

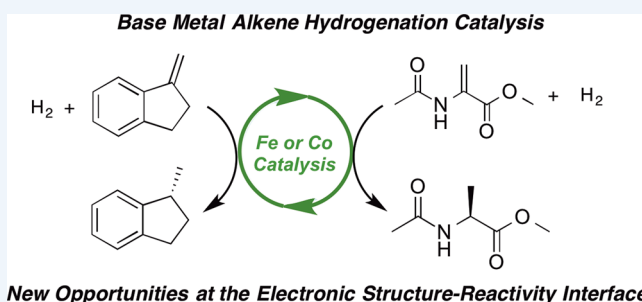
Iron- and Cobalt-Catalyzed Alkene Hydrogenation: Catalysis with Both Redox-Active and Strong Field Ligands

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CONSPECTUS: The hydrogenation of alkenes is one of the most impactful reactions catalyzed by homogeneous transition metal complexes finding application in the pharmaceutical, agrochemical, and commodity chemical industries. For decades, catalyst technology has relied on precious metal catalysts supported by strong field ligands to enable highly predictable two-electron redox chemistry that constitutes key bond breaking and forming steps during turnover. Alternative catalysts based on earth abundant transition metals such as iron and cobalt not only offer potential environmental and economic advantages but also provide an opportunity to explore catalysis in a new chemical space. The kinetically and thermodynamically accessible oxidation and spin states may enable new mechanistic pathways, unique substrate scope, or altogether new reactivity. This Account describes my group's efforts over the past decade to develop iron and cobalt catalysts for alkene hydrogenation. Particular emphasis is devoted to the interplay of the electronic structure of the base metal compounds and their catalytic performance. First generation, aryl-substituted pyridine(diimine) iron dinitrogen catalysts exhibited high turnover frequencies at low catalyst loadings and hydrogen pressures for the hydrogenation of unactivated terminal and disubstituted alkenes. Exploration of structure–reactivity relationships established smaller aryl substituents and more electron donating ligands resulted in improved performance. Second generation iron and cobalt catalysts where the imine donors were replaced by *N*-heterocyclic carbenes resulted in dramatically improved activity and enabled hydrogenation of more challenging unactivated, tri- and tetrasubstituted alkenes. Optimized cobalt catalysts have been discovered that are among the most active homogeneous hydrogenation catalysts known. Synthesis of enantiopure, C_1 symmetric pyridine(diimine) cobalt complexes have enabled rare examples of highly enantioselective hydrogenation of a family of substituted styrene derivatives. Because improved hydrogenation performance was observed with more electron rich supporting ligands, phosphine cobalt(II) dialkyl complexes were synthesized and found to be active for the diastereoselective hydrogenation of various substituted alkenes. Notably, this class of catalysts was activated by hydroxyl functionality, representing a significant advance in the functional group tolerance of base metal hydrogenation catalysts. Through collaboration with Merck, enantioselective variants of these catalysts were discovered by high throughput experimentation. Catalysts for the hydrogenation of functionalized and essentially unfunctionalized alkenes have been discovered using this approach. Development of reliable, readily accessible cobalt precursors facilitated catalyst discovery and may, along with lessons learned from electronic structure studies, provide fundamental design principles for catalysis with earth abundant transition metals beyond alkene hydrogenation.



1. INTRODUCTION

The hydrogenation of alkenes is one of the most widely practiced metal-catalyzed reactions in organic synthesis and in the chemical industry.¹ The ability to rationally prepare single enantiomer compounds from abundant alkene precursors has been transformative in the pharmaceutical and agrochemical industries.^{2–4} For nearly 50 years, catalyst technology has principally relied on transition metals that are among the least abundant and subsequently most valuable in the Earth's lithosphere. While at first this may seem counterintuitive or perhaps even imprudent, the high activity, predictable selectivity, availability of reliable synthetic precursors and

general ease of handling has rendered Rh, Ir, Pd, Pt, and Ru catalysts among the most widely deployed in synthetic contexts.

Motivations for base metal catalysis extend beyond cost. The environmental impact and associated carbon dioxide footprint associated with extraction of scarce elements from the earth's crust coupled with uncertainty in supply and concerns with toxicity provide additional incentives for using catalysts with earth abundant transition metals. Because of the now global emphasis on sustainable chemistry, it is unsurprising that catalysis with earth abundant elements has undergone explosive

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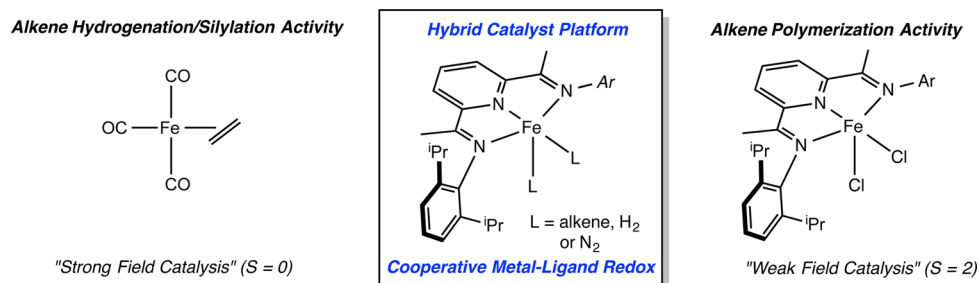


Figure 1. Observation of iron catalysis in both strong and weak ligand field inspired the concept for new platforms exploiting cooperative metal–ligand redox.

growth during the past decade.⁵ Perhaps most significant to the synthetic chemist, new catalysts based on iron and cobalt may uncover new reactivity or overcome limitations in substrate scope commonly encountered with precious metals. The variable coordination geometries (e.g., T_d vs D_{4h}), multiple spin states, and high density of states of first row transition metals offer a new frontier for the rational manipulation of electronic structure as applied to catalytic chemistry. In addition, the substitutional lability of these metals, in contrast to second and third row transition elements, may allow broader functional group compatibility, especially with heterocycles that often act as catalyst poisons.

One of the enabling features of precious metal catalysts is that, when surrounded by strong field ligands such as phosphines, carbenes, carbon monoxide, alkyls, and hydrides typically used in catalysis, predictable two-electron chemistry is observed. As such, fundamental transformations such as oxidative addition and reductive elimination are enabled and constitute the key bond breaking and making steps in many catalytic cycles. Strong field organometallic compounds of the first row transition metals are by no means rare and in fact, compounds such as ferrocene and $\text{Fe}(\text{CO})_5$ launched the field of organometallic chemistry. These early organometallic complexes often contained saturated, 18-electron configurations that limited their utility in catalytic reactions. Nevertheless, many successful catalytic reactions, such as alkene hydroformylation, have been reported where the base metal catalyst operates in the traditional, strong field limit.⁶

A more intriguing possibility is to exploit the electronic structures of first row transition metals to explore catalysis in a weak ligand field. While prevalent in Nature with metalloenzymes, examples of homogeneous catalysis applied to organic transformations such as alkene hydrogenation and hydrometalation were comparatively underdeveloped at the outset of our program and offered the opportunity to explore new catalyst space. We became interested in the application of redox-active ligands—those that undergo reversible electron transfer with a transition metal—to homogeneous catalysis^{7–11} and through collaboration with Karl Weighardt's laboratory determined the role of redox-active chelates in base metal catalyst precursors. We surmised that, by enabling cooperative redox-events between the supporting ligand and the base metal, net multielectron chemistry could be achieved. With first row metals, it was unclear what redox couples would be the most effective—in fact, this ambiguity presents and opportunity to perhaps tune reactivity based on what redox couples are accessed. This Account details our development of iron and cobalt catalysts for alkene hydrogenation and hydrosilylation. The interplay of electronic structure and catalyst performance is

highlighted as is the significant role an industrial collaboration with Merck has played in catalyst development.

