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Nickel and Iron Pincer Complexes as Catalysts for the Reduction of Carbonyl Compounds

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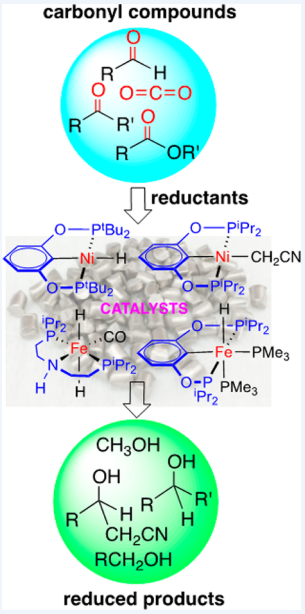
CONSPECTUS: The reductions of aldehydes, ketones, and esters to alcohols are important processes for the synthesis of chemicals that are vital to our daily life, and the reduction of CO_2 to methanol is expected to provide key technology for carbon management and energy storage in our future. Catalysts that affect the reduction of carbonyl compounds often contain ruthenium, osmium, or other precious metals. The high and fluctuating price, and the limited availability of these metals, calls for efforts to develop catalysts based on more abundant and less expensive first-row transition metals, such as nickel and iron. The challenge, however, is to identify ligand systems that can increase the thermal stability of the catalysts, enhance their reactivity, and bypass the one-electron pathways that are commonly observed for first-row transition metal complexes. Although many other strategies exist, this Account describes how we have utilized pincer ligands along with other ancillary ligands to accomplish these goals. The bis(phosphinite)-based pincer ligands (also known as POCOP-pincer ligands) create well-defined nickel hydride complexes as efficient catalysts for the hydrosilylation of aldehydes and ketones and the hydroboration of CO_2 to methanol derivatives. The hydride ligands in these complexes are substantially nucleophilic, largely due to the enhancement by the strongly *trans*-influencing aryl groups. Under the same principle, the pincer-ligated nickel cyanomethyl complexes exhibit remarkably high activity (turnover numbers up to 82,000) for catalytically activating acetonitrile and the addition of H−CH_2CN across the C═O bonds of aldehydes without requiring a base additive. Cyclometalation of bis(phosphinite)-based pincer ligands with low-valent iron species "$Fe(PR_3)_4$" results in diamagnetic Fe(II) hydride complexes, which are active catalysts for the hydrosilylation of aldehydes and ketones. Mechanistic investigation suggests that the hydride ligand is not delivered to the carbonyl substrates but is important to facilitate ligand dissociation prior to substrate activation. In the presence of CO, the amine-bis(phosphine)-based pincer ligands are also able to stabilize low-spin Fe(II) species. Iron dihydride complexes supported by these ligands are bifunctional as both the FeH and NH moieties participate in the reduction of C═O bonds. These iron pincer complexes are among the first iron-based catalysts for the hydrogenation of esters, including fatty acid methyl esters, which find broad applications in industry. Our studies demonstrate that pincer ligands are promising candidates for promoting the first-row transition metal-catalyzed reduction of carbonyl compounds with high efficiency. Further efforts in this research area are likely to lead to more efficient and practical catalysts.



INTRODUCTION

One of the rapidly growing areas of research involves the development of first-row transition metal-based catalysts for chemical transformations. The need for such efforts has been motivated by the fact that precious metals, which are widely used today for synthesizing commodity and specialty chemicals, are expensive, limited in supply, and sometimes difficult to remove from organic products. Although elements in the same group of the periodic table are expected to show similar chemical behaviors, the principles that govern the reactivity of precious metal-based complexes are not always extended to their first-row counterparts. Because of small covalent radii and narrow energy gaps between the d orbitals, first-row transition metals often form complexes with low thermal stability and with a tendency to generate paramagnetic species (or prefer one-electron pathways). Unless radical-mediated processes are desired, these properties pose a great challenge for the utilization of first-row transition metals in catalytic reactions.

The general strategy for replacing precious metals with first-row transition metals in homogeneous catalysis is to identify ligands that can not only bind tightly to the metals but also promote precious metal-like reactivity or de-emphasize metal's role. The following are some useful guidelines for ligand selection: (1) strong chelation to metals increases the stability of the metal complexes and potentially minimizes the degradation of the catalysts; (2) ligands such as hydride, alkyl/aryl, and CO provide a strong ligand field that favors low-

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spin states and diamagnetic species, which are more commonly observed for precious metal-based complexes; (3) redox-active ligands store and release electrons readily, thus obviating the need to change the oxidation states of the metals;[1,2] and (4) ligands capable of activating a substrate via secondary coordination sphere interactions diminish the reactivity difference among the metals in the same group. While electronic and steric properties of ligands and coordination geometry remain critical to controlling the catalytic activity of metal complexes, the ligand features described above have been key to the success of many catalytic systems employing a first-row transition metal.

