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Hydrogenation and Dehydrogenation Iron Pincer Catalysts Capable of Metal–Ligand Cooperation by Aromatization/Dearomatization

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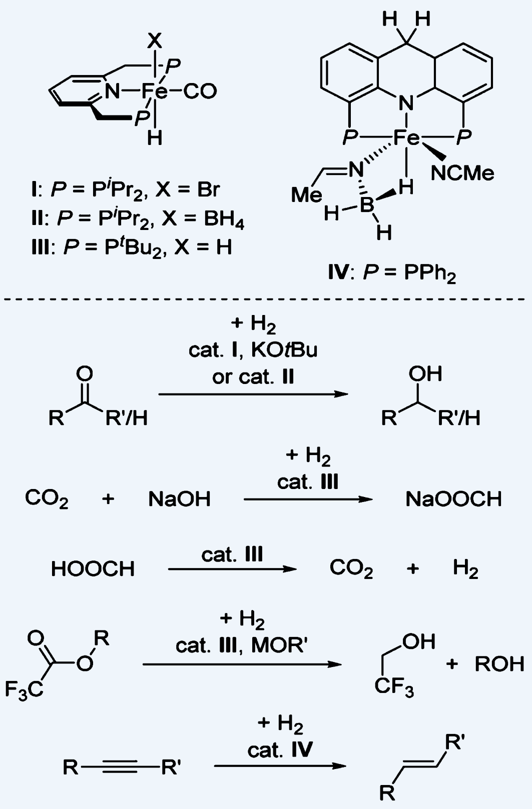

CONSPECTUS: The substitution of expensive and potentially toxic noble-metal catalysts by cheap, abundant, environmentally benign, and less toxic metals is highly desirable and in line with green chemistry guidelines.

We have recently discovered a new type of metal–ligand cooperation, which is based on the reversible dearomatization/aromatization of different heteroaromatic ligand cores caused by deprotonation/protonation of the ligand. More specifically, we have studied complexes of various transition metals (Ru, Fe, Co, Rh, Ir, Ni, Pd, Pt, and Re) bearing pyridine- and bipyridine-based PNP and PNN pincer ligands, which have slightly acidic methylene protons. In addition, we have discovered long-range metal–ligand cooperation in acridine-based pincer ligands, where the cooperation takes place at the electrophilic C-9 position of the acridine moiety leading to dearomatization of its middle ring. This type of metal–ligand cooperation was used for the activation of chemical bonds, including H–H, C–H (sp^2 and sp^3), O–H, N–H, and B–H bonds. This unusual reactivity likely takes place in various catalytic hydrogenation, dehydrogenation, and related reactions.

In this Account, we summarize our studies on novel bifunctional iron PNP and PNN pincer complexes, which were designed on the basis of their ruthenium congeners. Iron PNP pincer complexes serve as efficient (pre)catalysts for hydrogenation and dehydrogenation reactions under remarkably mild conditions. Their catalytic applications include atom-efficient and industrially important hydrogenation reactions of ketones, aldehydes, and esters to the corresponding alcohols. Moreover, they catalyze the hydrogenation of carbon dioxide to sodium formate in the presence of sodium hydroxide, the selective decomposition of formic acid to carbon dioxide and hydrogen, and the *E*-selective semihydrogenation of alkynes to give *E*-alkenes. These catalysts feature, compared to other iron-based catalysts, very high catalytic activities which in some cases can even exceed those of state-of-the-art noble-metal catalysts. For the iron PNP systems, we describe the synthesis of the pyridine- and acridine-based PNP iron complexes and their performances and limitations in catalytic reactions, and we present studies on their reactivity with relevance to their catalytic mechanisms. In the case of the bipyridine-based PNN system, we summarize the synthesis of new complexes and describe studies on the noninnocence of the methylene position, which can be reversibly deprotonated, as well as on the noninnocence of the bipyridine unit.

Overall, this Account underlines that the combination of cheap and abundant iron with ligands that are capable of metal–ligand cooperation can result in the development of novel, versatile, and efficient catalysts for atom-efficient catalytic reactions.

INTRODUCTION

The properties and the reactivity of transition-metal complexes are influenced by the electronic and steric properties of the surrounding ligands.[1,2] Traditionally, elementary steps of catalytic reactions take place solely on the metal centers whereas the ligands do not actively participate in bond formation or bond breaking events.

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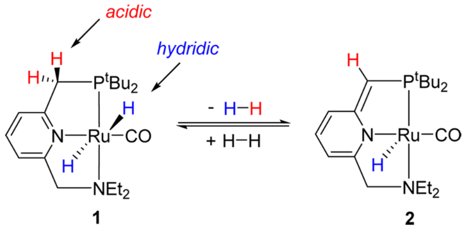
Scheme 1. Reversible Activation of H_2 by a Ru−PNN Complex Based on MLC



In recent years, the field of bifunctional catalysis, in which the metal center and the ligands bound to it cooperate during catalytic cycles, has gained much interest, and bifunctional catalysts have been proven as a powerful tool in organic chemistry.[3] Studies on bifunctional catalysts, in particular, metal complexes with active ligand sites, have led in many cases to enhanced catalytic activities and to the development of new catalytic reactions.

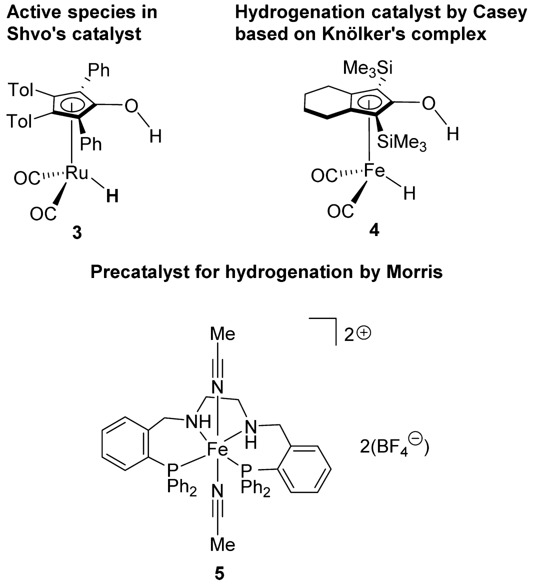
Over the past few years our group has studied metal complexes with noninnocent ligands in bifunctional substrate activation reactions and catalytic transformations.[4−10] We have discovered a new mode of metal−ligand cooperation (MLC) based on dearomatization/aromatization processes of the ligand. More specifically, we have developed metal complexes and catalysts with pyridine- and bipyridine-based pincer ligands, which undergo dearomatization/aromatization caused by deprotonation/protonation of the benzylic arm of the ligands. Furthermore, we have discovered a unique long-range MLC in acridine-based pincer ligands, where the cooperation takes place at the electrophilic C-9 position of the acridine moiety leading to dearomatization of its middle ring.

This type of MLC was used for the activation of various chemical bonds including H−H, C−H (sp^2 and sp^3), O−H, N−H, and B−H bonds. Dearomatized complexes can activate these E−H bonds by cooperation between the metal and the ligand and thereby regain aromatization of the ligand by protonation of the benzylic carbon atom (Scheme 1).[9]

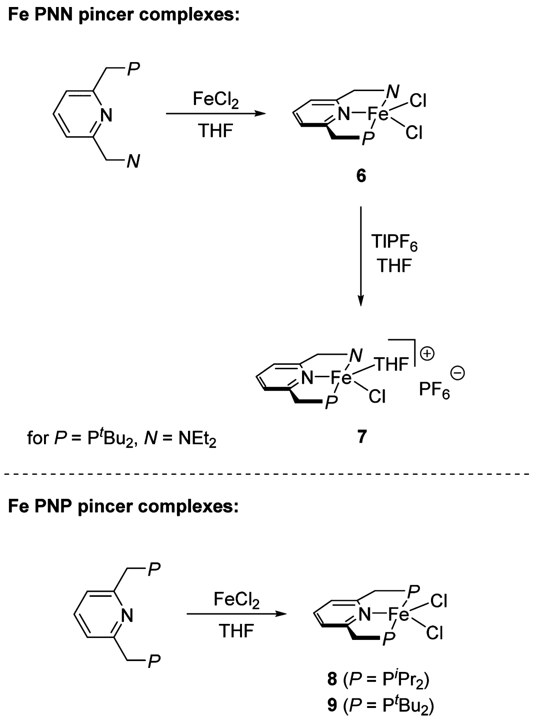
On the basis of this unique reactivity, we have developed several pincer complexes of Ru, Fe, Co, Rh, Ir, Ni, Pd, Pt, and Re, which are capable of MLC, and we have shown that complexes of this type, mainly based on Ru, Fe, and Re, are versatile catalysts for hydrogenation, dehydrogenation, and related reactions. The catalytic applications of Ru(II) pincer complexes have recently been reviewed comprehensively elsewhere.[4−10]

The substitution of expensive and potentially toxic noble-metal catalysts by inexpensive, abundant, and environmentally benign metals is a prime goal in chemistry. In this Account, we provide an overview of our work with iron pincer complexes capable of MLC, and their application in catalytic reactions, which include the hydrogenation of ketones, aldehydes, CO_2, and esters, as well as the *E*-selective semihydrogenation of alkynes and the decomposition of formic acid to H_2 and CO_2. These bifunctional catalysts were designed on the basis of their Ru congeners, in order to answer the question of how far iron, as a cheap, earth-abundant, and environmentally benign metal with low toxicity can mimic these unusual catalysts.