2. ALKENE HYDROGENATION WITH PYRIDINE(DIIMINE) IRON COMPOUNDS

In 2003, we reported that Wilkinson's compound, $(\text{Ph}_3\text{P})_3\text{RhCl}$, was an effective catalyst for the hydrogenative ring opening of cyclopropanes.¹² These investigations raised the question of whether less expensive iron catalysts could be effective for the same transformation. Somewhat surprisingly, few iron compounds were known for catalytic alkene hydrogenation let alone for potentially more challenging C–C oxidative addition chemistry.^{13,14} This motivated our program to develop new base metal catalysts, particularly with iron and cobalt, for alkene hydrogenation reactions.

Two observations inspired our concept for catalyst design (Figure 1). First, it was known that thermolysis or irradiation of $\text{Fe}(\text{CO})_5$ and other iron carbonyl compounds generated alkene hydrogenation catalysts with high turnover frequencies but with short lifetime.^{15,16} Second, Brookhart et al.¹⁷ and Gibson et al.¹⁸ had independently demonstrated that aryl-substituted pyridine-(diimine) iron halide complexes, when treated with excess methylaluminoxane (MAO), were highly active for ethylene polymerization, suggesting this ligand class may be “privileged” for supporting base metal catalysts.¹⁹ More notable, however, was the observation of high activity C–C bond forming chemistry with precatalysts that were high spin ($S_{\text{Fe}} = 2$) and hence in a weak ligand field. Subsequent experimental work from our laboratory^{20–22} and from Bryliakov and co-workers²³ established that the high spin state was maintained during chain propagation.

In alkene hydrogenation catalysis, extensive spectroscopic studies had implicated $[(\text{CO})_3\text{Fe}]$ as the active species^{24,25} and we reasoned that a related, reduced pyridine(diimine) fragment, $[(\text{PDI})\text{Fe}]$ would, in principle, be isolobal. Because pyridine(diimines) are straightforward to synthesize and highly modular,²⁶ libraries of iron catalysts would be available and offer a steric and electronic tunability lacking with the carbonyl compounds. We were also drawn to the known redox-activity of this class of chelate and recognized the challenges associated with elucidating the electronic structure of reduced metal compounds.^{27–29}

Reduction of $(i^{\text{Pr}}\text{PDI})\text{FeBr}_2$ with either excess sodium amalgam or 2 equiv of NaBET_3H under an N_2 atmosphere yielded, following recrystallization from pentane, the desired iron bis(dinitrogen) compound, $(i^{\text{Pr}}\text{PDI})\text{Fe}(\text{N}_2)_2$.³⁰ Our hypothesis proved correct as $(i^{\text{Pr}}\text{PDI})\text{Fe}(\text{N}_2)_2$ is an effective precatalyst for the hydrogenation of unactivated, unfunctionalized terminal, 1,1- and 1,2-disubstituted alkenes. Turnover

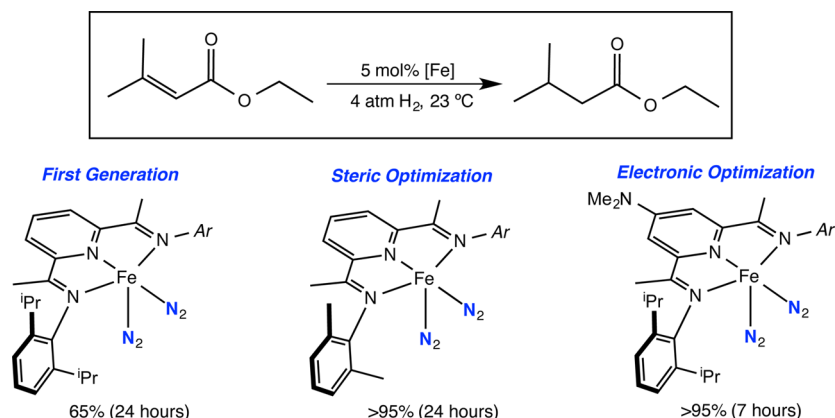


Figure 2. Steric and electronic optimization of bis(imino)pyridine iron dinitrogen compounds for the hydrogenation of ethyl-3-methylbut-2-enoate. All iron precatalysts depicted as monomers for simplicity.

frequencies as high as 1800 mol/h were observed at 0.3 mol % catalyst loadings with 4 atm of H_2 at 23 °C with 1-hexene, activity unprecedented with base metals and superior to Pd/C, $(Ph_3P)_3RhCl$ and $[(COD)Ir(PCy_3)Py]PF_6$ under identical conditions. It should be noted that such comparisons are often tenuous as different catalyst classes have optimized performances under different conditions. The iron catalyst was also effective for the hydrogenation of terminal alkenes with amine and ether substituents as well as α - and disubstituted olefins containing esters and ketones and did not require polar media for activity.³¹ More hindered tri- and tetrasubstituted alkenes were not reduced with $(iPrPDI)Fe(N_2)_2$ and α,β -unsaturated carbonyl compounds resulted in deactivation. In the absence of H_2 , C–O bond cleavage of allyl ethers was also identified as a catalyst deactivation pathway.³²

Straightforward modification of the pyridine(diimine) architecture was explored to improve catalyst performance (Figure 2). Reducing the size of the aryl substituents posed challenges for catalyst synthesis due to competing formation of bis(chelate) compounds, $(PDI)_2Fe$, which are catalytically inactive but have interesting electronic structures and highlight the redox activity of the pyridine(diimine).³³ Conditions were ultimately identified for the synthesis of $[(^ArPDI)Fe(N_2)_2](\mu_2,\eta^1,\eta^1-N_2)$ ($Ar = 2,6-Me_2-C_6H_3; 2,6-Et_2-C_6H_3$) and iron compounds with smaller aryl substituents were dramatically more active for the hydrogenation of ethyl-3-methylbut-2-enoate.³⁴ Introduction of electron donating substituents such as $[NMe_2]$ into the 4-position of the chelate³⁵ also had a profound effect on catalytic alkene hydrogenation activity as markedly improved hydrogenation activity was observed even when the relatively large $[2,6-^iPr_2-C_6H_3]$ aryl rings were maintained in the structure.³⁶

Further investigations into alterations of the ligand architecture highlighted the privileged nature of the pyridine(diimine) chelate. Simply replacing the methyl imine substituents with hydrogen atoms significantly reduced the catalytic activity of the reduced iron compounds and synthesis of the target dinitrogen complexes has remained elusive.³⁷ Transitioning from a tridentate supporting ligand to a bidentate chelate also had a deleterious effect on catalytic performance. Reduced iron complexes bearing redox-active α -diimine (DI) ligands, a class of compounds initially studied by tom Dieck in the context of diene cycloaddition,^{38,39} were also targeted.⁴⁰ The consequences of reducing the coordination number of the supporting ligand about the iron became immediately apparent

when attempts were made to synthesize catalytically active α -diimine iron precursors. Arene coordination to form coordinatively saturated, 18-electron and inactive $(DI)Fe(\eta^6\text{-arene})$ complexes was problematic.⁴¹ Similar deactivation pathways were eventually identified in reduced pyridine(diimine) iron chemistry.⁴²

It is useful at this point to comment on the electronic structure of bis(imino)pyridine iron dinitrogen compounds and related neutral ligand derivatives. Extensive studies between our group and the Weighardt laboratory and later Serena DeBeer's group established the electronic structure of the pyridine(diimine)iron dinitrogen compounds. The 18-electron, 5-coordinate compound, $(iPrPDI)Fe(N_2)_2$, is a highly covalent molecule, with the pyridine(diimine) ligand acting as a classic π -acceptor and the iron best described as a resonance hybrid between Fe(0) and Fe(II). The four-coordinate compounds, $(iPrPDI)FeN_2$, formed upon dissolution of $(iPrPDI)Fe(N_2)_2$ in common solvents, is an intermediate spin ferrous derivative ($S_{Fe} = 1$) antiferromagnetically coupled to a bis(imino)pyridine triplet dianion.^{43,44} In contrast to complexes with strong σ -donors,⁴⁵ the weakly π -accepting N_2 ligand results in a SOMO of essentially d_{z^2} parentage resulting in poor overlap with the magnetic orbitals of the pyridine(diimine), causing thermal population of the triplet state. This phenomenon is readily identified by NMR spectroscopy where temperature dependent shifts are observed.