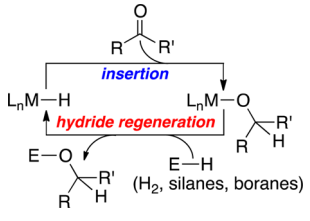
Over the past two decades, pincer or pincer-type ligands have become one of the most extensively studied ligand scaffolds.[3] They are particularly effective for transition metal catalysis, largely due to their high tunability and strong chelating ability. Some of the pincer systems can also be tailored such that the ligand is redox active or contains functional groups for substrate activation. Therefore, these ligands could be well suited to promote first-row transition metal-catalyzed reactions.

This Account summarizes our efforts in developing nickel- and iron-based catalysts for the reduction of C═O bonds of aldehydes, ketones, CO_2, and esters. These processes have a broad range of potential applications, such as converting a greenhouse gas to liquid fuels and improving the existing methods of making detergent precursors. Until recently, metal complexes used to catalyze the reduction of carbonyl compounds were mainly based on precious metals. Our studies showed that the reactivity of Ni(II) and Fe(II) complexes was significantly enhanced by a bis(phosphinite)-based or bifunctional amine-bis(phosphine)-based pincer ligand. These complexes proved to be effective in catalyzing hydrosilylation of aldehydes and ketones, hydroboration of CO_2 to methanol derivatives, cyanomethylation of aldehydes, and hydrogenation of esters.

NICKEL POCOP-PINCER COMPLEXES

From a mechanistic point of view, there are a number of different approaches that can be used to catalytically reduce carbonyl compounds.[4] With a monohydride complex, the insertion of a C═O bond would generate an intermediate with a metal−oxygen bond, which could react with H_2, silanes, or boranes to regenerate the monohydride species and close the catalytic cycle (Scheme 1). Except in the case of using H_2, regenerating the hydride with silanes and borane should be rather straightforward given the high oxophilicity of silicon and boron. For the insertion step, it was shown by Hazari et al. that the ΔG° value for the reaction with CO_2 correlated with the natural bond orbital charge on the hydride.[5] More experimental data are needed to fully understand metal's effect on C═O insertion into a M−H bond; however, on the basis of the studies with noncarbonyl substrates,[6−9] it is generally believed that first-row transition metal hydrides are less reactive not only thermodynamically but also kinetically.

Scheme 1. Catalytic Reduction of Carbonyl Compounds with a Monohydride Complex



At the beginning of our projects, our research activities were centered on how to make first-row transition metal hydrides "hydridic" enough to donate H^- to a polar double bond. The bis(phosphinite)-based pincer (later better known as POCOP-pincer) complexes of nickel developed by Morales−Morales[10] and Zargarian[11] caught our attention. It was hypothesized that if the corresponding hydride complexes could be made, they could be very hydridic due to the strong *trans*-influencing aryl group (Figure 1). Because the POCOP-pincer core is typically

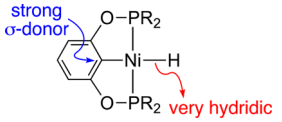
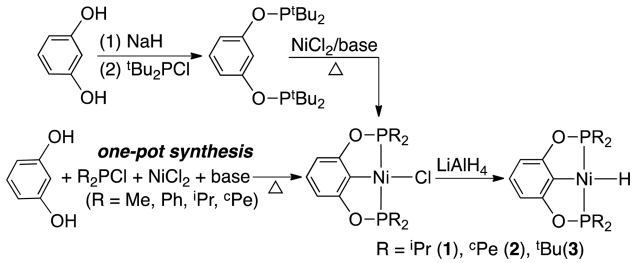


Figure 1. Nickel hydride complexes bearing a POCOP-pincer ligand.

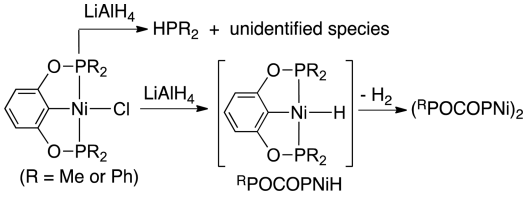
rigid and flat,[12] it was also anticipated that these square-planar d^8 metal hydride complexes would be reasonably stable. Another benefit of using this specific type of pincer ligand is that the precursors are relatively inexpensive (Scheme 2). In our laboratory, except for the bulky *tert*-butyl-substituted POCOP-pincer system, the nickel chloride complexes needed for preparing the hydrides were more conveniently synthesized in one pot from resorcinol, a chlorophosphine, $NiCl_2$, and a base (4-dimethylaminopyridine or triethylamine).[13] However, to isolate the hydride complexes, the phosphorus substituents are limited to medium-sized or bulky groups, such as isopropyl, cyclopentyl (^{c}Pe), and *tert*-butyl groups. A lack of sufficient steric protection would render the P−O bonds more exposed and susceptible to cleavage by nucleophiles[14] and also result in the loss of H_2 and the formation of a dinickel species as observed in other nickel pincer systems (Scheme 3).[15]

Scheme 2. Synthesis of Nickel POCOP-Pincer Hydride Complexes



To demonstrate the proof-of-principle of the approach illustrated in Scheme 1, we initially investigated the insertion and hydride regeneration steps. Hydride **1** was shown to react