Scheme 2. Bifunctional Catalysts 3−5[14,15]



Scheme 3. Synthesis of 6−9[18]

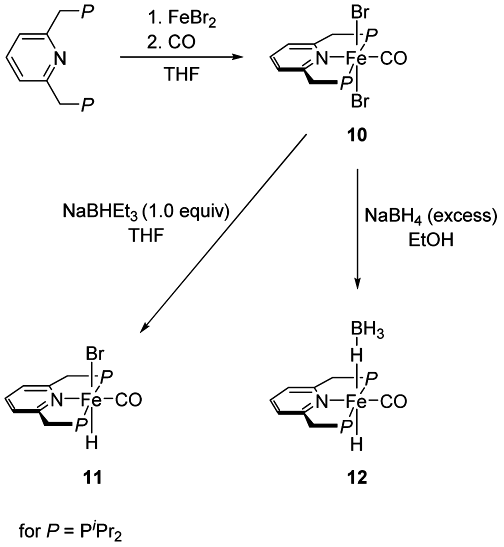


CATALYTIC HYDROGENATION OF KETONES AND ALDEHYDES

The catalytic reduction of ketones and aldehydes to alcohols using H_2 is an important and atom-economical process. These reactions often require the use of noble-metal catalysts based on Rh, Ir, or Ru.[11] In 2011 we reported on the use of a well-defined bifunctional iron catalyst for the hydrogenation of ketones.[12,13] At that time, only two examples of iron-catalyzed hydrogenation reactions of ketones had been reported.[14,15]

Pioneering work in the field of cooperative hydrogenation reactions catalyzed by iron complexes was reported by Casey and Guan in 2007. Following their studies on Shvo's catalyst (**3**, Scheme 2), they found that Knölker's complex (**4**, Scheme 2)

Scheme 4. Synthesis of 10−12[12,19]



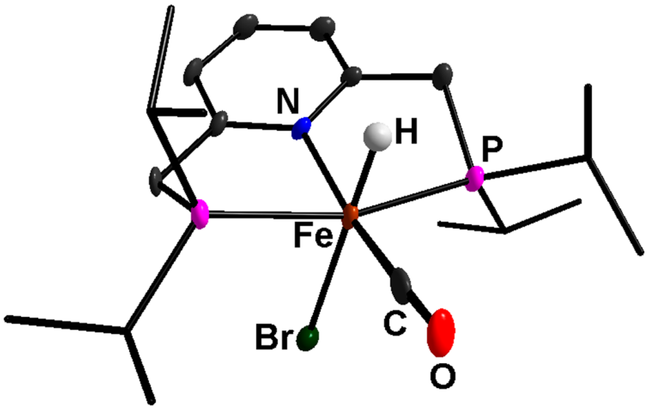


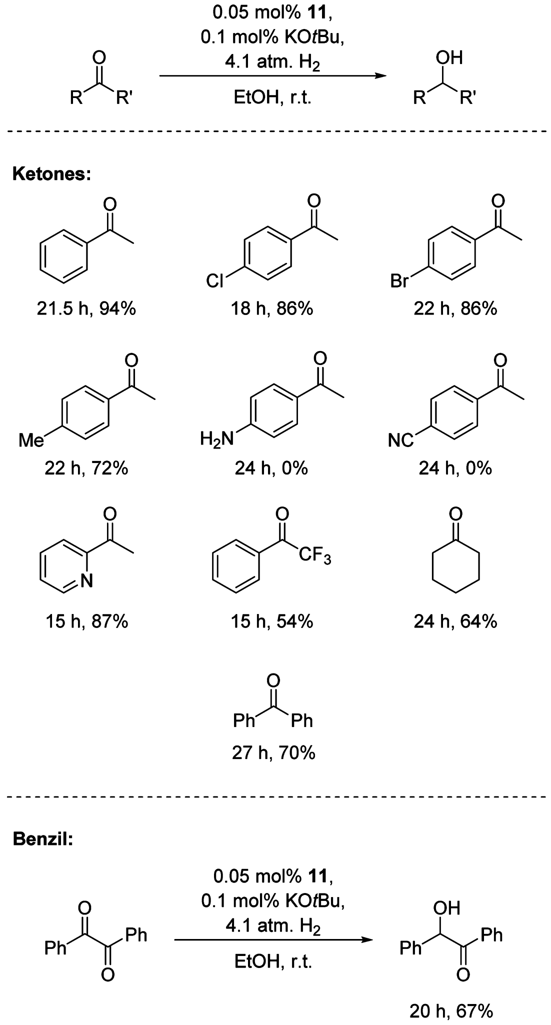
Figure 1. X-ray structure of **11**.[12]

catalyzes the hydrogenation of aldehydes and ketones under mild conditions (3 bar H$_2$, room temperature) with high chemo- and diastereoselectivity, resulting in turnover numbers (TONs) up to 50.[14] This cyclopentadienone complex operates by MLC based on the noninnocence of the η^5-hydroxocyclopentienyl/η^4-cyclopentadieneone ligand. In recent years, various derivatives of Knölker-type catalysts have been reported and used for different catalytic applications.[16] This work has recently been comprehensively reviewed.[17]

The Morris group described in 2009 a series of diiminodiphosphine and diaminodiphoshine iron complexes, which are precatalysts for the hydrogenation of acetophenone. Using precatalyst **5** (Scheme 2), TONs up to 222 were achieved under slightly harsher conditions (25 bar H$_2$, 50 °C).[15]

In continuation of our initial report on the ligation of FeCl$_2$ by various pincer ligands (complexes **6-9**, Scheme 3),[18] we reported on the synthesis and characterization of the new iron carbonyl pincer complexes **10−12** (Scheme 4). The crystallographically characterized complex [(^{i}Pr-PNP)Fe(H)(CO)(Br)] (**11**, ^{i}Pr-PNP = 2,6-bis(di-*iso*-propyl)phosphinomethyl)pyridine Figure 1), which is an efficient precatalyst for the hydrogenation of ketones under remarkably mild conditions, was synthesized by a reaction of the *trans*-di(bromo) carbonyl complex [(^{i}Pr-PNP)Fe(Br)$_2$(CO)] (**10**) with one equivalent of NaBHEt$_3$.

Scheme 5. Hydrogenation of Ketones Catalyzed by 11 and KO*t*Bu[12]

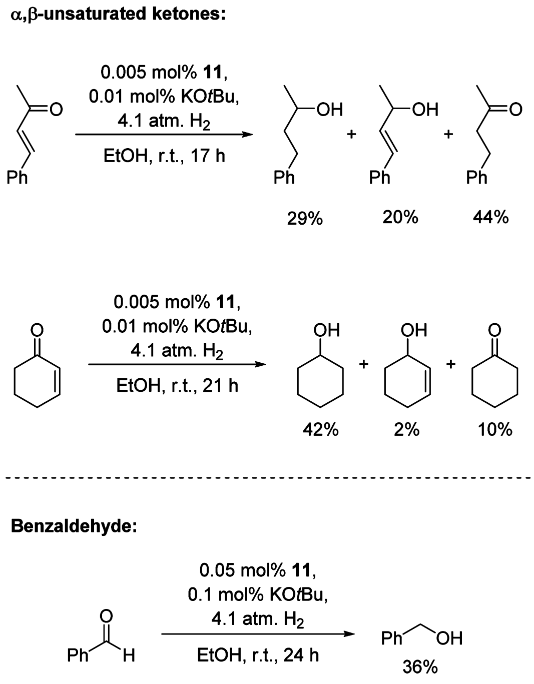


In a typical catalytic protocol, ketones were smoothly hydrogenated using 0.05 mol % precatalyst **11**, 0.10 mol % KO*t*Bu, 4.1 atm. H$_2$ pressure at room temperature in ethanol as solvent (Scheme 5). These remarkably mild conditions are applicable for various functionalized ketones achieving TONs up to 1880. In the hydrogenation reaction of acetophenone, a significant increase in turnover frequency (TOF) from 87 to 430 h^{-1} was observed when the temperature was raised to 40 °C. The diketone benzil was selectively monohydrogenated under these conditions to give benzoin (Scheme 5).

However, hydrogenation reactions of α,β-unsaturated ketones resulted in mixtures, including C═C double bond reduction products, and under these conditions benzaldehyde was hydrogenated in only 36% yield (Scheme 6).

Subsequently, we reported the synthesis of the iron hydrido borohydride carbonyl complex [(^{i}Pr-PNP)Fe(H)(CO)(BH$_4$)] (**12**), which was obtained by treatment of the di(bromo) carbonyl complex **10** with an excess of NaBH$_4$ in EtOH (Scheme 4, Figure 2).[19] This η^1-coordinated borohydride iron complex shows similar activity in the hydrogenation of ketones as the previously reported precatalyst **11**, but unlike with the latter complex, the addition of a base is not required in these

Scheme 6. Limitations of the Hydrogenation Reactions Catalyzed by 11 and KO*t*Bu[12]



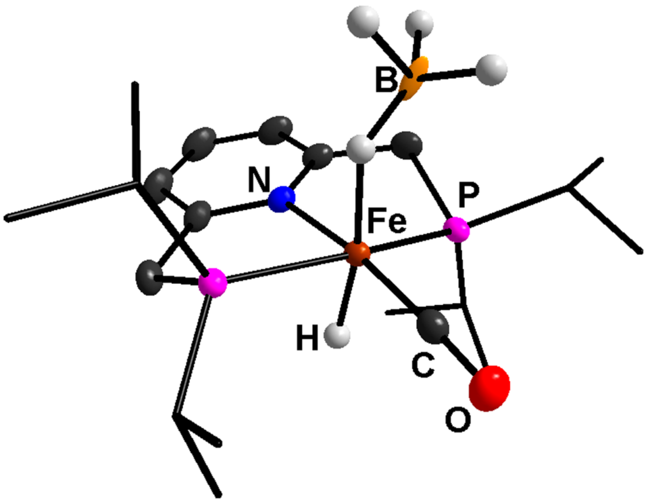
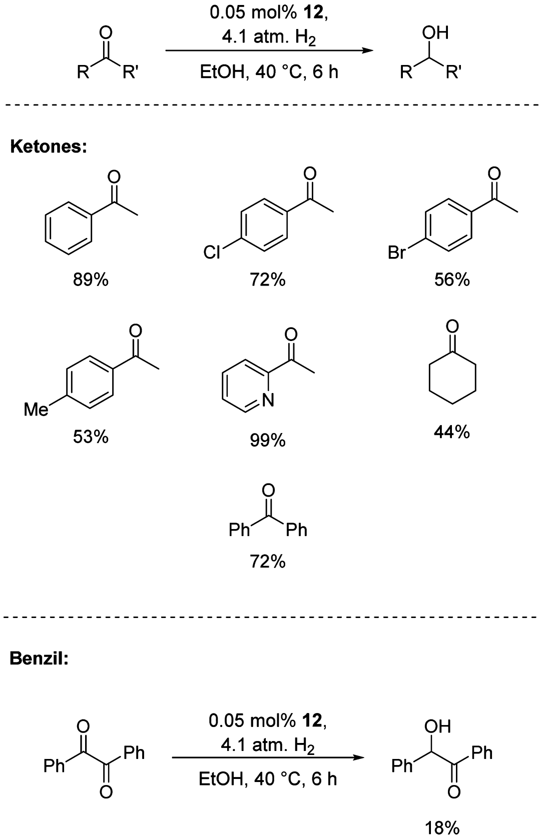
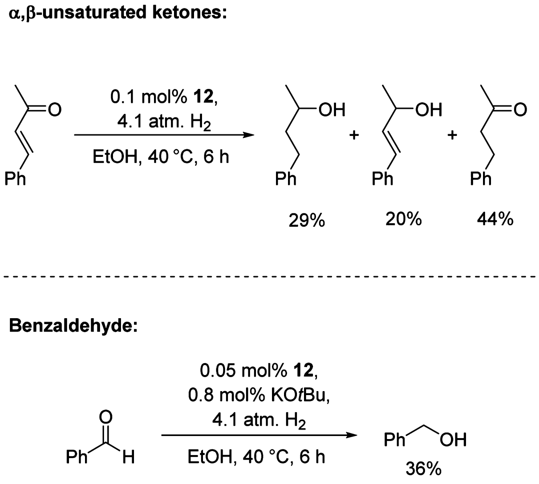