With a comprehensive view of the electronic structure of $(iPrPDI)FeN_2$ in hand, attention was devoted to how electrons flow in oxidative addition—a key, two-electron bond activation step in hydrogenation catalysis. Due to the formation of σ -complexes rather than oxidative addition products from the addition of H_2 or $PhSiH_3$ to $(iPrPDI)FeN_2$,³⁰ C–C bond cleavage of biphenylene was explored due to the thermodynamic driving force of forming two strong metal-aryl bonds in the iron product. The electronic structure of the iron metallocycle was studied by a combination of X-ray diffraction, SQUID magnetometry, NMR spectroscopy, X-ray absorption and emission spectroscopies, and DFT.⁴⁶ The combined experimental and computational data established a ferric product with a bis(imino)pyridine radical anion. Tracking the electron flow in the C–C oxidative addition reaction highlights the cooperative metal–ligand redox chemistry available in the pyridine(diimine)iron platform—the net two electron process occurs with concomitant one electron oxidation at both the supporting ligand and the iron center (Figure 3).

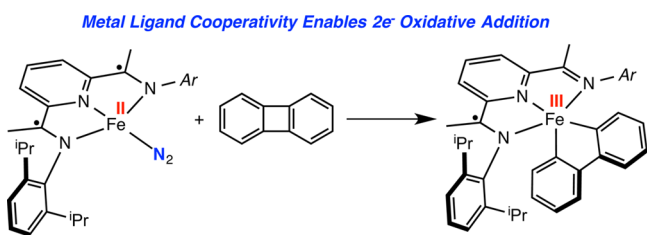


Figure 3. Electronic structure of the four-coordinate pyridine-(diimine)iron dinitrogen complex highlighting metal–ligand cooperativity in C–C oxidative addition.

3. ALKENE HYDROGENATION WITH [(CNC)Fe] AND [(CNC)Co] COMPOUNDS

The observation of improved hydrogenation activity upon introduction of more electron donating chelates inspired the evaluation of the electronic structure and catalytic activity of $(iPrCNC)Fe(N_2)_2$ ($iPrCNC = 2,6-(2,6-iPr_2-C_6H_3-imidazol-2-ylidene)_2-C_5H_3N$), a compound originally reported by Danopoulos and co-workers.⁴⁷ Infrared spectroscopy demonstrated that the [CNC] chelate is significantly more electron donating than the corresponding pyridine(diimine) compounds. More detailed spectroscopic studies established that the [CNC] pincer acts as a classical π -acceptor with no evidence for ligand radical character.⁴⁸ The preference for this electronic description is manifested in the reactivity of the compound as only 5-coordinate bis(neutral) ligand compounds have been observed; no evidence for formation of 4-coordinate complexes has been obtained. As anticipated from the electronic trend, $(iPrCNC)Fe(N_2)_2$ is more active than the $[(^R)PDI]Fe$ compounds for the hydrogenation of ethyl-3-methylbut-2-enoate and *trans*-methylstilbene.⁴⁴ Reducing the steric profile of the catalyst again increased activity as $(MeCNC)Fe(N_2)_2$ proved modestly active for the hydrogenation of the relatively challenging substrate methylcyclohexene.⁴⁴

Although the iron dinitrogen complexes are some of the most active base metal catalysts for alkene hydrogenation known, they are somewhat difficult to prepare and handle. Precedent with pyridine(diimine) cobalt alkyl complexes, $(^Ar)PDI)CoR$ ^{49,50} for the catalytic hydrogenation of α -olefins coupled with the relative ease of synthesis and established redox-activity of the chelate in these compounds^{51–53} inspired exploration of related $[(CNC)Co]$ derivatives.⁵⁴ The cobalt methyl derivative, $(iPrCNC)CoCH_3$, proved exceptionally active for the hydrogenation of tri- and tetrasubstituted alkenes

(Figure 4).⁵⁵ The cobalt-hydride, $(iPrCNC)CoH$ was identified upon hydrogenation of the alkyl complex. Under a dinitrogen atmosphere, migration of the cobalt-hydride to the 4-position of the pyridine ring of the chelate was observed, suggesting ligand-radical character. Similar reactivity was observed upon addition of 1,1-diphenylethylene and alkyl migration was identified as a possible catalyst deactivation pathway. Structural, spectroscopic, and computational studies identified bis-(arylimidazol-2-ylidene)pyridine radicals in the ground state. Spin density calculations revealed pyridine localized radicals, in contrast to the pyridine(diimine) chelates, accounting for the observed hydride and alkyl migration chemistry.

4. STEREOSELECTIVE ALKENE HYDROGENATION WITH PYRIDINE(DIIMINE) AND BIS(PHOSPHINE) COBALT COMPLEXES

The hydrogenation of prochiral alkenes to yield single enantiomer alkane products in the presence of chiral metal catalysts has emerged as one of the most powerful methods in asymmetric catalysis. Despite popular perception, most precious metal catalysts are effective for only small classes of specifically functionalized olefins that engage in two-point coordination with the metal.⁵⁶ Thus, base metal catalysts that expand the range of substrates that can be hydrogenated with synthetically useful enantioselectivity would be valuable. While selected examples of asymmetric alkene hydrogenation are known,^{57–61} H_2 is often not the stoichiometric reductant and the yields and selectivities are typically not synthetically useful. The discovery of high activity iron and cobalt complexes for alkene hydrogenation suggested that asymmetric variants should be within reach if appropriate chiral ligand architectures could be realized. We reasoned that lowering the pincer symmetry from C_{2v} to C_1 may provide the appropriate stereochemical environment to promote asymmetric hydrogenation with high enantioselectivity.

Our design for chiral, C_1 -pyridine(diimines) was inspired by an approach initially outlined by Bianchini et al.,⁶² where one imine contains a large aryl ring to sterically protect the complex while the other is derived from a single enantiomer of a readily available and inexpensive chiral amine. The cobalt methyl complex, $(S)-1-CH_3$ was effective for the hydrogenation of a family of substituted styrene derivatives with high enantioselectivity (Figure 5).⁶³ The most selective hydrogenations occurred with the use of sterically crowded alkenes and electron-rich styrenes. Cyclometalation of the chiral imine substituent was found to be competitive with formation of the

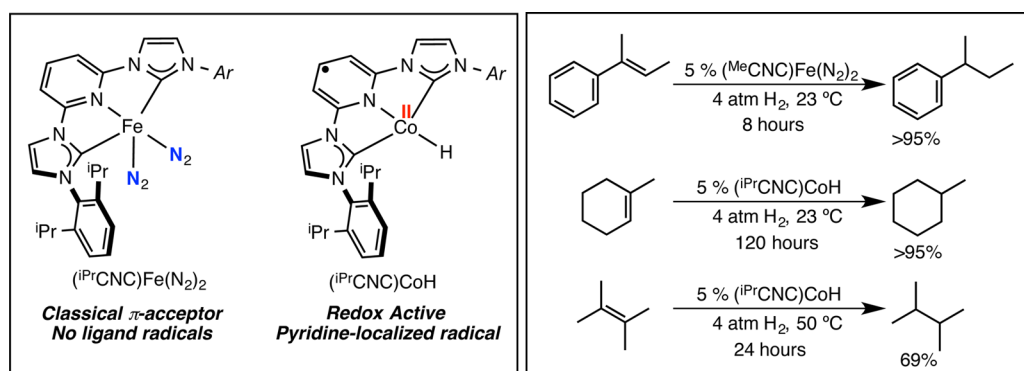


Figure 4. Electronic structures and catalytic hydrogenation performance of $(iPrCNC)Fe(N_2)_2$ and $(iPrCNC)CoH$.