Scheme 3. Potential Challenges for Synthesizing Nickel Hydride Complexes



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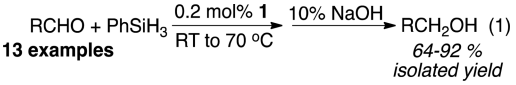
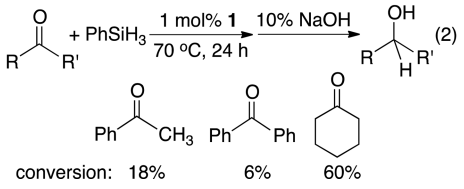
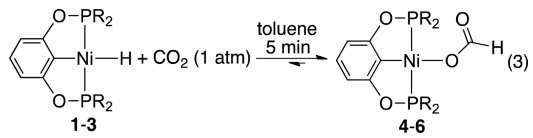
with PhCHO at a moderate rate (complete within 30 min) to generate a nickel benzyloxide complex, which upon mixing with $PhSiH_3$ or Ph_2SiH_2 provided silyl ether products and reformed **1**.[16] These results suggested that hydrosilylation of aldehydes should be catalyzed by **1**. Consistent with this hypothesis, aldehydes bearing various functional groups (e.g., OMe, NMe_2, Cl, NO_2, CN, pyridyl, and furyl groups) were catalytically and selectively reduced to their alcohols by $PhSiH_3$ following basic hydrolysis of the silyl ethers (eq 1). Ketones were also

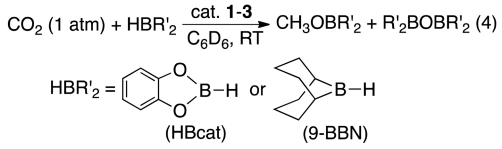




amenable to the catalytic hydrosilylation conditions; however, the conversions were much lower despite using a higher catalyst loading and temperature (eq 2). When the bulkier hydride **3** was employed as the catalyst, hydrosilylation reactions were sluggish, which is consistent with the observation that PhCHO inserted slowly into the Ni–H bond of **3**.

Once the catalytic activity of the nickel hydrides was established, our attention shifted to the reduction of CO_2. The insertion of CO_2 into the Ni–H bond of **1**–**3** was found to be substantially faster but reversible at room temperature, resulting in a nearly quantitative formation of nickel formate





complexes **4**–**6** (eq 3).[13] The subsequent treatment of **6** (R = ^{t}Bu) with $PhSiH_3$ unfortunately failed to yield the hydride. In contrast, the reaction of **6** with pinacolborane (HBpin) gave anticipated hydride **3** along with HCO_2Bpin as the reduced product for CO_2. More interestingly, mixing **6** with excess catecholborane (HBcat) not only regenerated **3** but also led to the methanol derivative CH_3OBcat. Hydrides **1**–**3** were all demonstrated to be active catalysts for CO_2 reduction under mild conditions (room temperature, 1 atm of CO_2) with turnover frequencies of up to 495 h^{-1} (eq 4, Table 1).[17] In addition to HBcat, 9-BBN also proved to be an effective borane for nickel-catalyzed reduction of CO_2.

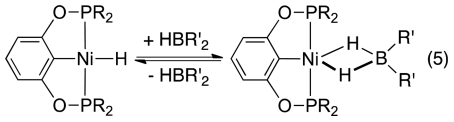
A detailed mechanistic study of the catalytic system using density functional theory (DFT) calculations suggested that CO_2 was reduced sequentially to HCO_2Bcat, HCHO, and CH_3OBcat in three separate catalytic cycles (Scheme 4).[18] The elemental steps in each of the cycles were described as either insertion or hydride regeneration, except for the step

Table 1. Catalytic Activities of Nickel Hydride Complexes in the Reduction of CO_2

catalyst	borane	borane/NiH	time (h)	TON	TOF (h^{-1})
1	HBcat	100	2	100	50
2	HBcat	100	12	30	2.5
3	HBcat	100	0.75	100	133
3	HBcat	500	1	495	495
1	9-BBN	100	1.5	100	67
2	9-BBN	100	4	100	25
3	9-BBN	100	1	100	100

converting [Ni]OCH_2OBcat to [Ni]OBcat and HCHO, which is a β-alkoxy elimination process. The individual steps in Cycle I were experimentally studied and verified. Cycle III is analogous to the mechanism for nickel-catalyzed hydrosilylation of aldehydes mentioned earlier, supported by the viability of using **3** to catalyze the hydroboration of paraformaldehyde to CH_3OBcat. Experimental investigation of Cycle II, especially the insertion of HCO_2Bcat into the nickel hydrides, was challenging due to the instability of HCO_2Bcat. A recent study by Maron, Fontaine, and co-workers reveals that the reduction of HCO_2Bcat (generated in situ) by HBcat to HCHO and catBOBcat does not necessarily need a metal catalyst.[19] Nevertheless, according to the DFT calculations, the kinetic barrier for the reduction of HCO_2Bcat is lowered by 7.5 kcal/mol when using catalyst **3**.[18]