Figure 2. X-ray structure of **12**.[19]

Scheme 7. Base-Free Hydrogenation of Ketones Catalyzed by 12[19]



Scheme 8. Limitations of the Base-Free Hydrogenation Reactions Catalyzed by 12[19]

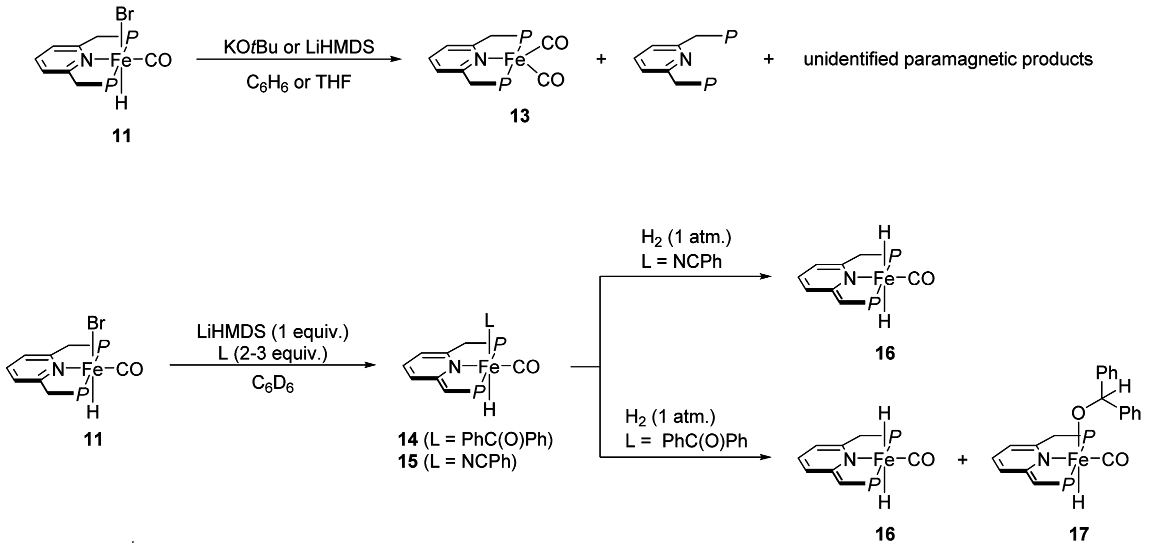


reactions. Various ketones were hydrogenated by **12**, using 0.05 mol % catalyst loading, 4.1 atm. H_2 pressure at 40 °C in ethanol as solvent (Scheme 7). Under these conditions, TONs up to 1980 were observed after only 6 h. In contrast to the hydrogenation of benzil using precatalyst **11** in the presence of KO*t*Bu (Scheme 5), only 18% of the monohydrogenated benzoin were obtained using **12** in the absence of base (Scheme 7).

Similar to catalysis by complex **11** and KO*t*Bu, hydrogenation reactions using complex **12** under base-free conditions gave no selective hydrogenation of *α*,*β*-unsaturated ketones, such as *trans*-4-phenyl-3-buten-2-one, and the reduction of benzaldehyde was unsatisfying (Scheme 8).

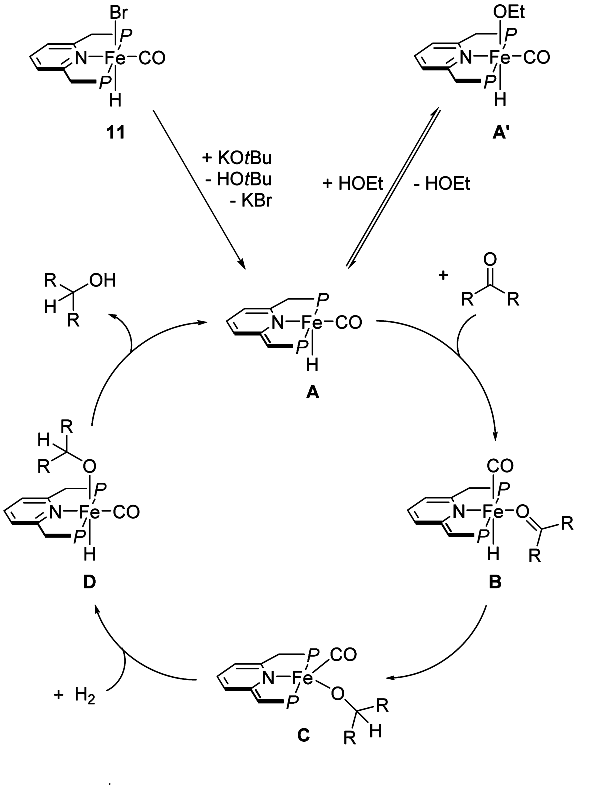
The reactivity of complex **11** was investigated in stoichiometric reactions to gain mechanistic understanding of these hydrogenation reactions. Treatment of the hydrido bromo complex **11** with one or two equivalents of base (KO*t*Bu or LiHMDS) in aprotic solvents (THF, benzene, or toluene) resulted in the formation of the Fe(0) complex $[({}^{i}\text{Pr-PNP})\text{Fe(CO)}_2]$ (**13**) together with the free ligand ^{i}Pr-PNP and unidentified paramagnetic products (Scheme 9).[12] No reaction was observed when 2 equivalents of KO*t*Bu was added to an EtOH solution of complex **11**. However, reactions of **11** with LiHMDS in the presence of 2−3 equivalents of the ancillary ligands benzophenone or benzonitrile resulted in deprotonation of benzylic arm with formation of the dearomatized complexes $[({}^{i}\text{Pr-PNP*})\text{Fe(H)(CO)(L)}]$ (**14**: L = PhC(O)Ph, **15**: L = NCPh, Scheme 9, the asterisk denotes a

Scheme 9. Stoichiometric Experiments



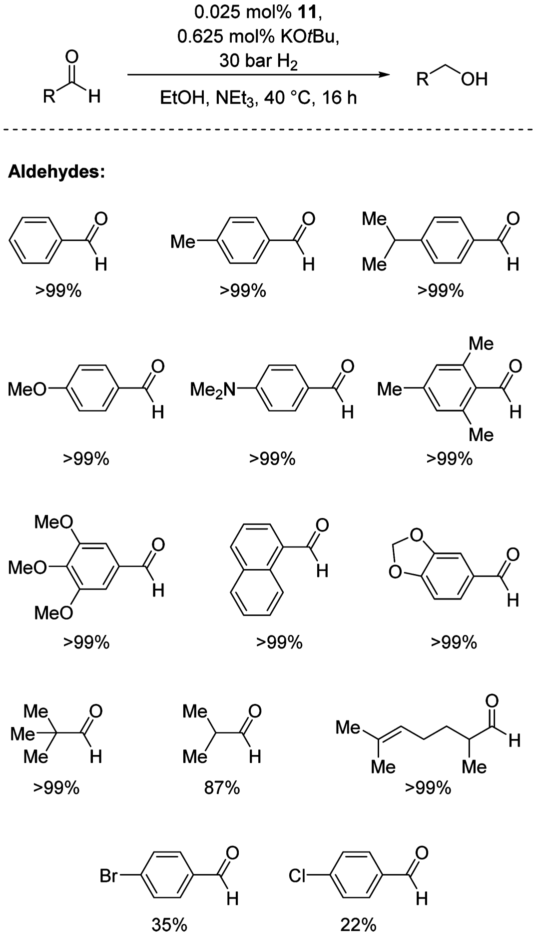
for $P = P^iPr_2$

Scheme 10. Proposed Mechanism for the Hydrogenation of Ketones Catalyzed by 11 and KO*t*Bu[12]



for $P = P^iPr_2$

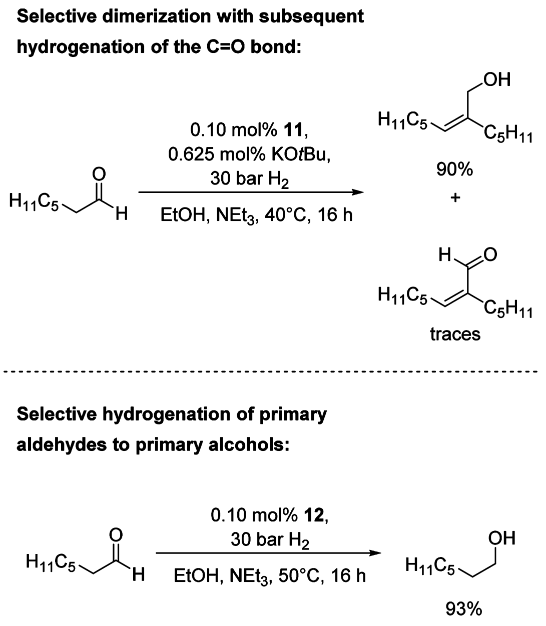
Scheme 11. Hydrogenation of Aldehydes Catalyzed by 11 and KO*t*Bu[24]



dearomatized pincer ligand). Furthermore, we found that complex **14** reacts readily with hydrogen (1 atm.) to give the corresponding alkoxide complex **17** along with the dihydride complex **16.** Notably in this experiment the three equivalents of benzophenone, which were employed to stabilize **14**, were quantitatively converted to the corresponding alkoxide. In contrast to this experiment, complex **15** reacts slowly under 1 atm. of hydrogen pressure to give the dihydride complex **16**. Thus, it is unlikely that ketone hydrogenation can take place directly by the dihydride complex **16** without precoordination of the ketone to the iron center. Decoordination of one the phosphorus arms is at room temperature energetically unfeasible.

On the basis of these experiments and a comprehensive DFT study, a catalytic cycle for the hydrogenation of ketones using precatalyst **11** was proposed.[12,19] Scheme 10 shows a simplified

Scheme 12. Hydrogenation of Heptanal Catalyzed by 11/KO*t*Bu and 12[24]



catalytic inner sphere mechanism. Deprotonation of precatalyst **11** results in the formation of dearomatized intermediate A. Ketone coordination to A accompanied by isomerization of the complex leads to the dearomatized intermediate B. Subsequent insertion of the ketone into the Fe−H bond of B, followed by bifunctional activation of hydrogen by intermediate C gives the aromatized intermediate D. Product release from D by MLC regenerates the dearomatized intermediate A.