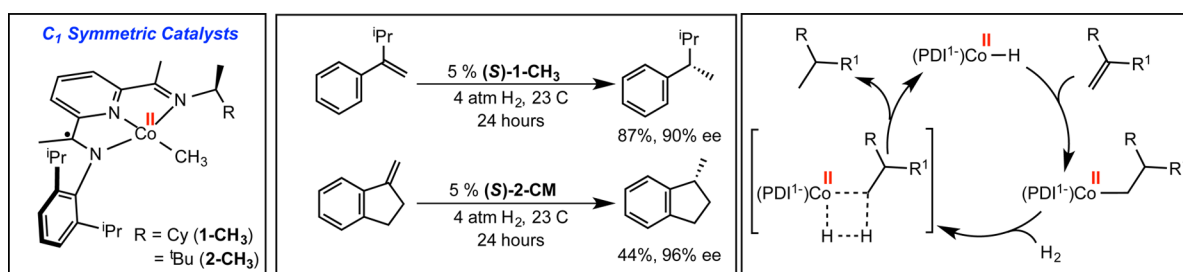


Figure 5. Cobalt-catalyzed asymmetric hydrogenation of styrene derivatives using enantiopure C_1 symmetric pyridine(diimine) supporting ligands and proposed mechanism.

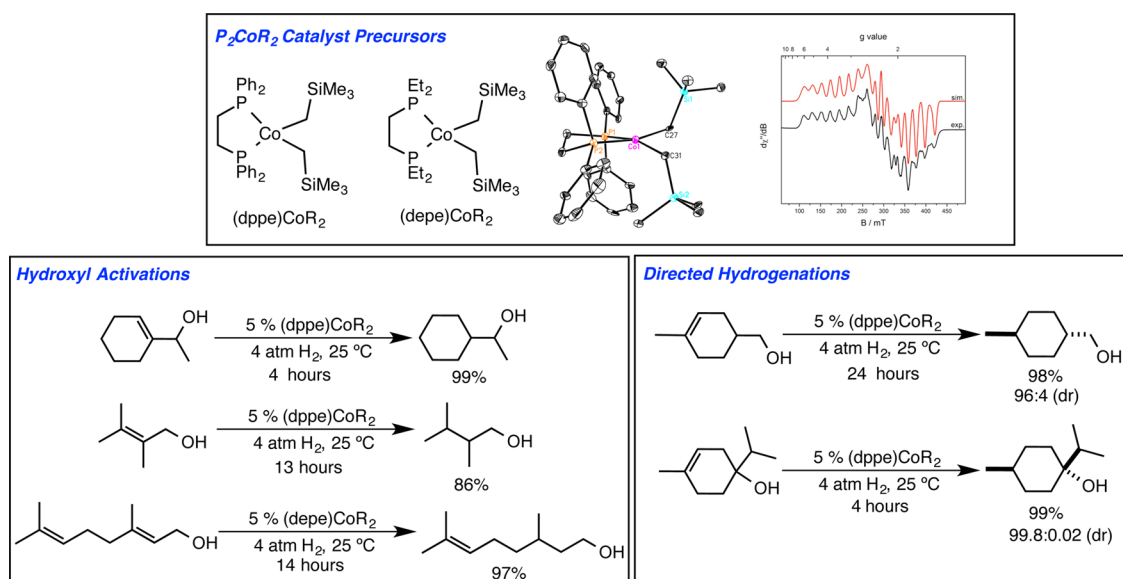


Figure 6. Directed alkene hydrogenation with bis(phosphine)cobalt(II) dialkyl complexes. The solid state structure and X-band EPR spectrum (10 K) of **(dppe)Co(CH₂SiMe₃)₂** are also shown.

cobalt hydride. Subsequent DFT studies by Hopmann⁶⁴ examined the origin of selectivity as well as the reaction energies and barriers for catalyst activation and cyclometalation. Experimental studies to establish a stereochemical model are ongoing.

Much of the success of precious metals in asymmetric alkene hydrogenation can be attributed to the availability of reliable and versatile starting materials. Diene complexes of the group 9 metals such as **[(COE)₂RhCl]₂**, **[(NBD)RhCl]₂** and **[(COD)-IrCl]₂** (COE = cyclooctene, NBD = norbornadiene, COD = 1,5-cyclooctadiene) undergo reproducible, rapid and high yielding substitution by a variety of neutral ligands, many of which are commercially available, thus enabling the synthesis of scores of olefin hydrogenation precatalysts. This procedure has now been automated, allowing for rapid evaluation of hundreds of metal–ligand combinations and accelerated the discovery of Merck's catalyst for the asymmetric hydrogenation used in the industrial manufacture of Sitagliptin.^{3,65} We reasoned that the development of analogous synthetic precursors in base metal chemistry could be equally transformative and open the field to the use of high throughput experimentation.

The observation that electron rich [CNC]-ligated iron and cobalt precursors were among the most active base metal hydrogenation catalysts suggested that classic, strong field ligands such as phosphines may support base metal alkene hydrogenation catalysts. Reports from Nindakova and co-workers demonstrated that mixtures of cobalt dichloride and

mono- or bidentate phosphines were active for alkene hydrogenation upon activation with NaBH₄ in the presence of 30 atm of H₂.⁶⁶ With methyl *N*-acetamidocinnamate, a 42% enantiomeric excess was observed using (–)-DIOP as the diphosphine.

The synthesis of four-coordinate cobalt(II) dialkyls was targeted as hydrogenation of the cobalt-alkyl bonds seemed like an attractive strategy for catalyst activation using H₂. Displacement of pyridine from **(py)₂Co(CH₂SiMe₃)₂** with ubiquitous and readily available bis(phosphines) such as dppe, depe, dmpe, and dppBz yielded the desired bis(phosphine)cobalt dialkyl products. X-ray crystallographic studies, magnetic measurements and X-band EPR spectroscopy established formation of planar, low-spin Co(II) compounds.⁶⁸ Notably, these compounds were active in the presence of hydroxyl groups, functionality that is typically a poison for other reduced first row transition metal hydrogenation catalysts (Figure 6). Experiments with analogous methyl ethers or methyl esters produced little to no turnover. Facile hydrogenation of tri- and tetrasubstituted alkenes was observed and in some cases with high diastereoselectivity.

Hydrogenation activity of Co(II) compounds with *redox innocent* phosphine donors likely invokes metal-based redox. Support for a Co(0)–Co(II) couple derived from isolation and use of **(dppe)Co(COD)** for the hydrogenation of both α -methylstyrene and terpinen-4-ol. These results highlight the potential benefit of controlling the electronic structure in base

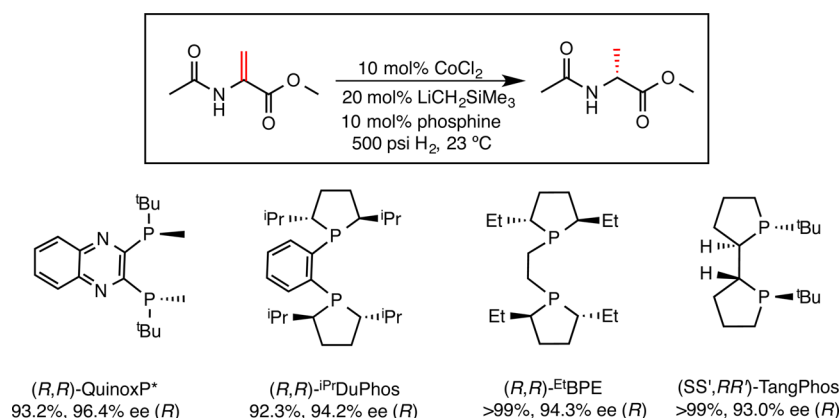


Figure 7. Representative examples of C_2 symmetric bidentate phosphines with two carbon bridges for the cobalt-catalyzed asymmetric hydrogenation of MAA.