Calculations also suggested that the insertion of HCO_2Bcat crossed the highest kinetic barrier of the complete catalytic cycles. Because **1** was found to be more reactive than **3** for aldehyde insertion, it was expected that the reaction of **1** with HCO_2Bcat would also be more favorable and hence a better catalyst for CO_2 reduction. Contrary to this prediction, catalytic activity followed a decreasing order: **3** > **1** > **2** (Table 1).[13] To reconcile the discrepancy, we proposed hydridoborate complexes (eq 5) as the dormant species resting outside the



catalytic cycles.[20] The equilibria were observable by NMR spectroscopy, and one of the hydridoborate complexes was characterized by X-ray crystallography (Figure 2). For the less bulky hydrides **1** or **2**, it is more likely to be trapped by a borane, thus decreasing the steady-state concentration of the active hydride. The decay of the catalyst through the cleavage of P–O bonds by HBR'_2 (to release $R_2PH{\cdot}HBR'_2$) is another issue with **1** and **2**.

The success of the nickel hydrides in catalyzing the reduction of carbonyl compounds was attributed to the high reactivity of the hydride moiety promoted by the POCOP-pincer ligand. In addition to the resorcinol-derived complexes **1**–**3**, hydride **7** (Figure 3) bearing an aliphatic backbone was shown by Jonasson and Wendt to react rapidly with CO_2 to give a nickel formate complex.[21] Similarly fast CO_2 insertion was observed by Hazari and co-workers with the phosphine-based nickel pincer hydride complexes (**8**,[22] **9**,[23] and **10**[23]), all of which involve a strongly *trans*-influencing central donor. In contrast, the insertion of CO_2 into PNP-pincer nickel hydrides was reported to be very slow; **11**[24] needed 24 h to complete the insertion, whereas **12**[25] required 10 days. The calculated $\Delta G^{\ddagger}$

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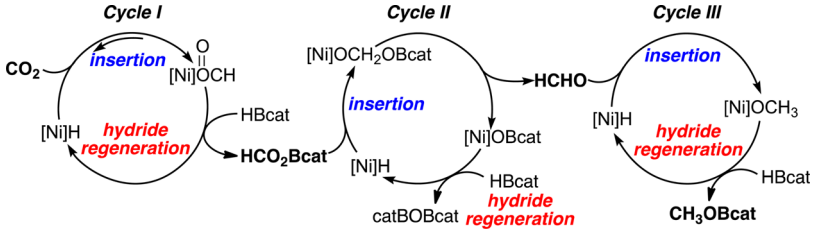
Scheme 4. Proposed Catalytic Cycles for Nickel-Catalyzed Reduction of CO_2



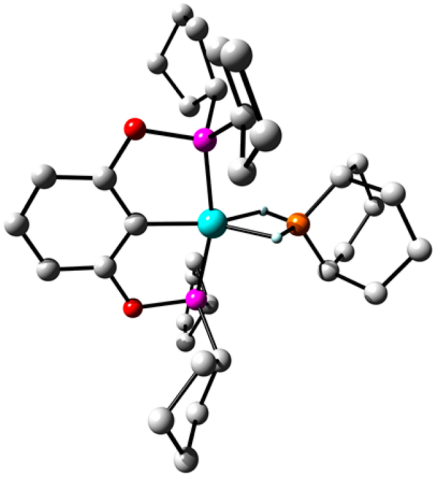


Figure 2. Structure of a hydridoborate complex generated from **2**/9-BBN.

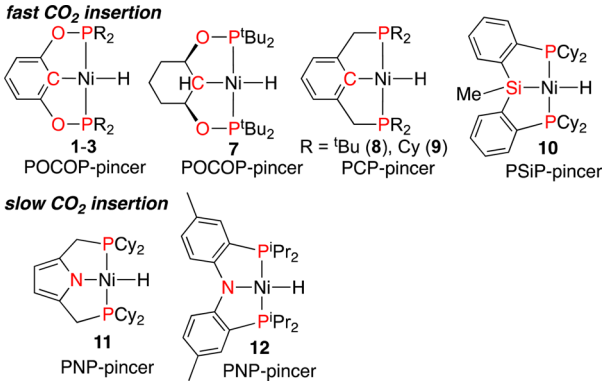
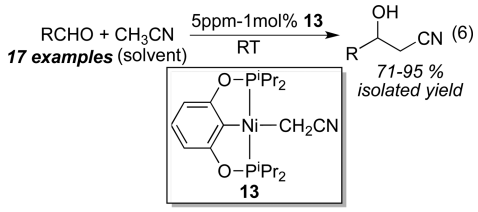


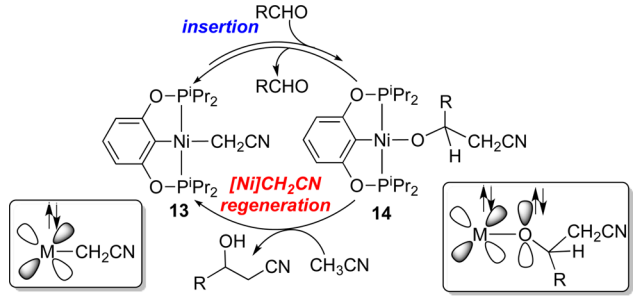
Figure 3. Nickel pincer hydride complexes tested for CO_2 insertion.

values for CO_2 insertion into nickel hydrides with various pincer ligands agree reasonably well with the experimental data.[23] Meanwhile, the comparison between nickel and palladium systems through the computational study suggests the possibility that a judicious selection of ligand could lead to even better reactivity for a nickel hydride than a palladium hydride.