Whereas iron-catalyzed hydrogenation reactions of ketones are now well documented, iron-catalyzed hydrogenation reactions of aldehydes are significantly less investigated.[20−24] Very recently, we reported on highly efficient hydrogenation reactions of aldehydes using complexes **11** and **12** as (pre)catalysts.[24] A significant improvement of catalytic activity was observed in the presence of additives which suppress catalyst deactivation by traces of carboxylic acids. These are formed by base-mediated Cannizarro reactions of the aldehydes with trace water present in the solvent. Under optimized reaction conditions, hydrogenation reactions using 0.025 mol % **11**, 0.625 mol % KO*t*Bu, and 30 bar H_2 pressure at 40 °C in an EtOH/NEt_3 mixture as solvent gave good to quantitative yields using various aldehydes after 16 h (Scheme 11). In these reactions TONs up to 4000 were observed for many substrates, which stands as the highest TON reported to date for the iron-catalyzed aldehyde hydrogenation.

Under these reaction conditions, primary aldehydes dimerize via base-catalyzed aldol condensation. Subsequent hydrogenation of the C═O bond gave in the case of heptanal (*Z*)-2-pentylnon-2-en-1-ol in 90% yield (Scheme 12). The selective hydrogenation of primary aldehydes to primary alcohols in high yield was achieved under base-free conditions using catalyst **12** (Scheme 12).

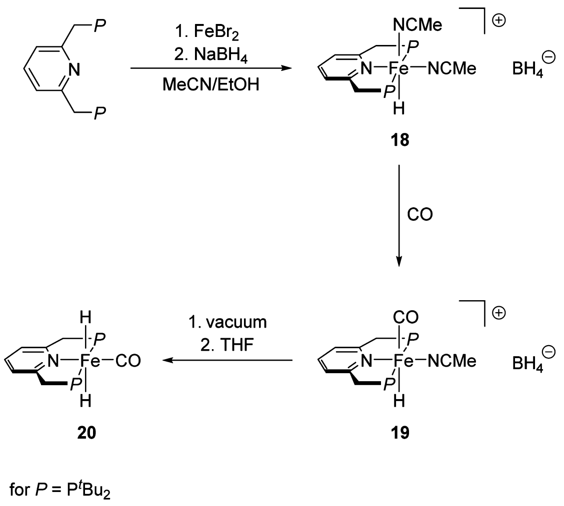
Kirchner and co-workers demonstrated later on that related iron(II) hydride complexes featuring PNP pincer ligands based on 2,6-diaminopyridine serve as well as (pre)catalysts for the hydrogenation of aldehydes and ketones under mild conditions.[25]

CATALYTIC HYDROGENATION OF CARBON DIOXIDE

In 2011, we reported on the synthesis of the *trans*-dihydride carbonyl complex *trans*-[(^{t}Bu-PNP)Fe(H)$_2$(CO)] (**20**, ^{t}Bu-PNP=2,6-bis(di-*tert*-butylphosphinomethyl)pyridine, Scheme 13, Figure 3).[26] Complex **20** is an efficient catalyst for the low-pressure hydrogenation of carbon dioxide to sodium formate in aqueous solutions of sodium hydroxide. This reaction usually requires high pressures and the use of noble-metal catalysts. Iron-based catalysts for the hydrogenation of CO_2 to formate salts are limited to a few examples.[27−29] The most effective iron catalyst system at that time was reported in 2010 by Laurency and Beller and prepared in situ from $Fe(BF_4)_2{\cdot}6H_2O$ and the tetradentate ligand $P(CH_2CH_2PPh_2)_3$ (PP_3). For the hydrogenation of sodium bicarbonate to sodium formate a TON of 610 was observed using 60 bar of H_2 pressure at 80 °C. Complex **20** catalyzes the reduction of CO_2 efficiently at significantly lower pressures, and its catalytic activity under these mild reaction conditions compares well with those of state-of-the-art noble-metal-based catalysts. Carbon dioxide and sodium bicarbonate are hydrogenated by **20** at remarkably low pressures (6−10 bar). A catalytic hydrogenation reaction using 0.1 mol % **20**, 3.33 bar CO_2, and 6.66 bar H_2 pressure in a 2 M NaOH solution in H_2O/THF (10:1) resulted after 5 h at 80 °C in a TON of 788 with a TOF of 156 h^{-1} (Scheme 14).

Upon reaction of the *trans*-dihydride complex **20** with CO_2 insertion into the Fe−H bond takes place to give the hydrido η^1-formate complex [(^{t}Bu-PNP)Fe(H)(CO)(η^1−OOCH)] (**21**, Scheme 15, Figure 4). Dissolving **21** in D_2O results in the formation of a new complex, which is likely the monocationic aqua complex $[(^t\text{Bu-PNP})\text{Fe(H)(CO)}(D_2O)]^+$ (**22**, Scheme 15). A possible catalytic mechanism was suggested on the basis of these experiments (Scheme 16). Addition of CO_2 to the dihydride complex **20** results in the oxygen-bound formate complex **21**. The formate ligand of **21** is easily displaced by water to give the monocationic complex **22**. Under hydrogen pressure the dihydrogen intermediate **A** is possibly formed. Complex **20** is regenerated either by direct deprotonation of the coordinated H_2 ligand, or by deprotonation of the benzylic position of the ligand of **A** to result in the dearomatized intermediate **C**. In the latter case, subsequent

Scheme 13. Synthesis of 18−20[26]



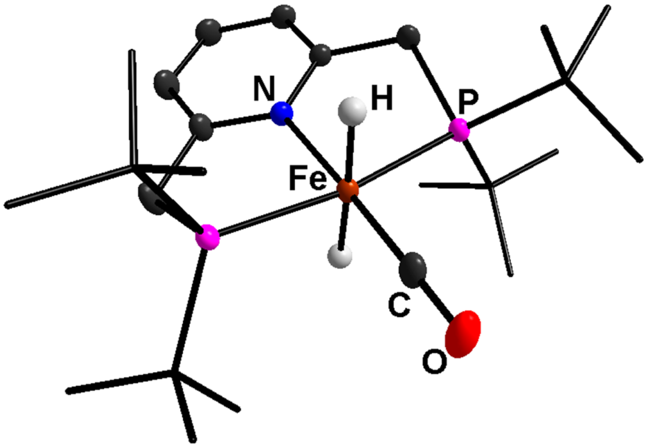


Figure 3. X-ray structure of **20**.[26]

Scheme 14. Hydrogenation of Bicarbonate and CO_2 Catalyzed by **20**[26]

Hydrogenation of bicarbonate to sodium formate:

$$\underset{}{NaHCO_3} + \underset{(8.3\ \text{bar})}{H_2} \xrightarrow[\substack{-\,H_2O\\ H_2O/THF\ (10:1)\\ 80\ °C,\ 16\ h}]{0.1\ \text{mol\%}\ \mathbf{20}} NaOOCH$$

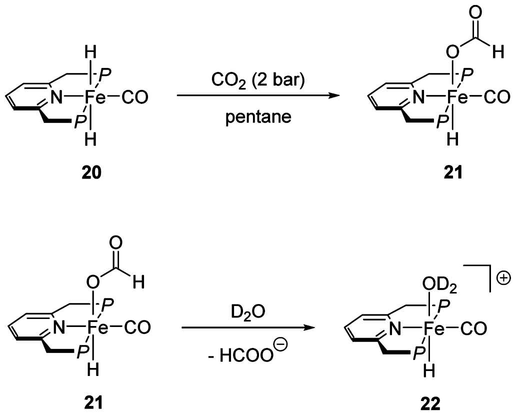
TON = 320, TOF = 20 h^{-1}

Hydrogenation of carbon dioxide to sodium formate:

$$\underset{(3.33\ \text{bar})}{CO_2} + \underset{(6.66\ \text{bar})}{H_2} \xrightarrow[\substack{-\,H_2O\\ H_2O/THF\ (10:1)\\ 80\ °C,\ 5\ h}]{\substack{0.1\ \text{mol\%}\ \mathbf{20}\\ NaOH\ (2\ M)}} NaOOCH$$

TON = 788, TOF = 156 h^{-1}

Scheme 15. Synthesis of 21 and 22[26]



for *P* = P^{t}Bu$_2$

proton migration from **C** could then regenerate the dihydride complex **20**.

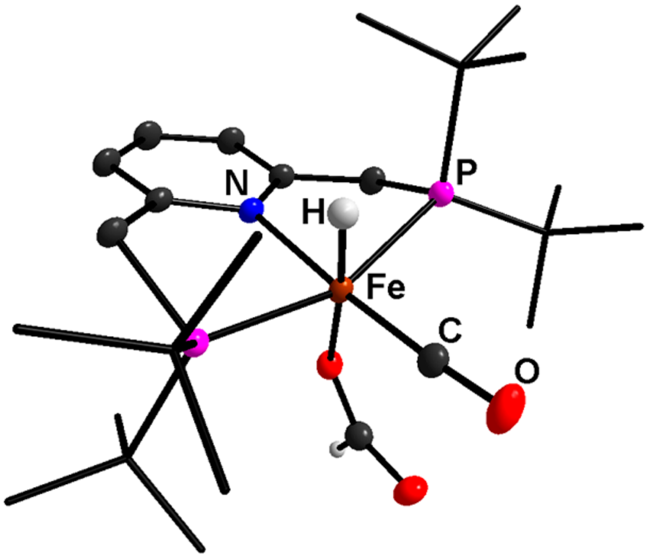
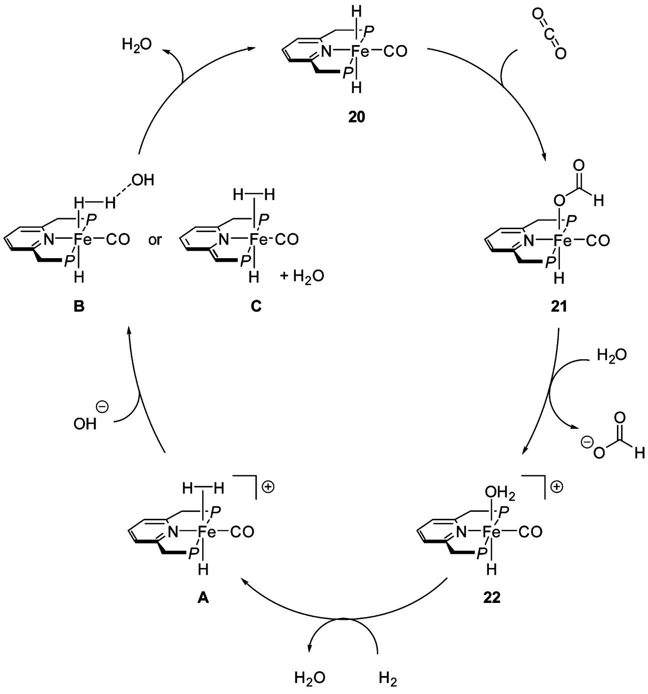


Figure 4. X-ray structure of **21**.[26]