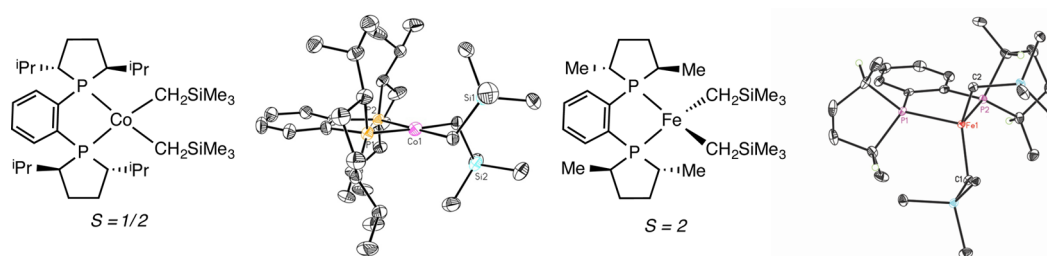


Figure 8. Comparison of the structures and spin states of (*R,R*)-(*i*Pr)DuPhosCo(CH₂SiMe₃)₂ and (*R,R*)-(^{Me})DuPhosFe(CH₂SiMe₃)₂.

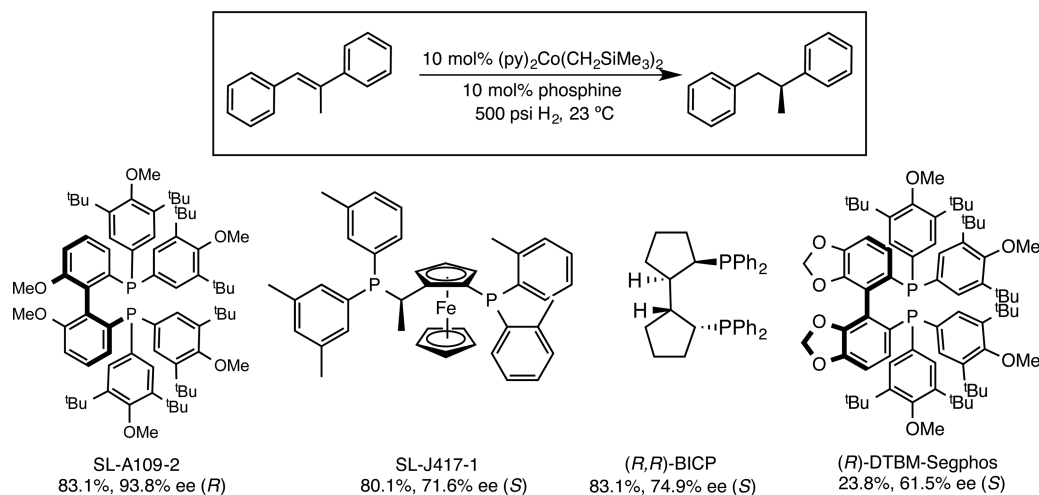


Figure 9. Enantioselective hydrogenation of *trans*-methyl stilbene with enantiopure cobalt phosphine catalysts.

metal catalysis. Notably, two different classes of catalysts have been discovered—those with redox-active ligands that maintain the Co(II) oxidation state during turnover and compounds bearing strong field donors that enable a more traditional metal based two-electron redox cycle.

The ubiquity of chiral bidentate phosphines suggested that enantioselective variants of cobalt-catalyzed hydrogenation could be realized. A collaboration with the catalysis group at Merck was initiated to accelerate catalyst discovery. This group had demonstrated success in the discovery of the rhodium catalyst used in the manufacture of Sitagliptin.³ The first generation of catalyst screening relied on (py)₂Co(CH₂SiMe₃)₂ and made assumption that all 192 of the phosphines in the ligand library would rapidly displace pyridine from the

coordination sphere of cobalt. Only a select few phosphines produced reasonable conversion and enantioselectivity for the hydrogenation of methyl 2-acetamidoacrylate (MAA).⁶⁹ Suspecting pyridine may inhibit phosphine coordination and hence catalyst formation, activation of bisphosphine/CoCl₂ combinations with two equivalents of LiCH₂SiMe₃ was explored. This evaluation demonstrated that C_2 symmetric phosphines that form 5-membered chelate rings were highly effective as many examples were found to give product in high yield and with high levels of enantioselectivity of product (Figure 7). A variety of other readily available cobalt precursors such as CoBr₂, Co(OBz)₂, and Co(ClO₄)₂ hydrate, when activated with LiCH₂SiMe₃ or other organometallic reagents

including Grignard and alkyl zinc reagents, were also effective using (R,R)-*iPr*DuPhos as the chiral ligand.

Well-defined cobalt complexes were then explored using the phosphines that gave the best results in the high throughput evaluations. Low spin, $S = 1/2$ (R,R)-(*iPr*)₂DuPhos cobalt dialkyl, dichloride and bis(benzoate) compounds were synthesized in high yields. X-ray diffraction established nearly idealized planar compounds in each case (Figure 8). The dialkyl complex proved active for the hydrogenation of MAA reaching quantitative conversion with 96.1% ee in 12 h at 22 °C. Analogous four-coordinate iron dialkyl compounds were also prepared and in each case, high spin tetrahedral compounds were isolated and characterized.⁷⁰ Unfortunately the hydrogenation performance was inferior to cobalt and in many cases suffered from decomposition to heterogeneous iron particles.

The enantioselective hydrogenation of *trans*-methylstilbene, an alkene with little coordinating functionality and a type of substrate that is among the most challenging for precious metal catalysts, was pursued with base metals.⁵⁶ Using the library of 192 chiral bidentate phosphines in combination with (py)₂Co(CH₂SiMe₃)₂, catalysts were identified that produced high activity and good enantioselectivity. Four-carbon tethered, principally axially chiral diphosphines were preferred. These structures contrast the most effective ligand motifs for the asymmetric hydrogenation of MAA. Additional experiments with both antipodes of the Biphep derivative, SL-A109, established a 1:1 ligand to cobalt stoichiometry and that once the phosphine is coordinated to the metal it is not labile on the time scale of the alkene hydrogenation (Figure 9). Perhaps most importantly, versatile cobalt precursors have been identified that allow evaluation of ligands to solve disparate and contemporary problems in asymmetric hydrogenation catalysis.

5. CONCLUSIONS AND OUTLOOK

The chemistry described above clearly establishes that iron and cobalt compounds are effective catalysts for alkene hydrogenation and opens a new frontier for catalyst development. Despite being a mature technology recognized with a Nobel prize, there are many unsolved problems in hydrogenation catalysis that can potentially be addressed with new base metal technology. Unlike heavy metals, catalysts based on earth abundant first row transition metals offer not only economic and environmental advantages but also the ability to tune coordination geometry as well as oxidation and spin states to overcome challenges in substrate scope, activity, and selectivity.