The *trans*-influence of the POCOP-pincer ligand on the reactivity of nickel pincer complexes was further manifested in our discovery of nickel-catalyzed cyanomethylation of aldehydes (eq 6).[26] The CH_2CN moiety of complex **13** was proposed to be sufficiently nucleophilic to attack an aldehyde to generate a nickel alkoxide complex **14** (Scheme 5). This step can also be described as aldehyde insertion into a Ni−C bond. The subsequent deprotonation of acetonitrile by **14** would release the organic product and regenerate **13**. This mechanism differs from that proposed for Lewis-acid-catalyzed cyanomethylation reactions, where acetonitrile first coordinates to a metal and then is deprotonated by an externally added base.[27,28] In our case, the conversion of **14** to **13** was believed to be driven by the relief of dπ-pπ repulsion[29,30] between the occupied nickel d orbital and the oxygen lone pair. A simple sodium alkoxide would not be basic enough to deprotonate acetonitrile.



Scheme 5. Proposed Catalytic Cycle for Nickel-Catalyzed Cyanomethylation of Aldehydes



The advantage of this particular catalytic system lies in the fact that no external base is needed. Thus, a broad range of aldehydes, including base-sensitive ones such as aliphatic aldehydes and those containing an ester group, were successfully coupled with acetonitrile to yield β-hydroxy nitriles, which are important building blocks for pharmaceutical synthesis. Catalyst **13** is air stable and tolerates impurities present in undistilled aldehydes and acetonitrile. Furthermore, the reaction is highly efficient at room temperature with turnover numbers up to 82,000 and turnover frequencies up to 1,139 h^{-1}.

Monitoring the reaction with ^{31}P NMR identified **13** as the resting state of the catalytic cycle, suggesting that the insertion is the turnover-limiting step. Kinetic data further supported the mechanistic hypothesis as overall a second-order reaction was observed. An independent synthesis of **14** led to the formation of **13** and RCHO, implying that the insertion step is reversible. Analogous to the hydrosilylation of aldehydes catalyzed by the nickel hydrides, replacing the isopropyl groups in **13** with bulkier *tert*-butyl groups (catalyst **15**, eq 7) resulted in a much poorer catalyst, likely due to slow insertion of the aldehydes.

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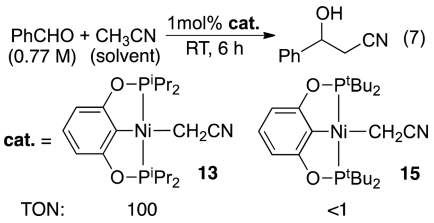
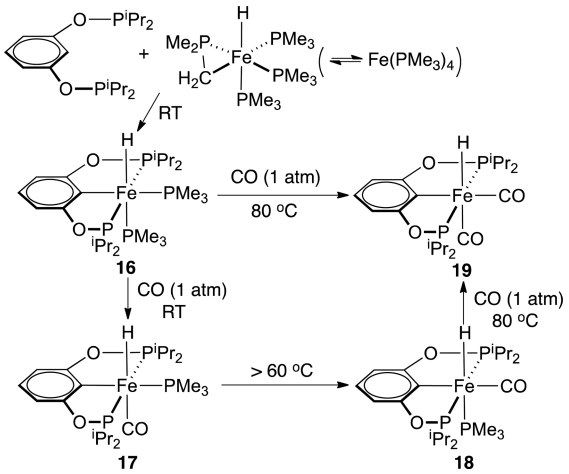


IRON POCOP-PINCER COMPLEXES

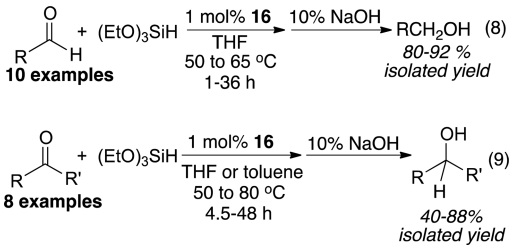
The rigidity of the POCOP ligand framework and the remarkable catalytic activity observed for the nickel system prompted us to explore the possibility of preparing iron-based pincer complexes[31] as catalysts for reduction reactions. The cyclometalation strategy (Scheme 2) used for making nickel complexes failed with various combinations of an Fe(II) salt and a base. To our delight, (κ^C,κ^P-Me_2PCH_2)Fe(PMe_3)$_3$H, which is equivalent to Fe(PMe_3)$_4$, activated the C–H bond of 1,3-bis(diisopropylphosphinito)benzene to generate isolable iron pincer complex **16** (Scheme 6).[32] With this synthetic