Scheme 16. Proposed Mechanism for the Hydrogenation of CO_2 Catalyzed by **20**[26]

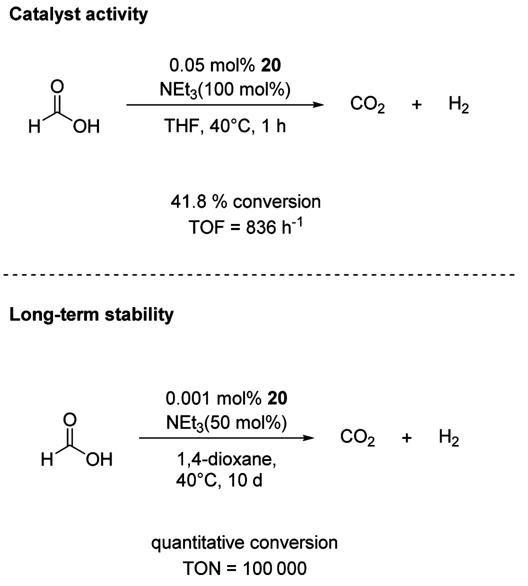


for *P* = P^{t}Bu$_2$

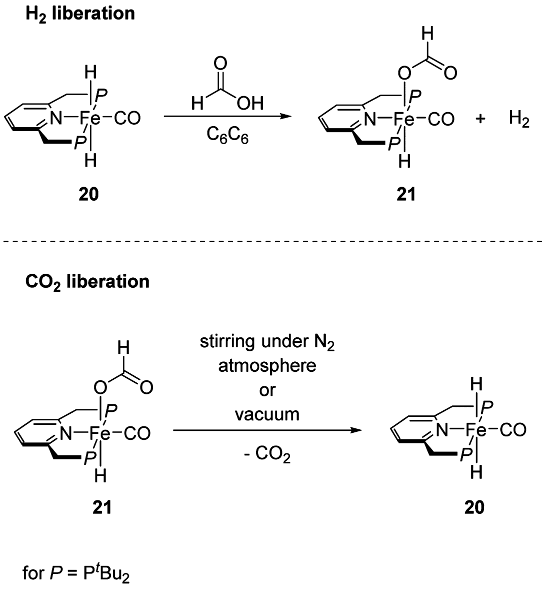
CATALYTIC DEHYDROGENATION OF FORMIC ACID

An attractive approach to reversible hydrogen storage applications is based on the decomposition of formic acid.[30−32] In 2011, Beller and co-workers reported the selective catalytic decomposition of formic acid to hydrogen and carbon dioxide catalyzed by an in situ generated iron catalyst. This catalyst system is composed of $Fe(BF_4)_2{\cdot}6H_2O$ and a slight excess of the tetradentate phosphine ligand PP_3.[33] A very high TOF of 9425 h^{-1} and TONs up to 92 417 were observed when the iron salt and the ligand were employed in a ratio of 1:4 in propylene carbonate at 80 °C and without further additives. In 2013, we reported on the application of complex **20** as catalyst

Scheme 17. Formic Acid Decomposition Catalyzed by 20[34]

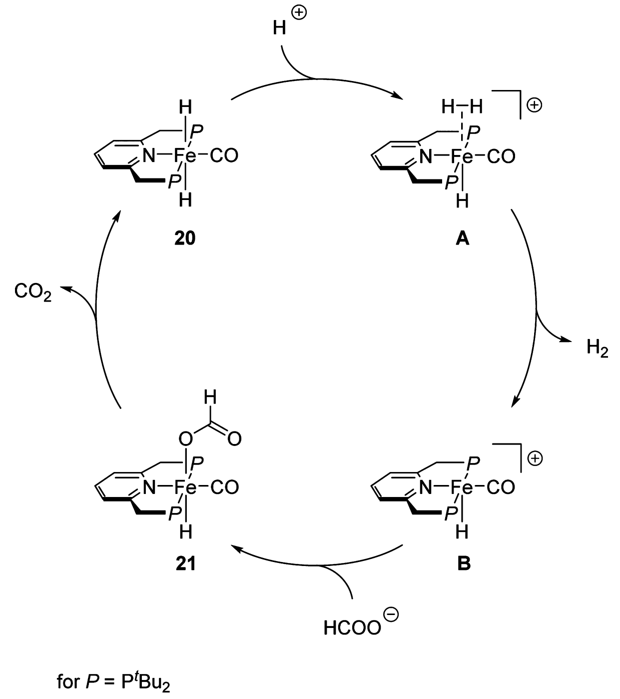


Scheme 18. Stoichiometric Experiments[34]



for the selective decomposition of formic acid to H_2 and CO_2 at low temperatures.[34] Complex **20** efficiently catalyzes this reaction at 40 °C in the presence of trialkylamines. When formic acid was decomposed in a 1:1 mixture with triethylamine in THF a TOF of 836 h^{-1} was achieved at 40 °C in the first hour, using only 0.05 mol % of catalyst **20** (Scheme 17). It is noteworthy that the activity of **20** at this temperature is higher than that of the most active iron-based catalyst reported earlier.[33] Studies regarding the long-term stability of catalyst **20** led to a total TON of 100 000. Full conversion of 1 mol formic acid was observed with a catalyst loading of 0.001 mol % **20** in the presence of 50% mol NEt_3 in dioxane at 40 °C after 10 days (Scheme 17).

Scheme 19. Proposed Mechanism of Formic Acid Decomposition Catalyzed by 20[34]



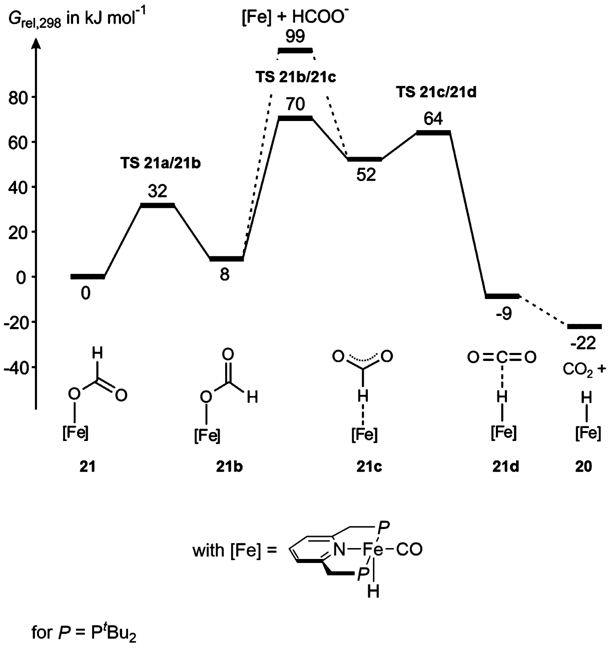


Figure 5. Reversible, nontraditional β-hydride elimination from a formate ligand.[34]

The mechanism of formic acid decomposition catalyzed by the dihydride complex **20** was investigated experimentally and computationally. Reaction of **20** with a stoichiometric amount or a slight excess of formic acid leads rapidly to the formation of the hydride η^1-formate complex **21**, concomitant with liberation of hydrogen gas (Scheme 18). CO_2 liberation from **21** to give the dihydride complex **20** was observed upon exposure of **21** to vacuum, or upon prolonged stirring of a solution of **21** under nitrogen atmosphere (Scheme 18).

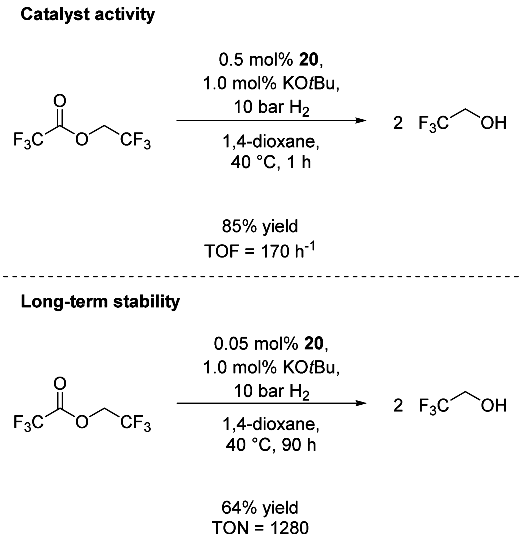
The proposed mechanism for H_2 and CO_2 liberation from formic acid (Scheme 19) involves protonation of the dihydride complex **20**. This might result in the formation of the cationic dihydrogen intermediate A.[26] Hydrogen liberation from A would result in the formation of the unsaturated, five-coordinate, cationic complex B. Coordination of a formate anion to B gives the hydrido formate complex **21**, and upon CO_2 elimination from **21** the dihydride complex **20** is regenerated. The latter step is a nontraditional β-hydride elimination, as **21** is coordinatively saturated and does not have a vacant coordination site (Figure 5). According to DFT studies, this step is strictly intramolecular and does not involve the dissociation of the formate anion followed by recoordination through the hydrogen atom. This β-hydride elimination step is reversible, which implies that the direct addition of the CO_2 to the iron hydride moiety of **20** forming the oxygen-bound formate complex **21**, which was observed in the hydrogenation of CO_2 (Scheme 16), proceeds via the same outer-sphere mechanism.

■ CATALYTIC HYDROGENATION OF ESTERS

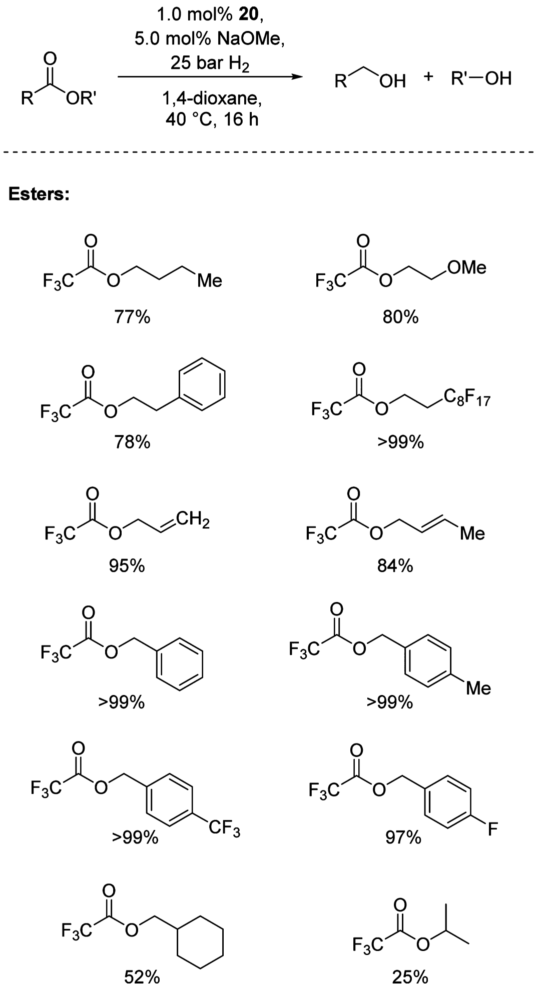
The catalytic hydrogenation of esters to alcohols is an environmentally benign, waste-free and atom-economical process, which is used industrially on a large scale with fatty esters under harsh conditions employing heterogeneous catalysts. Homogeneous catalysts for this reaction are based on Ru, Ir, or Os. Until very recently, no iron-catalyzed hydrogenation of esters or any other carboxylic acid derivates were reported. We accomplished the first example of an iron-catalyzed hydrogenation of esters,[35,36] using dihydride complex **20**, which is an efficient catalyst for the hydrogenation of trifluoroacetates under mild conditions. Initially the hydrogenation of 2,2,2-trifluoroethyl trifluoroacetate to trifluoroethanol was investigated. For this substrate TOFs up to 170 h^{-1} and a maximal TON of 1280 were observed in catalytic reactions using 10 bar of H_2 at 40 °C (Scheme 20). Various other trifluoroacetates were hydrogenated in good to quantitative yields using 1.0 mol % **20**, 5.0 mol % NaOMe, under 25 bar of H_2 pressure at 40 °C after 16 h (Scheme 21). Notably, other functional groups, such as ethers, aryl groups, and terminal or internal C═C bonds stayed intact during the catalytic hydrogenation.