Highly active and stereoselective base metal alkene hydrogenation catalysts have been discovered in two distinct electronic structure regimes. Redox-active pyridine(diimine)-chelates enable cooperative electron flow with both the ligand and the metal giving rise to the net two-electron chemistry required for the fundamental organometallic transformations that comprise the catalytic cycle. Use of strong field phosphine donors confined the redox events to the metal in cobalt catalyzed hydrogenation chemistry and not only expanded the scope of the reaction to more functionalized molecules and enantioselective variants, but also opened base metal catalysis to commercially available and readily accessible ligand platforms found in most synthetic laboratories. While important progress has been made, significant challenges need to be addressed through catalyst design and include expanding the substrate scope, ease of catalyst handling as well as further development of metal precursors to facilitate catalyst discovery.

Perhaps most importantly, this work highlights the value of a redox flexible catalyst toolbox that will likely find applications in other synthetic contexts beyond alkene hydrogenation.

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Notes

The authors declare no competing financial interest.

Biography

Paul Chirik received his B.S. in Chemistry in 1995 from Virginia Tech and his Ph.D. from Caltech in 2000. After a brief postdoctoral stay with Christopher Cummins at MIT, he was appointed Assistant (2001), Associate (2006), and Peter J. W. Debye Professor (2009) at Cornell University. In 2011, he moved to Princeton University and is currently the Edwards S. Sanford Professor of Chemistry. His research group is interested in sustainable chemistry, including new methods for N₂ fixation as well as base metal catalysis. Chirik has been recognized with an NSF CAREER Award, a Cottrell Scholarship, a David and Lucile Packard Fellowship in Science and Technology, a Camille Dreyfus Teacher-Scholar Award, and the Blavatnik Award from the New York Academy of Sciences. In 2015, Chirik was named Editor-in-Chief of *Organometallics*.

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REFERENCES

- (1) Blaser, H.-U.; Spindler, F.; Thommen, M. In *The Handbook of Homogeneous Hydrogenation*; de Vries, J. G., Elsevier, C. J., Eds.; Wiley-VCH: Weinheim, 2008; Chapter 37, pp 1279–1324.
- (2) Johnson, N. B.; Lennon, I. C.; Moran, P. H.; Ramsden, J. A. Industrial-Scale Synthesis and Applications of Asymmetric Hydrogenation Catalysts. *Acc. Chem. Res.* **2007**, *40*, 1291–1299.
- (3) Shultz, C. S.; Krska, S. W. Unlocking the Potential of Asymmetric Hydrogenation at Merck. *Acc. Chem. Res.* **2007**, *40*, 1320–1326.
- (4) Blaser, H.-U.; Pugin, B.; Spindler, F.; Thommen, M. From a chiral switch to a ligand portfolio for asymmetric catalysis. *Acc. Chem. Res.* **2007**, *40*, 1240–1250.
- (5) Bauer, I.; Knölker, H.-J. Iron Catalysis in Organic Synthesis. *Chem. Rev.* **2015**, *115*, 3170–3387 DOI: 10.1021/cr500425u.
- (6) Gao, K.; Yoshikai, N. Low-Valent Cobalt Catalysis: New Opportunities for C–H Functionalization. *Acc. Chem. Res.* **2014**, *47*, 1208–1219.
- (7) Chirik, P. J.; Wieghardt, K. Radical Ligands Confer Nobility on Base-Metal Catalysts. *Science* **2010**, *327*, 794–795.
- (8) Chirik, P. J. Preface: Forum on Redox-Active Ligands. *Inorg. Chem.* **2011**, *50*, 9737–9740.
- (9) Knijnenburg, Q.; Gambarotta, S.; Budzelaar, P. H. M. Ligand-centered reactivity in diiminepyridine complexes. *Dalton Trans.* **2006**, 5442–5448.
- (10) Lyaskovskyy, V.; de Bruin, B. Redox Non-innocent Ligands: Versatile New Tools to Control Catalytic Reactions. *ACS Catal.* **2012**, *2*, 270–279.