Scheme 6. Synthesis of Iron POCOP-Pincer Hydride Complexes

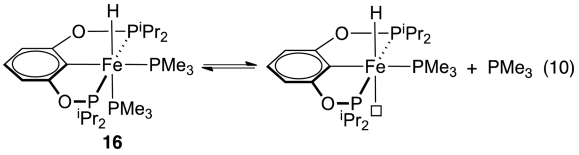


method, the structure of **16** could be altered through the introduction of a substituent (e.g., methoxy and fluorine) on the aromatic ring, the use of PMe_2Ph instead of PMe_3,[33] and the replacement of the isopropyl groups with phenyl or cyclopentyl groups (but not with *tert*-butyl groups). One or both PMe_3 ligands from **16** could be substituted by CO to generate monocarbonyl complexes **17** and **18** and dicarbonyl complex **19**, depending on the conditions used. Air and thermal stabilities of these complexes were shown to increase as more CO ligand is introduced (**16** < **17** < **18** < **19**). A solution of **19** could be exposed to air for hours without noticeable decomposition.

Hydrides **16**–**19** were demonstrated to be active catalysts for the hydrosilylation of aldehydes and ketones, and **16** was found to be the most effective catalyst in this series (eqs 8 and 9).[32] Compared to nickel catalyst **1** (eq 1), **16** is less reactive for the reduction of aldehydes (requiring heating and a higher catalyst loading, eq 8) but much more reactive for the hydrosilylation of ketones (achieving higher conversions at lower temperatures, eq 9). The iron system was also shown to be compatible with many functional groups, such as OMe, NMe_2, F, CF_3, NH_2, pyridyl, and furyl groups.

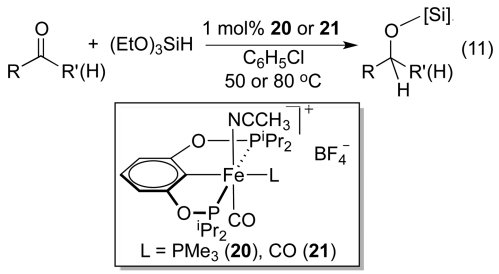


Mechanistically, the iron pincer catalysts behave drastically different than the nickel catalysts. Benzaldehyde did not insert into any of the iron POCOP-pincer hydride complexes illustrated in Scheme 6. The deuterium-labeled benzaldehyde (PhCD=O) did not undergo H/D exchange with **16**, thus ruling out the possibility that the insertion is thermodynamically uphill but kinetically accessible. Labeling both substrates (PhCD=O and Ph_2SiD_2) and treating them with a stoichiometric amount of **16** led to hydrosilylation products with no deuterium incorporated into the iron hydride. Although DFT calculations of our system by Wei et al. supported an insertion mechanism,[34] our labeling studies suggested that the hydride ligand was not involved in the catalytic cycle. Our preferred mechanism for catalyst **16** starts with the dissociation of the PMe_3 ligand that is *trans* to the hydride (eq 10) as evidenced by



the inhibition of the catalytic reaction with added PMe_3. Subsequently, either the carbonyl compound or the silane is activated by the iron center, leading to the hydrosilylation product. This Lewis-acid-type mechanism appears to be more consistent with the observation that the reactivity difference for aldehydes versus ketones is not as big as one would anticipate for C=O insertion, particularly into an Fe–H bond situated in a sterically demanding environment.

In fact, cationic iron complexes **20** and **21**, prepared via the removal of the hydride ligand with HBF_4·Et_2O, remain active as hydrosilylation catalysts (eq 11).[35] They were shown to be



catalytically more reactive than the corresponding neutral complexes **17** and **19** (Table 2), presumably due to more efficient activation of the substrates by more Lewis acidic iron centers in **20** and **21**. Although the reaction mechanism may change going from neutral species to cationic ones, this study nevertheless demonstrates that the hydride ligand is not necessarily needed for the reduction reaction.

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Table 2. Catalytic Activities of Iron Pincer Complexes in Hydrosilylation Reactions

catalyst	substrate	temp.	time	TON
20	PhCHO	50 °C	24 h	100
17	PhCHO	50 °C	24 h	15
21	PhCHO	50 °C	48 h	10
19	PhCHO	50 °C	48 h	0
20	$PhCOCH_3$	80 °C	48 h	79
17	$PhCOCH_3$	80 °C	48 h	54
21	$PhCOCH_3$	80 °C	48 h	63
19	$PhCOCH_3$	80 °C	48 h	56

IRON PNP-PINCER COMPLEXES

Our interest in iron-catalyzed hydrogenation of esters[36] was sparked by the Procter & Gamble Company's (P&G) need to develop catalytic systems that are less energy intensive than their current ones using heterogeneous copper chromite catalysts.[37] Ruthenium-based pincer complexes were tested as catalysts for homogeneous hydrogenation of fatty acid methyl esters to fatty alcohols, which operated under much milder conditions than the heterogeneous catalysts.[38] The turnover numbers (up to 1860) obtained with these ruthenium catalysts were respectable, but when the costs of preparing these catalysts are factored in, the hydrogenation method is too expensive to be commercially viable. Although more active ruthenium catalysts could, and should, be developed in the future, efforts were made to replace ruthenium with iron for catalytic hydrogenation of esters. It was envisioned that a promising iron catalyst (Figure 4) would possess the following