A possible bifunctional mechanism for the hydrogenation of trifluoroacetates catalyzed by complex **20** was proposed on the basis of stoichiometric reactions. Most importantly, when complex **20** was reacted with 1.5 equivalents of benzyl trifluoroacetates in CD_3CN, transfer of one of the hydride ligands of **20** to the ester was observed generating the monocationic acetonitrile complex $[(^tBu\text{-PNP})Fe(H)(CO)(MeCN)]^+$ (**23**).

Scheme 20. Hydrogenation of 2,2,2-Trifluoroethyl Trifluoroacetate Catalyzed by 20[35]



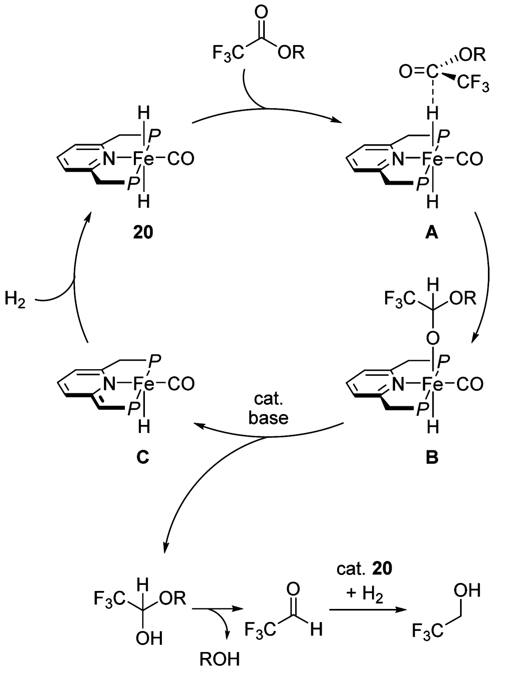
Scheme 21. Hydrogenation of Trifluoroacetic Esters Catalyzed by 20[35]



As we have shown, the *trans*-dihydride complex **20** is capable of direct, outer sphere hydride transfer to benzyl trifluoroacetate. This reaction is likely to proceed via intermediate **A** (Scheme 22), leading to oxygen-bound hemiacetaloxide intermediate **B** (which in acetonitrile forms complex **23**). A similar outer sphere nucleophilic addition of the hydride was already described for the reversible insertion of CO_2 in the Fe—H bond of **15** to give the formate complex **21** (Figure 5). OH elimination of the hemiacetal through MLC generates the dearomatized intermediate **C**. It is likely that this step is facilitated by the presence of a catalytic amount of base. H_2 activation by MLC subsequently regenerates the dihydride complex **20**. The hemiacetal is in equilibrium with the aldehyde, which under these conditions is likely to get hydrogenated.

Shortly after our publication, Guan and co-workers[37] and the Beller group[38] reported independently on the use of the hydrido borohydrido pincer complex $[(PHNP)Fe(H)(CO)(BH_4)]$ (**24**, PHNP = bis(di-*iso*-propylphosphinoethyl)amine) as catalyst hydrogenation of esters. Whereas the reported substrate scope of catalyst **20** is limited to trifluoroacetic esters, **24** was applied in hydrogenation reactions of various esters in

Scheme 22. Proposed Mechanism for the Hydrogenation of Esters Catalyzed by 20[35]



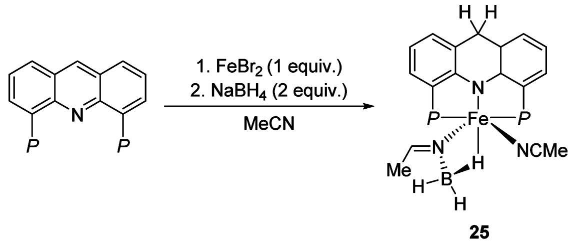
for *P* = P^{t}Bu$_2$

the absence of additional base. Using **24**, typical catalytic reactions were conducted with catalyst loadings of 1−3 mol % under H_2 pressures of 10−52 bar at significantly higher temperatures (100−135 °C). In a related study, Schneider and co-workers reported that the same iron complex catalyzes the reversible acceptorless dehydrogenation of alcohols to ketones and esters.[39]

■ *E*-SELECTIVE SEMIHYDROGENATION OF ALKYNES

The semihydrogenation of alkynes to alkenes is an important reaction, which is intensively used for the synthesis of biologically relevant compounds, including natural products, fragrances, and pharmaceuticals. These compounds have very often C=C bonds with defined *E* or *Z* configurations. Whereas catalytic methods for the *Z*-selective hydrogenation of alkynes have been developed, the *E*-selective hydrogenation of alkynes remains challenging. Practically all common methods for the *E*-selective synthesis of alkenes from alkynes are stoichiometric and suffer from poor atom economy. Very recently, Fürstner and co-workers found that alkynes can be semihydrogenated in the presence of stoichiometric amounts of [(Cp*)Ru(COD)(Cl)] (COD = 1,5-cyclooctadiene) and AgOTf with high *E*-selectivity.[40] These reactions were performed using 5.5 mol % [(Cp*)Ru(COD)(Cl)] and 5.0 mol % AgOTf under 10 bar H_2 pressure at room temperature. In 2013, we reported on the synthesis of the novel acridine-based PNP iron complex [($^{\text{HACR}}$PNP)Fe(CH_3CN)(κ^2-$CH_3CHCNBH_3$)] (**25**, $^{\text{HACR}}$PNP = 4,5-bis(diphenylphosphino)-9*H*-acridine-10-ide, Scheme 23, Figure 6).[41] This is the first iron catalyst which provides chemo- and stereoselective semihydrogenation of alkynes to *E*-alkenes.

Scheme 23. Synthesis of 25[41]



25

for *P* = PPh$_2$

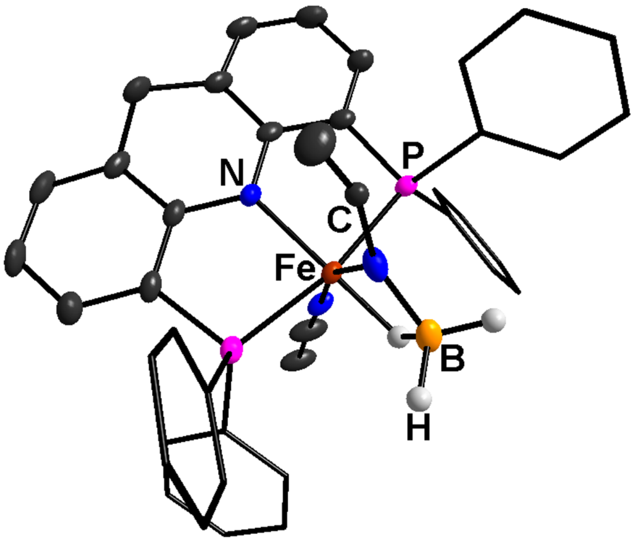


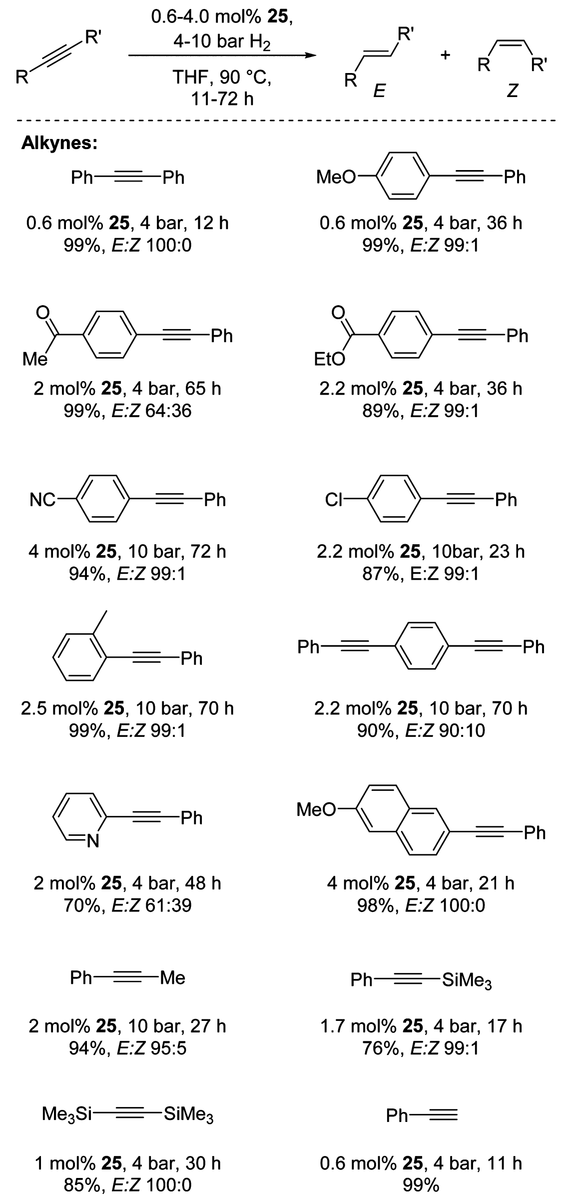
Figure 6. X-ray structure of **25**.[41]

Various alkynes are efficiently semihydrogenated by **25** in high yields and high *E*-selectivities under remarkably mild conditions (Scheme 24). Typically the catalytic hydrogenation reactions were conducted with catalyst loadings between 0.6 and 4.0 mol % and H_2 pressures between 4 and 10 bar in THF at 90 °C. Ether, carbonyl, ester, nitrile, silyl, and chloro substituents remained intact during the hydrogenation reactions catalyzed by **25**. The high *E*-selectivity obtained in these catalytic hydrogenation reactions is a result of facile isomerization of the *Z*-isomers, formed during the hydrogenation, to the *E*-isomers in the presence of **25**. Indeed, isomerization to *E*-stilbene was observed when a solution of *Z*-stilbene and 0.6 mol % **25** was stirred at 90 °C in the absence of H_2.