- (11) Praneeth, V. K. K.; Ringenberg, M. R.; Ward, T. R. Redox-Active Ligands in Catalysis. *Angew. Chem., Int. Ed.* **2012**, *51*, 10228–10234.
- (12) Bart, S. C.; Chirik, P. J. Selective, Catalytic Carbon-Carbon Bond Activation and Functionalization Promoted by Late Transition Metal Catalysts. *J. Am. Chem. Soc.* **2003**, *125*, 886–887.
- (13) Bianchini, C.; Mantovani, G.; Meli, A.; Miglacci, F.; Zanobini, F.; Laschi, F.; Sommazzi, A. Oligomerization of ethylene to linear α -olefins by new Cs- and C1-symmetric [2,6-bis(imino)pyridyl]iron and -cobalt dichloride complexes. *Eur. J. Inorg. Chem.* **2003**, 1620–1631.
- (14) Daida, E. J.; Peters, J. C. Considering Fe^{II/IV} Redox Processes as Mechanistically Relevant to the Catalytic Hydrogenation of Olefins by [PhBP^{Pr}]₃Fe-H_x Species. *Inorg. Chem.* **2004**, *43*, 7474–7485.
- (15) Schroeder, M. A.; Wrighton, M. S. Pentacarbonyliron(0) photocatalyzed hydrogenation and isomerization of olefins. *J. Am. Chem. Soc.* **1976**, *98*, 551–558.
- (16) Harmon, R. E.; Gupta, S. K.; Brown, D. J. Hydrogenation of organic compounds using homogeneous catalysts. *Chem. Rev.* **1973**, *73*, 21–52.
- (17) Small, B. L.; Brookhart, M.; Bennett, A. M. A. Highly Active Iron and Cobalt Catalysts for the Polymerization of Ethylene. *J. Am. Chem. Soc.* **1998**, *120*, 4049–4050.
- (18) Britovsek, G. J. P.; Bruce, M.; Gibson, V. C.; Kimberley, B. S.; Maddox, P. J.; Mastroianni, S.; McTavish, S. J.; Redshaw, C.; Solan, G. A.; Strömberg, S.; White, A. J. P.; Williams, D. J. Iron and Cobalt Ethylene Polymerization Catalysts Bearing 2,6-Bis(Imino)Pyridyl Ligands: Synthesis, Structures, and Polymerization Studies. *J. Am. Chem. Soc.* **1999**, *121*, 8728–8740.
- (19) Knijnenburg, Q.; Horton, A. D.; Van Der Heijden, H.; Gal, A. W.; Budzelaar, P.; Henricus, M. PCT Int. Appl. WO 2003304231, 2003, 26 pp.
- (20) Bouwkamp, M. W.; Lobkovsky, E.; Chirik, P. J. Bis(imino)pyridine Iron(II) Alkyl Cations for Olefin Polymerization. *J. Am. Chem. Soc.* **2005**, *127*, 9660–9661.
- (21) Tondreau, A. M.; Milsmann, C.; Patrick, A. D.; Hoyt, H. M.; Lobkovsky, E.; Wieghardt, K.; Chirik, P. J. Synthesis and Electronic Structure of Cationic, Neutral and Anionic Bis(imino)pyridine Iron Alkyl Complexes: Evaluation of Redox Activity in Single-Component Polymerization Catalysts. *J. Am. Chem. Soc.* **2010**, *132*, 15046–15059.
- (22) Atienza, C. C. H.; Milsmann, C.; Lobkovsky, E.; Chirik, P. J. Synthesis, Electronic Structure, and Ethylene Polymerization Activity of Bis(imino)pyridine Cobalt Alkyl Cations. *Angew. Chem., Int. Ed.* **2011**, *50*, 8143–8147.
- (23) Bryliakov, K. P.; Talsi, E. P.; Semikolvenova, N. V.; Zakharov, V. A. Formation and Nature of the Active Sites in Bis(imino)pyridine Iron-Based Polymerization Catalysts. *Organometallics* **2009**, *28*, 3225–3232.
- (24) Whetten, R. L.; Fu, K.-J.; Grant, E. R. Pulsed-laser photocatalytic isomerization and hydrogenation of olefins. *J. Am. Chem. Soc.* **1982**, *104*, 4270–4272.
- (25) Kismartoni, L. C.; Weitz, E.; Cedeño, D. L. Density Functional Study of Fe(CO)₃ and Fe(CO)₃(L) with H₂ and C₂H₄, where L = H₂ or C₂H₄; Reactions Relevant to Olefin Hydrogenation. *Organometallics* **2005**, *24*, 4714–4720.
- (26) Gibson, V. C.; Redshaw, C.; Solan, G. A. Bis(imino)pyridines: Surprisingly Reactive Ligands and a Gateway to New Families of Catalysts. *Chem. Rev.* **2007**, *107*, 1745–1776.
- (27) Toma, H. E.; Chavez-Gil, T. E. Synthesis and Characterization of a Polymetallic Supermolecule Containing Four Ruthenium(II)-Bipyridine Complexes Attached to an Iron(II) Polyimine Center. *Inorg. Chim. Acta* **1997**, *257*, 197–202.
- (28) de Bruin, B.; Bill, E.; Bothe, E.; Weyermüller, T.; Wieghardt, K. Molecular and Electronic Structures of Bis(pyridine-2,6-diimine)metal Complexes [ML₂](PF₆)_n (n = 0, 1, 2, 3; M = Mn, Fe, Co, Ni, Cu, Zn). *Inorg. Chem.* **2000**, *39*, 2936–2947.
- (29) Budzelaar, P. H. M.; de Bruin, B.; Gal, A. W.; Wieghardt, K.; van Lenthe, J. H. Metal-to-Ligand Electron Transfer in Diiminopyridine Complexes of Mn-Zn. *Inorg. Chem.* **2001**, *40*, 4649–4655.
- (30) Bart, S. C.; Lobkovsky, E.; Chirik, P. J. Preparation and Molecular and Electronic Structures of Iron(0) Dinitrogen and Silane Complexes and Their Application to Catalytic Hydrogenation and Hydrosilation. *J. Am. Chem. Soc.* **2004**, *126*, 13794–13807.
- (31) Trovitch, R. J.; Lobkovsky, E.; Bill, E.; Chirik, P. J. Functional Group Tolerance and Substrate Scope in Bis(imino)pyridine Iron Catalyzed Alkene Hydrogenation. *Organometallics* **2008**, *27*, 1470–1478.
- (32) Trovitch, R. J.; Lobkovsky, E.; Bouwkamp, M. W.; Chirik, P. J. Carbon-Oxygen Bond Cleavage by Bis(imino)pyridine Iron Compounds: Catalyst Deactivation Pathways and Observation of Acyl C-O Bond Cleavage in Esters. *Organometallics* **2008**, *27*, 6264–6278.
- (33) Wile, B. M.; Trovitch, R. J.; Bart, S. C.; Tondreau, A. M.; Lobkovsky, E.; Milsmann, C.; Bill, E.; Wieghardt, K.; Chirik, P. J. Reduction Chemistry of Aryl- and Alkyl-Substituted Bis(imino)pyridine Iron Dihalide Compounds: Molecular and Electronic Structures of [(PDI)₂Fe] Derivatives. *Inorg. Chem.* **2009**, *48*, 4190–4200.
- (34) Russell, S. K.; Darmon, J. M.; Lobkovsky, E.; Chirik, P. J. Synthesis of aryl-substituted bis(imino)pyridine iron dinitrogen complexes. *Inorg. Chem.* **2010**, *49*, 2782–2792.
- (35) Darmon, J. M.; Turner, Z. R.; Lobkovsky, E.; Chirik, P. J. Electronic Effects in 4-Substituted Bis(imino)pyridines and the Corresponding Reduced Iron Compounds. *Organometallics* **2012**, *31*, 2275–2285.
- (36) Yu, R. P.; Darmon, J. M.; Hoyt, J. M.; Margulieux, G. W.; Turner, Z. R.; Chirik, P. J. High-Activity Iron Catalysts for the Hydrogenation of Hindered, Unfunctionalized Alkenes. *ACS Catal.* **2012**, *2*, 1760–1764.
- (37) Russell, S. K.; Milsmann, C.; Lobkovsky, E.; Weyhermüller, T.; Chirik, P. J. Bis(aldimino)pyridine Iron Compounds: Experimental Evidence for Ligand Participation. *Inorg. Chem.* **2011**, *50*, 3159–3169.
- (38) tom Dieck, H.; Dietrich, J. Diazadienes as Controlling Ligands in Catalysis, 5 Synthesis of Chiral Diazadienes R*–N=CR'–N–R. *Chem. Ber.* **1984**, *117*, 694–701.
- (39) tom Dieck, H.; Dietrich, J. Selectivity and Mechanism of Diene Cyclodimerization on Iron(0) Complexes. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 781–783.
- (40) Bart, S. C.; Hawrelak, E. J.; Schmisser, A. K.; Lobkovsky, E.; Chirik, P. J. Synthesis, Reactivity, and Solid State Structures of Four-Coordinate Iron(II) and Manganese(II) Alkyl Complexes. *Organometallics* **2004**, *23*, 237–246.
- (41) Bart, S. C.; Hawrelak, E. J.; Lobkovsky, E.; Chirik, P. J. Low-Valent α -Diimine Iron Complexes for Catalytic Olefin Hydrogenation. *Organometallics* **2005**, *24*, 5518–5527.
- (42) Archer, A. M.; Bouwkamp, M. W.; Cortez, M.-P.; Lobkovsky, E.; Chirik, P. J. Arene Coordination in Bis(imino)pyridine Iron Complexes: Identification of Catalyst Deactivation Pathways in Iron-Catalyzed Hydrogenation and Hydrosilation. *Organometallics* **2006**, *25*, 4269–4278.
- (43) Stieber, S. C. E.; Milsmann, C.; Hoyt, J. M.; Turner, Z. R.; Finkelstein, K. D.; Wieghardt, K.; DeBeer, S.; Chirik, P. J. Bis(imino)pyridine Iron Dinitrogen Complexes Revisited: Differences in Electronic Structure Between Four- and Five-Coordinate Derivatives. *Inorg. Chem.* **2012**, *51*, 3770–3785.
- (44) Bart, S. C.; Chlopek, K.; Bill, E.; Bouwkamp, M. W.; Lobkovsky, E.; Neese, F.; Wieghardt, K.; Chirik, P. J. Electronic Structure of Bis(imino)pyridine Iron Dichloride, Monochloride, and Neutral Ligand Complexes: A Combined Structural, Spectroscopic and Computational Study. *J. Am. Chem. Soc.* **2006**, *128*, 13901–13912.
- (45) Bart, S. C.; Lobkovsky, E.; Bill, E.; Wieghardt, K.; Chirik, P. J. Neutral-Ligand Complexes of Bis(imino)pyridine Iron: Synthesis, Structure and Spectroscopy. *Inorg. Chem.* **2007**, *46*, 7055–7063.
- (46) Darmon, J. M.; Stieber, S. C. E.; Sylvester, K. T.; Fernández, I.; Lobkovsky, E.; Semproni, S. P.; Bill, E.; Wieghardt, K.; DeBeer, S.; Chirik, P. J. Oxidative Addition of Carbon-Carbon Bonds with a Redox-Active Bis(imino)pyridine Iron Complex. *J. Am. Chem. Soc.* **2012**, *134*, 17125–17137.
- (47) Danopoulos, A. A.; Wright, J. A.; Motherwell, W. B. Molecular N₂ Complexes of Iron Stabilised by N-Heterocyclic ‘Pincer’ Dicarbene Ligands. *Chem. Commun.* **2005**, 784–786.