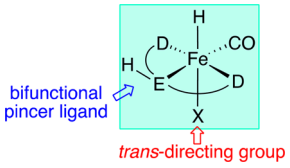


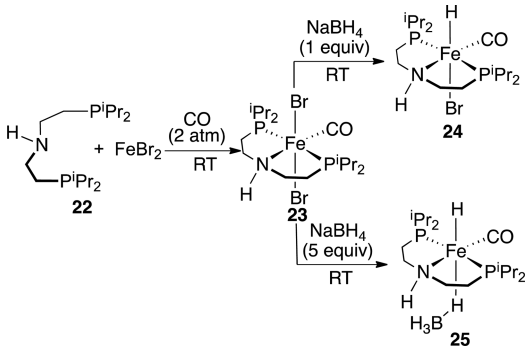
Figure 4. Design principles for an iron-based catalyst for ester hydrogenation.

structural features: (1) a bifunctional pincer ligand that has a high binding affinity for iron and can facilitate the hydrogenation process through proton transfer, (2) an ancillary ligand such as CO that forces a low-spin state for the iron, and (3) a strong *trans*-directing group that can help deliver the *trans*-hydride during reduction.

After initial screening of a few tridentate ligands, **22** was identified as the pincer ligand capable of building the target molecular structure around iron. Mixing **22** with $FeBr_2$ led to a paramagnetic species, which, upon exposure to CO, was converted to six-coordinate, diamagnetic Fe(II) complex **23** (Scheme 7).[39] Through controlling the amount of $NaBH_4$ that was added, two different hydride complexes, **24** and **25**, were isolated. Although they have the "wrong" configuration for the hydride with respect to the NH hydrogen (*anti* rather than *syn* as shown in Figure 4), both capture the general features for which we had wished. It should be mentioned that, during the development of this chemistry, **23**–**25** and the related iron chloride complexes were also studied by several other research groups.[40−42]

Of particular note is that the stability of the iron complexes is highly sensitive to the electronic and steric properties of the pincer ligand. Synthesis of **26** and **27** (Figure 5), following the

Scheme 7. Synthesis of Iron PNP-Pincer Complexes



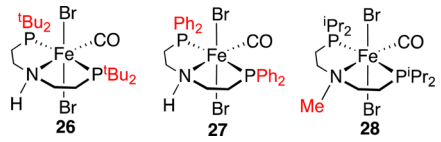
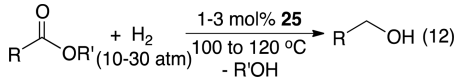


Figure 5. Iron pincer complexes that either do not form or show low stability.

same procedures used for **23**, failed as the paramagnetic intermediates did not bind CO. **28** was spectroscopically observed under a CO atmosphere but readily lost CO upon isolation. X-ray crystallographic studies revealed that the Fe−N bond of **28** is 0.1 Å longer than that of **23**, likely due to increased steric congestion around the iron center or perhaps due to the lack of hydrogen-bonding interactions (N−H···Br) as observed in **23**.[39] These results seem to suggest that the preferred ligands for iron should be small to medium size and sufficiently electron-rich to strengthen the interaction between iron and CO through back-donation.

25 was reported by both the Beller group[43] and us[39] to be an active catalyst for the hydrogenation of esters (eq 12).



Functional groups tolerated by this catalytic system included CF_3, MeO, Cl, furyl, pyridyl, and benzothiazyl groups; however, the reduction of an ester with a phenol moiety was unsuccessful. Under the hydrogenation conditions, C═C bonds were intact unless they are conjugated to the ester functionality, in which case both C═C and C═O bonds were reduced. Cyano groups were hydrogenated to NH_2 groups, thus providing a convenient method for the synthesis of primary amines from nitriles.[44] Catalyst **25** (1 mol % catalyst loading) was also employed to hydrogenate a P&G sample containing a mixture of fatty acid methyl esters, producing fatty alcohols in high yield.[39] The reaction was carried out under neat conditions; however, because of the lower reactivity for these substrates, hydrogen pressure had to be raised to 50 atm. Direct hydrogenation of refined coconut oil to fatty alcohols and glycerol was also possible with **25** (2 wt % catalyst loading), though the yield was very low (12% yield), mainly due to decomposition of the catalyst.[38] **24** alone was not an active hydrogenation catalyst, but when mixed with a base (e.g., NaOMe or KO^{t}Bu), it was shown to catalyze the hydrogenation of methyl benzoate, fatty acid methyl esters,[39] and even some *N*-heterocycles.[42] The interest in **24**, **25**, and their derivatives went beyond ester hydrogenation; they were also demonstrated

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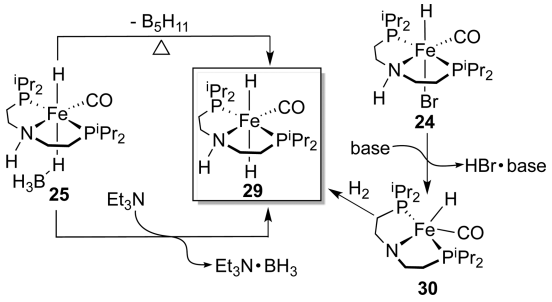
as excellent catalysts for the hydrogenation of ketones[45,46] and dehydrogenation of alcohols[40,45,47−49] and HCO_2H.[50]