■ IRON AND RUTHENIUM COMPLEXES WITH BIPYRIDINE-BASED PNN PINCER LIGANDS

Over the past few years our group has investigated catalytic applications of the bipyridine-based Ru pincer complexes **26**−**28** (Scheme 25). These complexes are extraordinary versatile catalysts and have been applied in hydrogenation reactions of carboxylic and carbonic acid derivates,[42−46] dehydrogenative coupling reactions,[47−49] the oxidation of alcohols using water as oxygen source,[50] the deuteration of alcohols using D_2O as deuterium source,[51] and in direct olefination reactions of alcohols using sulfones (Scheme 25).[52] Prompted by these studies, we investigated the ligation reactions of $FeCl_2$ and $FeBr_2$ with the three differently phosphine-substituted bipyridine-based pincer ligands ^{t}Bu-PNN (6-(di-*tert*-butylphosphino)methyl)-2,2′-bipyridine), ^{i}Pr-PNN (6-((di-*iso*-propylphosphino)methyl)-2,2′-bipyridine), and Ph-PNN (6-((diphenylphosphino)methyl)-2,2′-bipyridine). Depending on the steric demand of the phosphine moiety and the stoichiometric ratio between ligand and iron precursor,

Scheme 24. *E*-Selective Semihydrogenation of Alkynes Catalyzed by 25[41]



monochelated neutral high-spin (S = 2) complexes [(R-PNN)Fe(X)$_2$] (**29**−**32**, Scheme 26) and bis-chelated dicationic low-spin (S = 0) complexes [(R-PNN)$_2$Fe]$^{2+}$ (**33**−**36**, Scheme 26) were obtained.[53] The doubly deprotonated complexes [(R-PNN*)$_2$Fe] (**37** and **38**, Scheme 27) were synthesized by reactions of **34** and **36**, respectively, with KO*t*Bu. The dearomatized nature of the ligands was established for the first time for an iron complex by means of X-ray diffraction analysis of **38** (Figure 7). Independently from our studies, Huang and co-workers have shown that the dihalide complexes **29**[54] and **31**[55] are, upon activation with NaBHEt$_3$, efficient catalysts for the hydroboration of alkenes with pinacolborane. Although experimental mechanistic data was not presented, a mechanism was proposed that is initiated by the reduction of the complex **29** to give the four-coordinated iron(0) alkene complex [(^{t}Bu-PNN)Fe(η^2-H$_2$C═CHR)].[54] In stoichiometric experiments we found that the dihalide complexes **29**−**32** can be reduced in the presence of CO to form the iron(0) dicarbonyl complexes [(R-PNN)Fe(CO)$_2$] (**39** and **40**, Scheme 28).[56] The analogue phenyl substituted complex **41** was synthesized by a reaction of the free ligand with Fe(CO)$_5$ (Scheme 28). The diamagnetic low-spin complexes (S = 0) **39**−**41** exhibit shortened interpyridine C−C bonds of ~1.43 Å (Figure 8), as compared to other structurally characterized complexes bearing these PNN ligands.[42,50,53] A comparison with known examples, theoretically described as metal complexes with π-radical anionic bipyridine ligands (bpy$^{\bullet-}$),[57] suggests that the complexes can be described as Fe(I) complexes with one electron antiferromagnetically coupled to the ligand-based radical anions. However, in a comprehensive experimental and computational study (NEVPT2/CASSCF level of theory) we were able to prove that the bond shortening is a result of extensive π-backbonding of the iron centers into the antibonding orbital of the bipyridine units (Figure 8).

■ CONCLUDING REMARKS

In recent years, we have developed a new mode of MLC based on reversible dearomatization/aromatization processes of the pyridine and bipyridine pincer ligand cores upon deprotonation/protonation of the ligand. Additionally, acridine-based pincer complexes which undergo dearomatization of the central acridine ring were also investigated. This has led to the development of remarkably versatile Ru catalysts, which were used for the development of novel, atom-economic and environmentally benign catalytic processes.

In this Account, we have reviewed our studies on iron complexes bearing pyridine- and acridine-based PNP pincer ligands, and bipyridine-based PNN pincer ligands. Iron complexes bearing these ligands are, as in the case of metal complexes with precious metals, capable of MLC. The combination of iron with these ligands has led to the development of novel and efficient iron catalysts for hydrogenation and dehydrogenation reactions under mild conditions. Their catalytic applications include green, atom-efficient, and industrially important hydrogenation reactions of ketones, aldehydes, carbon dioxide, and trifluoroacetic esters as well as the semihydrogenation of alkynes to give the *E*-alkenes in high selectivity, and the selective decomposition of formic acid to hydrogen and carbon dioxide. In recent years, the research area of base-metal catalysis and the research area of noninnocent ligands have developed rapidly. In this Account, we have shown that combining these two research areas has led to the development of efficient and selective iron catalysts. These novel catalysts feature activities which in some cases can even be compared to those of state-of-the-art noble-metal catalysts.

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Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

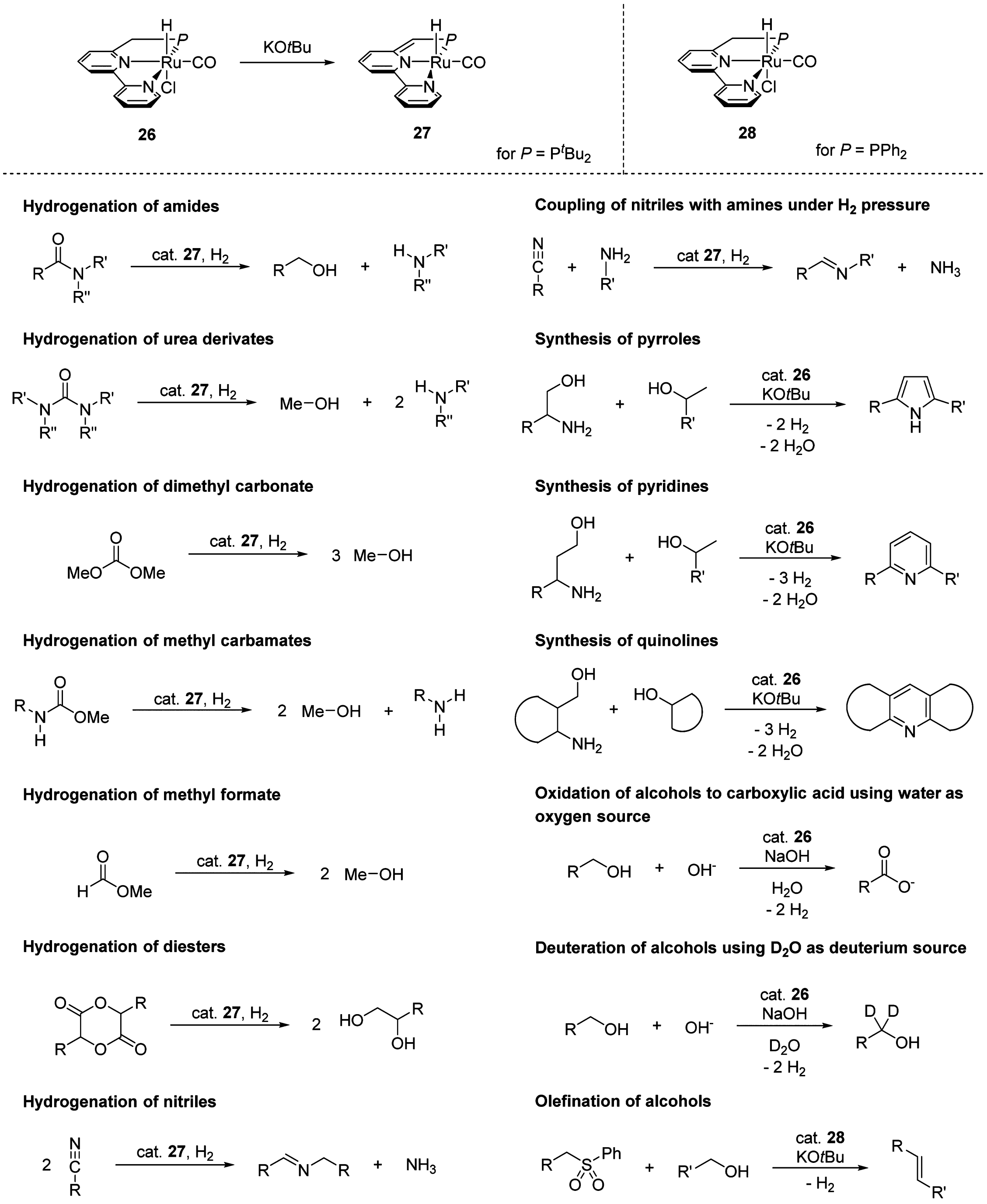
Notes

The authors declare no competing financial interest.