- (48) Darmon, J. M.; Yu, R. P.; Semproni, S. P.; Turner, Z. R.; Stieber, S. C. E.; DeBeer, S.; Chirik, P. J. Electronic Structure Determination of Pyridine N-Heterocyclic Carbene Iron Dinitrogen Complexes and Neutral Ligand Derivatives. *Organometallics* **2014**, *33*, 5423–5433.
- (49) Gibson, V. C.; Humphries, M. J.; Tellmann, K. P.; Wass, D. F.; White, A. J. P.; Williams, D. J. The Nature of the Active Species in the Bis(imino)pyridyl Cobalt Ethylene Polymerization Catalysts. *Chem. Commun.* **2001**, 2252–2253.
- (50) Gibson, V. C.; Tellmann, K. P.; Humphries, M. J.; Wass, D. F. Bis(imino)pyridine Cobalt Alkyl Complexes and Their Reactivity Towards Ethylene. *Chem. Commun.* **2002**, 2316–2317.
- (51) Knijnenburg, Q.; Hettterscheid, D.; Kooistra, T. M.; Budzelaar, P. H. M. The Electronic Structure of (Diiminopyridine)cobalt(I) Complexes. *Eur. J. Inorg. Chem.* **2004**, 1204–1211.
- (52) Bowman, A. C.; Milsman, C.; Atienza, C. C. H.; Lobkovsky, E.; Chirik, P. J. Synthesis and Molecular Structures of Reduced Bis(imino)pyridine Cobalt Dinitrogen Complexes: Ligand versus Metal Reduction. *J. Am. Chem. Soc.* **2010**, *132*, 1676–1684.
- (53) Bowman, A. C.; Milsman, C.; Bill, E.; Lobkovsky, E.; Weyhermuller, T.; Weighardt, K.; Chirik, P. J. Reduced N-Alkyl Substituted Bis(imino)pyridine Cobalt Complexes: Molecular and Electronic Structures for Compounds Varying by Three Oxidation States. *Inorg. Chem.* **2010**, *49*, 6110–6123.
- (54) Danopoulos, A. A.; Wright, J. A.; Motherwell, W. B.; Ellwood, S. N-Heterocyclic “Pincer” Dicarbene Complexes of Cobalt(I), Cobalt(II), and Cobalt(III). *Organometallics* **2004**, *23*, 4807–4810.
- (55) Yu, R. P.; Darmon, J. M.; Milsman, C.; Margulieux, G. W.; Stieber, S. C. E.; DeBeer, S.; Chirik, P. J. Catalytic Hydrogenation Activity and Electronic Structure Determination of Bis(arylimidazol-2-ylidene)pyridine Cobalt Alkyl and Hydride Complexes. *J. Am. Chem. Soc.* **2013**, *135*, 13168–13184.
- (56) Zhu, Y.; Burgess, K. Filling in Gaps in Asymmetric Hydrogenation Methods for Acyclic Stereocontrol: Applications to Chirons for Polyketide-Derived Natural Products. *Acc. Chem. Res.* **2012**, *45*, 1623–1636.
- (57) Ohgo, Y.; Takeuchi, S.; Natori, Y.; Yoshimura. Asymmetric reactions. X. Asymmetric hydrogenation catalyzed by bis-(dimethylglyoximate)cobalt(II)-chiral cocatalyst (amino alcohol) system. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 2124–2135.
- (58) Leutenegger, U.; Madin, A.; Pfaltz, A. Enantioselective Reduction of α,β -Unsaturated Carboxylates with NaBH_4 and Catalytic Amounts of Chiral Cobalt Semicorrin Complexes. *Angew. Chem.* **1989**, *101*, 61–62.
- (59) Corma, A.; Iglesias, M.; del Pino, C.; Sánchez, F. Optically Active Complexes of Transition Metals (Rhodium(I), Ruthenium(II), Cobalt(II) and Nickel(II)) with 2-Aminocarbonylpyrrolidine Ligands. Selective Catalysts for Hydrogenation of Prochiral Olefins. *J. Organomet. Chem.* **1992**, *431*, 233–246.
- (60) Nindakova, L. O.; Lebed, F. M.; Zamazei, Z. Y.; Shainyan, B. A. New C_2 -symmetric Optically Active Salen Ligands and Their Cobalt(II) Complexes. Hydridoborate Reduction of Prochiral C=C and C=C Bonds. *Russ. J. Org. Chem.* **2007**, *43*, 1322–1329.
- (61) Nindakova, L. O.; Shainyan, B. A. Borohydride reduction of acetophenone and esters of dehydrocarboxylic acids in the presence of chiral cobalt(II) diamine complexes. *Russ. Chem. Bull.* **2005**, *54*, 348–353.
- (62) Bianchini, C.; Mantovani, G.; Meli, A.; Migliacci, F.; Zanobini, F.; Laschi, F.; Sommazzi, A. Oligomerization of Ethylene to Linear α -Olefins by New C_s - and C_1 -symmetric [2,6-bis(imino)pyridyl]iron and -Cobalt Dichloride Complexes. *Eur. J. Inorg. Chem.* **2003**, 1620–1631.
- (63) Monfette, S.; Turner, Z. R.; Semproni, S. P.; Chirik, P. J. Enantiopure C_1 -Symmetric Bis(imino)pyridine Cobalt Complexes for Asymmetric Alkene Hydrogenation. *J. Am. Chem. Soc.* **2012**, *134*, 4561–4564.
- (64) Hopmann, K. H. Cobalt-Bis(imino)pyridine-Catalyzed Asymmetric Hydrogenation: Electronic Structure, Mechanism, and Stereoselectivity. *Organometallics* **2013**, *32*, 6388–6399.
- (65) Hansen, K. B.; Hsiao, Y.; Xu, F.; Rivera, N.; Clausen, A.; Kubryk, M.; Krska, S.; Rosner, T.; Simmons, B.; Balsells, J.; Ikemoto, N.; Sun, Y.; Spindler, F.; Malan, C.; Grabowski, E. J. J.; Armstrong, J. D. Highly Efficient Asymmetric Synthesis of Sitagliptin. *J. Am. Chem. Soc.* **2009**, *131*, 8798–8804.
- (66) Nindakova, L. O.; Shainyan, B. A.; Shmidt, F. K. Enantioselective Hydrogenation over Chiral Cobalt Complexes with (+)-(1*S*,2*S*,5*R*)-Neomenthylidiphosphine and (–)-(1*R*,2*R*)-2,2-Dimethyl-4,5-bis(diphenylphosphinomethyl)-1,3-dioxolane. *Russ. J. Org. Chem.* **2004**, *40*, 973–975.
- (67) Zhu, D.; Janssen, F. F. B.; Budzelaar, P. H. M. $(\text{Py})_2\text{Co}(\text{CH}_2\text{SiMe}_3)_2$ As an Easily Accessible Source of “ CoR_2 ”. *Organometallics* **2010**, *29*, 1897–1908.
- (68) Friedfeld, M. R.; Margulieux, G. W.; Schaefer, B. A.; Chirik, P. J. Bis(phosphine)cobalt Dialkyl Complexes for Directed Catalytic Alkene Hydrogenation. *J. Am. Chem. Soc.* **2014**, *136*, 13178–13181.
- (69) Friedfeld, M. R.; Shevlin, M.; Hoyt, J. M.; Krska, S. W.; Tudge, M. T.; Chirik, P. J. Cobalt Precursors for High-Throughput Discovery of Base Metal Asymmetric Alkene Hydrogenation Catalysts. *Science* **2013**, *342*, 1076–1080.
- (70) Hoyt, J. M.; Shevlin, M.; Margulieux, G. W.; Krska, S. W.; Tudge, M. T.; Chirik, P. J. Synthesis and Hydrogenation Activity of Iron Dialkyl Complexes with Chiral Bidentate Phosphine Ligands. *Organometallics* **2014**, *33*, 5781–5790.