amides took place using $[Fe_3(CO)_{12}]$ and inexpensive PMHS (Scheme 19).

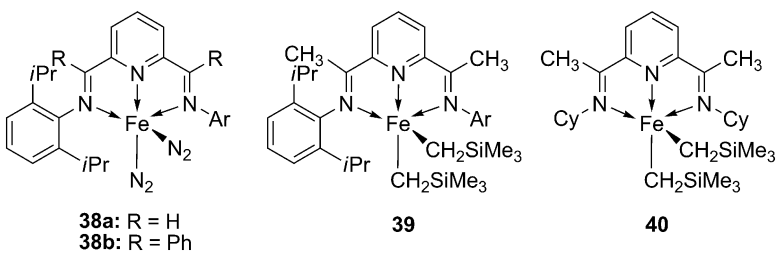
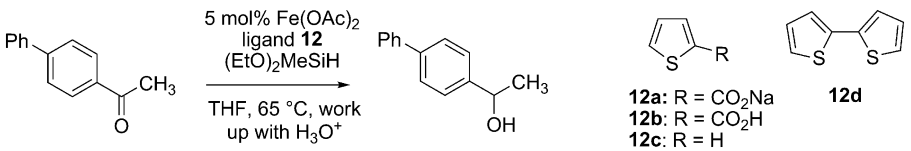
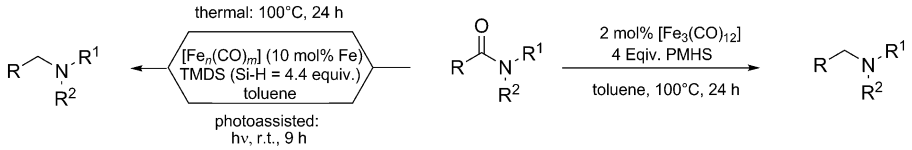


Fig. 10 Iron complexes containing tridentate nitrogen ligands according to Chirik *et al.*



Scheme 18 Asymmetric hydrosilylation of ketone with iron–thiophene derivatives.



Scheme 19 Iron-catalysed reduction of amides according to Beller and Nagashima.

Interestingly, a striking difference in reactivity for the reduction of the nitro group was noted. In contrast to ruthenium and platinum catalysts,[55] the iron-catalysed hydrosilylation of *N*,*N*-dimethyl-*p*-nitrobenzamide selectively occurred on the nitro function. However, using primary instead of secondary and tertiary amides as substrates clean conversion towards nitriles was observed.[56] This novel dehydration procedure proceeded in the presence of various iron sources. The general applicability of the method and the functional group tolerance of the iron catalyst systems were demonstrated in the dehydration of around 20 different aromatic, heteroaromatic, and aliphatic amides. Recently, also a comprehensive study on iron-catalysed reduction of nitroarenes using organosilanes was reported by us.[57] An inexpensive and convenient catalytic system consisting of $FeBr_2$/PPh_3 reduces a variety of nitro-substituted arenes and heteroarenes in good to excellent yields. Notably, other reducible functional groups such as cyano, ester, ether or alcohol groups as well as C=C double bonds are not affected under these conditions.

In summary, in the last few years it has been demonstrated that iron complexes represent viable alternative systems for precious metal catalysts. Chemo- and stereoselective hydrogenations, hydrosilylations and transfer hydrogenations which are typically performed in the presence of Rh, Ru, and Ir complexes are nowadays possible with defined organometallic iron catalysts. Clearly, the reported iron-catalysed reactions are still far off from immediate industrial applications and also the substrate scope has to be further improved. Nevertheless, for the mid-term future we expect a significant increase in the use of "iron catalysis" in organic synthesis and finally also in "real" applications. The advantages of biomimetic or bio-inspired iron complexes in catalysis are obvious and convincing. A pre-requisite for the further improvement of molecular-defined iron catalysts is an increased understanding of the mechanism and the detailed elementary steps in order to clarify relationships between structure and action. This will also lead to improved catalyst activity and productivity which are crucial issues with respect to practical applications.

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