Biographies

Thomas Zell received his diploma in chemistry from the University of Karlsruhe (TH) in Germany. In 2007, he joined the group of Prof. Dr. Radius, supported by a fellowship of the Landesgraduiertenförderung

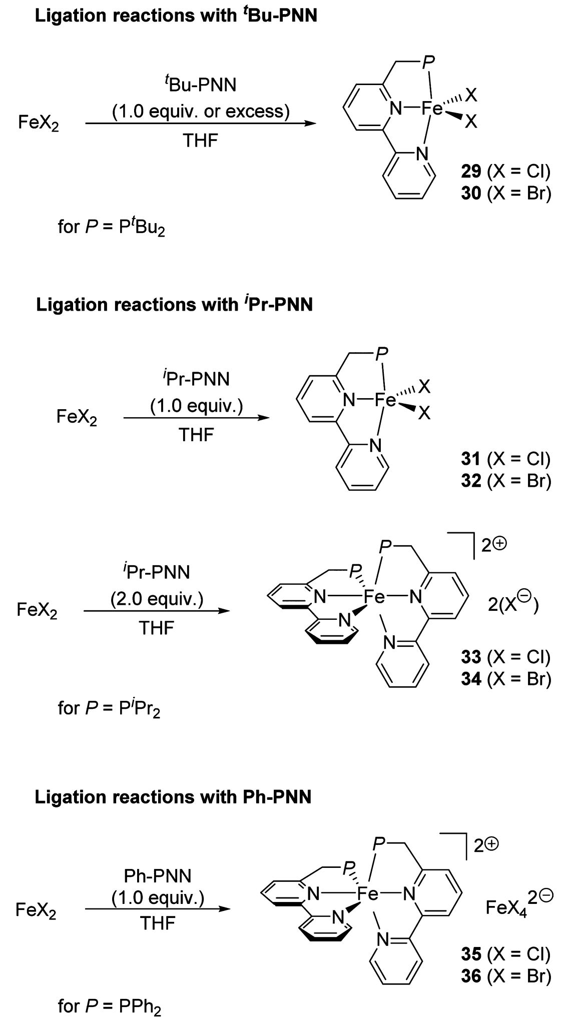
Scheme 25. Selected Catalytic Applications of 26–28[42–52]



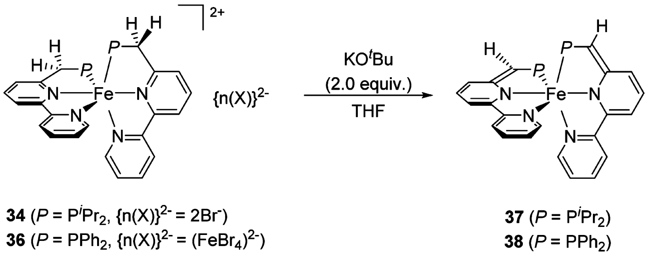
Baden-Württemberg. After completion of his doctoral studies in 2011, he was awarded with the Faculty prize of the Faculty of Chemistry and Pharmacy of the University of Würzburg. He then joined the group of Prof. Dr. David Milstein at the Weizmann Institute of Science to carry out his postdoctoral studies on bifunctional iron pincer complexes, supported by postdoctoral fellowship from the MINERVA Foundation.

David Milstein is the Israel Matz Professor of Organic Chemistry and the Director of the Kimmel Center for Molecular Design at the Weizmann Institute of Science in Israel. He received his Ph.D. degree at the Hebrew University in 1976 with Prof. Blum and performed postdoctoral research at Colorado State University, where together with his advisor, John Stille, he discovered the Stille Reaction. In 1979, he joined DuPont Company's CR&D department, and in 1986 he moved to the Weizmann Institute, where he headed the Department of Organic Chemistry in 1996–2005. His research interests include fundamental organometallic chemistry, particularly the activation of strong bonds, and the design and applications of environmentally benign processes and sustainable energy related processes catalyzed by transition metal complexes. He has received several awards, including the 2012 Israel Prize (Israel's highest honor) in Chemistry. He is a member of the Israel Academy of Sciences and Humanities, and the German National Academy of Sciences-Leopoldina.

Scheme 26. Synthesis of 29–36[53]



Scheme 27. Synthesis of 37 and 38[53]



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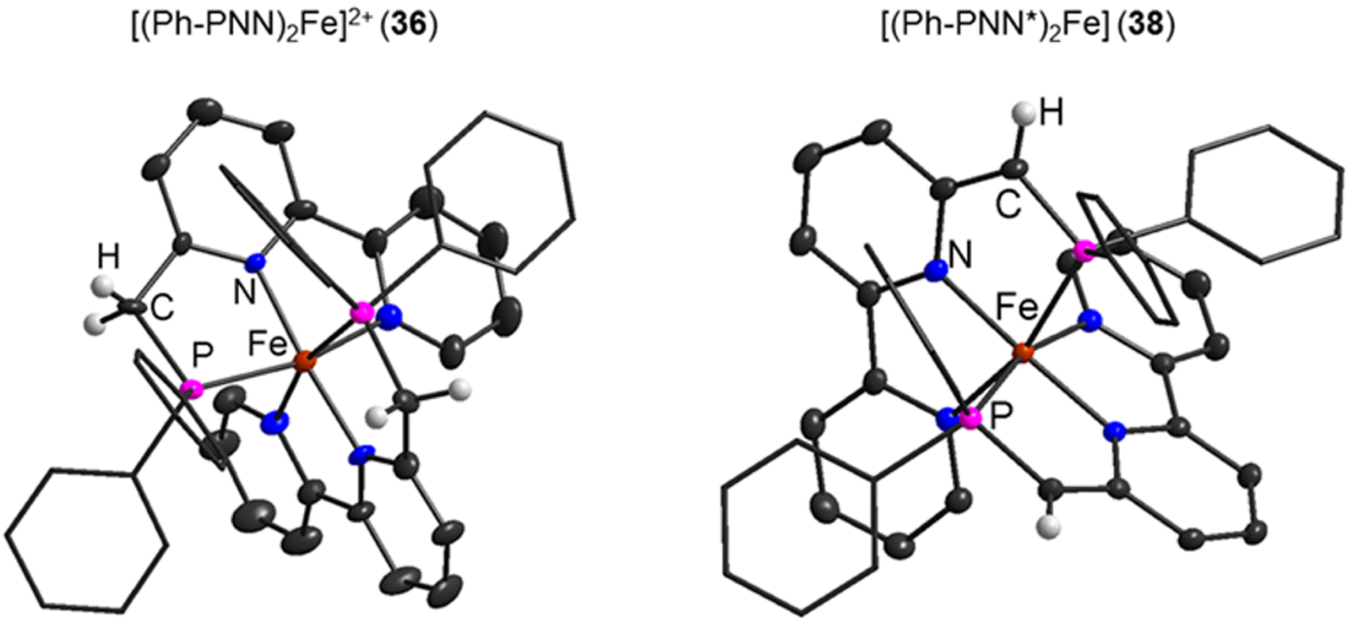
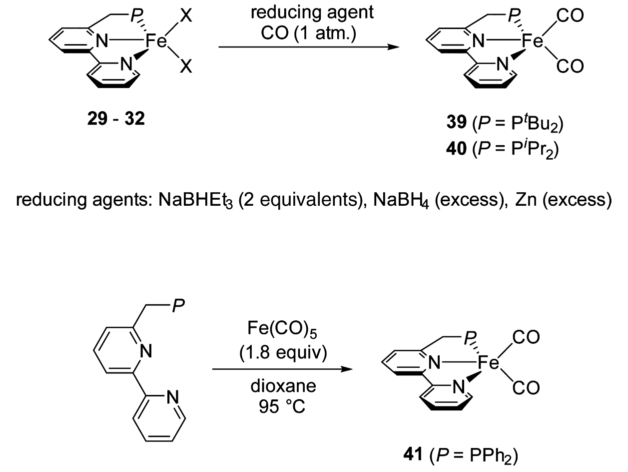


Figure 7. X-ray structures of **36** and **38**.[53]

Scheme 28. Synthesis of 39−41[56]



reducing agents: NaBHEt$_3$ (2 equivalents), NaBH$_4$ (excess), Zn (excess)

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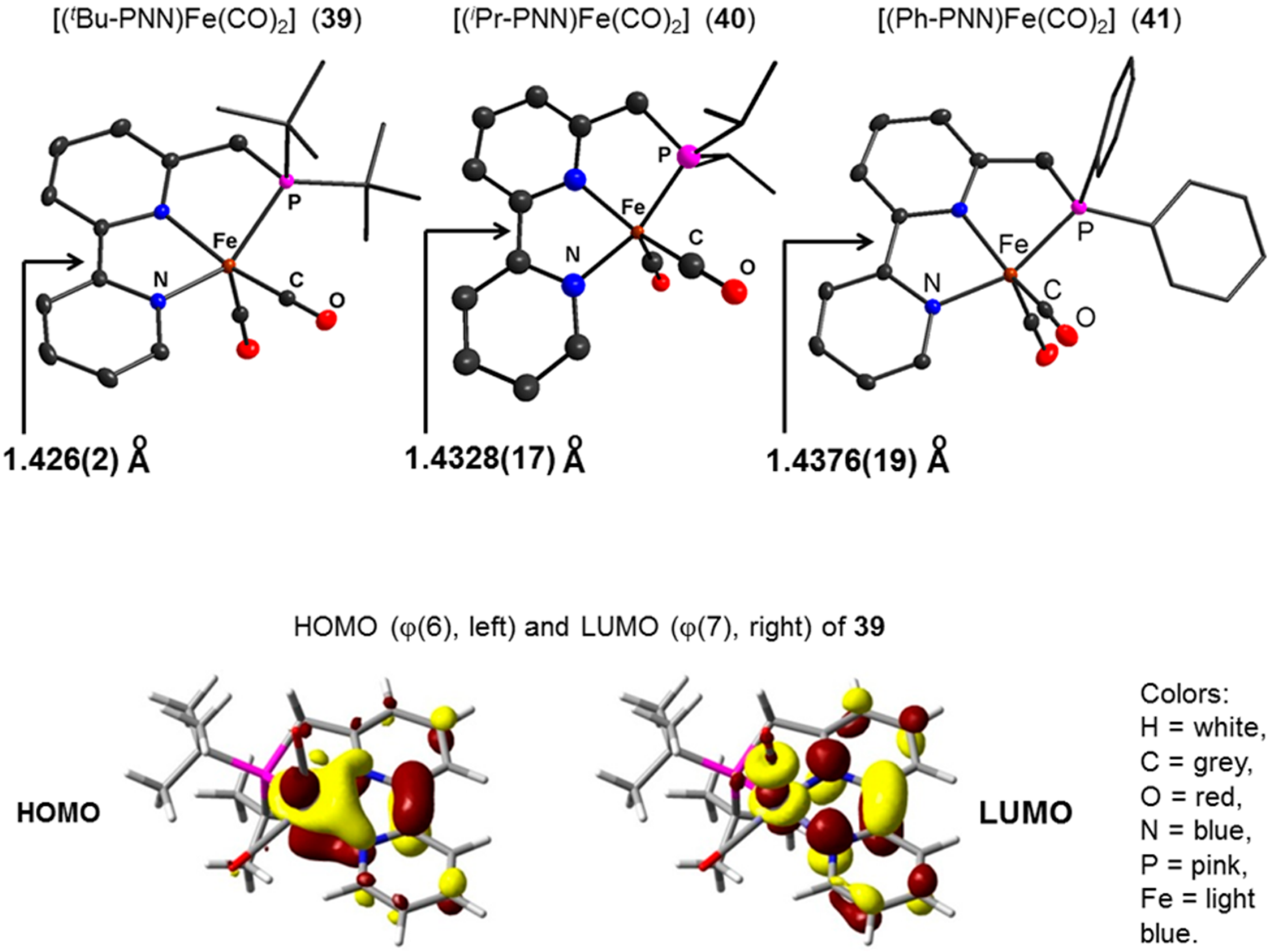

Figure 8. Top: X-ray structures of **39**–**41**. Bottom: HOMO (left) and LUMO (right) of **39**.[57]

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