The *trans*-dihydride complex **29** was proposed as the key species for the hydrogenation of esters.[39,43] It is accessible from **25** by either heating, which leads to the dissociation of BH_3 in the form of higher boranes, or at room temperature in the presence of Et_3N (or P^nBu_3), which traps BH_3 as an amine-borane (or a phosphine-borane) adduct (Scheme 8).[39,51]

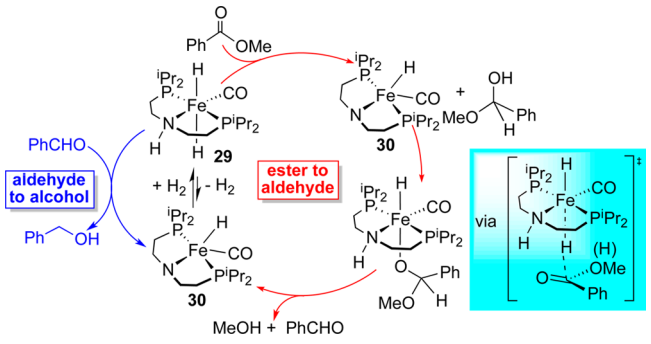
Scheme 8. Routes to Iron *trans*-Dihydride Complex



Alternatively, starting from **24**, the addition of a base generates five-coordinate species **30**, which activates H_2 readily to give **29** as the major product. **29** and **30** were spectroscopically observed by others[44,50] and us;[39] **30** was also crystallographically characterized by Jones and co-workers.[42]

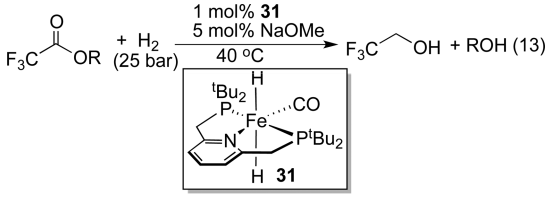
The mechanistic details for the ester hydrogenation were probed by DFT calculations using methyl benzoate as the substrate (Scheme 9).[51] The hydride ligand *syn* to NH is first

Scheme 9. Proposed Catalytic Cycles for Iron-Catalyzed Hydrogenation of Methyl Benzoate



transferred to the ester, followed by a low-barrier proton transfer leading to **30** and a hemiacetal. The latter decomposes to methanol and benzaldehyde. Further reduction of benzaldehyde to benzyl alcohol by **29** completes the hydrogenation process.

In addition to the iron PNP-pincer complexes described above, pyridine-derived PNP-pincer complex **31** was reported by Milstein et al. as a hydrogenation catalyst for fluorinated esters (eq 13).[52] It is interesting to note that the structure of



this catalyst is analogous to that of **29**. However, in this particular case, the methylene hydrogens serve as the proton source for the formation of the hemiacetal intermediate. The cocatalyst NaOMe is needed to facilitate proton transfer and dearomatization of the pyridine ring.[53]

SUMMARY AND OUTLOOK

In this Account, we have described the progress made toward our goal of building robust ligand scaffolds around first-row transition metals and, concurrently, to modulate the activity of the metal complexes to the extent that they can mimic or even outperform precious metal-based catalysts for carbonyl reduction. Many other research groups have made remarkable contributions in this specific research area.[54,55] Because of space limitations, these results are not discussed here. The utilization of pincer ligands appears to be a fruitful path to the development of catalytic processes with more abundant metals. The POCOP-pincer ligands are very effective in enhancing the nucleophilicity of square-planar nickel hydride and cyanomethyl complexes, resulting in highly efficient catalysts for the reduction of aldehydes and CO_2. These ligands are also able to stabilize Fe(II) species while maintaining a Lewis acidic metal center for catalytic hydrosilylation of aldehydes and ketones. The PNP-pincer ligands, when used in conjunction with CO, are successful at creating low-spin Fe(II) complexes as bifunctional catalysts for ester hydrogenation.

Our future efforts will be devoted to the development of more active nickel- and iron-based catalysts for the hydrogenation of CO_2 and esters. Improving turnover numbers and frequencies should be prioritized for chemists embarking on catalytic research, especially for those interested in using first-row transition metals. High catalyst loadings and long reaction times would erode the benefits of using these metals. One should also keep in mind that the cost of ligands can outweigh the cost of metal. The identification of inexpensive ligands capable of promoting high catalytic activity requires a deeper understanding of reaction mechanisms as well as the effects of metals and ligands on fundamentally important steps, such as the insertion of C═O bonds, activation of H_2, and hydrogenolysis of M−O bonds. Furthermore, biological systems perform catalytic reductions so well with first-row transition metals that we should all be inspired. One of the future directions in homogeneous catalysis could involve the development of new bifunctional catalysts mimicking the secondary coordination sphere interactions observed in enzymatic reactions.

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