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Bis(imino)pyridine Iron Complexes for Aldehyde and Ketone Hydrosilylation

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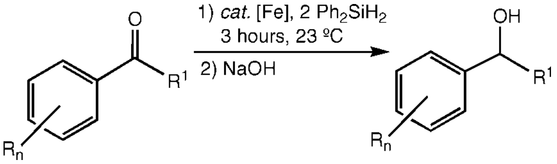
ABSTRACT



Bis(imino)pyridine iron dinitrogen and dialkyl complexes are well-defined precatalysts for the chemo- and regioselective reduction of aldehydes and ketones. Efficient carbonyl hydrosilylation is observed at low (0.1−1.0 mol %) catalyst loadings and with 2 equiv of either $PhSiH_3$ or Ph_2SiH_2, representing one of the most active iron-catalyzed carbonyl reductions reported to date.

The metal-catalyzed reduction of carbonyl compounds to alcohols by hydrogenation, hydrosilylation, or transfer hydrogenation has emerged as a powerful method in organic synthesis and has found application in the commercial production of fine chemicals, perfumes, and pharmaceuticals.[1] Precious metal catalysts, particularly those containing Rh(I) and Ru(II), are seminal and widely used examples.[1,2] The cost of the these metals, coupled with concerns about disposal and removal of trace metal residues, have motivated the search for base metal alternatives. Highly active and selective Ti,[3] Cu,[4] and organocatalytic methods[5] have become state of the art.

The high natural abundance, low cost, environmental capability, and biological importance of iron inspire efforts to expand its use in catalysis.[6] The iron-catalyzed reduction of organic carbonyl compounds has recently emerged as an area of intense investigation. Transfer hydrogenation[7] and direct H_2 addition reactions[8] have been reported by Beller and Casey. For Si−H addition, Nishiyama described that $Fe(OAc)_2$, in combination with various *N*-donor ligands and $(EtO)_3SiH$, is effective for ketone hydrosilylation at 65 °C in THF.[9] Beller has since modified this protocol to $Fe(OAc)_2$−phosphine mixtures with excess PMHS (poly(methylhydrosiloxane)) as the reductant.[10] Introduction of chiral phosphines produced high enantiomeric excesses for selected, hindered substrates.[10b] More well-defined iron precatalysts have also been described by Morris[11] and, more recently, Nikonov.[12] The latter example, $[(\eta^5\text{-}C_5H_5)\,Fe(PR_3)(CH_3CN)_2]^{2+}$, operates efficiently at ambient temperature although the substrate scope has yet to be reported. Here

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[1] (a) Nishiyama, H. *Transition Metals for Organic Synthesis*; Beller, M., Bolm, C., Eds.; Wiley-VCH: Weinheim, 2004. (b) Ohkuma, T.; Noyori, R. In *Comprehensive Asymmetric Catalysis*; Jacobsen, E. N., Pfaltz, A., Yamamoto, H., Eds.; Springer: Berlin, 1999. (c) Ikariya, T.; Blacker, J. *Acc. Chem. Res.* **2007**, *40*, 1300.

[2] Nishiyama, H.; Itoh, K. Asymmetric Hydrosilylation and Related Reactions. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; Wiley VCH: New York, 2000.

[3] Yun, J.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 5640.

[4] (a) Lipshutz, B. H.; Noson, K.; Chrisman, W.; Lower, A. *J. Am. Chem. Soc.* **2003**, *125*, 8779. (b) Lipshutz, B. H.; Frieman, B. A. *Angew. Chem., Int. Ed.* **2005**, *44*, 6345.

[5] Ouellet, S. G.; Walji, A. M.; MacMillan, D. W. C. *Acc. Chem. Res.* **2007**, *40*, 1327.

[6] (a) Bolm, C.; Legros, J.; Le Paih, J.; Zani, L. *Chem. Rev.* **2004**, *104*, 6217. (b) Fürstner, A.; Martin, R. *Chem. Lett.* **2005**, 624. (c) Enthaler, S.; Junge, K.; Beller, M. *Angew. Chem., Int. Ed.* **2008**, *47*, 3317.

[7] Enthaler, S.; Hagemann, B.; Erre, G.; Junge, K.; Beller, M. *Chem. Asian J.* **2006**, *1*, 598.

[8] Casey, C. P.; Guan, H. *J. Am. Chem. Soc.* **2007**, *129*, 5816.

[9] Nishiyama, H.; Furuta, A. *Chem. Commun.* **2007**, 760.

[10] (a) Shaikh, N. S.; Junge, K.; Beller, M. *Org. Lett.* **2007**, *9*, 5429. (b) Shaikh, N. S.; Enthaler, S.; Junge, K.; Beller, M. *Angew. Chem. Int. Ed.* **2008**, *47*, 2497.

[11] Sui-Seng, C.; Freutel, F.; Lough, A. J.; Morris, R. H. *Angew. Chem., Int. Ed.* **2008**, *47*, 940.

[12] Gutsulyak, D. V.; Kuzmina, L. G.; Howard, J. A. K.; Vyboishchikov, S. F.; Nikonov, G. I. *J. Am. Chem. Soc.* **2008**, *130*, 3732.

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we describe the application of readily accessible bis(imino)pyridine iron dialkyl compounds that are active precatalysts for the hydrosilylation of aldehydes and ketones at low catalyst loadings. These compounds are tolerant of many functional groups and are some of the most active iron-based reduction catalysts reported.

The bis(imino)pyridine iron bis(dintrogen) complex, (^{iPr}PDI)Fe(N$_2$)$_2$ (**1-(N$_2$)$_2$**), has proven to be an effective precursor for the catalytic hydrogenation and hydrosilylation of unactivated[13] and functionalized alkenes.[14] Seeking to extend the scope of this chemistry into aldehyde and ketone reductions, the hydrosilylation of *p*-tolualdehyde and acetophenone with Ph_2SiH_2 was initially examined. Both substrates were quantitatively converted to $PhCHROSiH_2Ph$ in less than 1 h with 1 mol % of **1-(N$_2$)$_2$** at 23 °C in a pentane solution. Hydrolysis with NaOH quantitatively produced the corresponding alcohol.

These initial results prompted exploration of different iron precatalysts. Because analogues of **1-(N$_2$)$_2$** with various bis(imino)pyridine ligands have thus far eluded isolation, dialkyliron compounds were targeted. Cámpora and coworkers have described a straightforward method for the synthesis of bis(imino)pyridine iron dialkyl compounds by substitution of the pyridine ligands in $(py)_2Fe(CH_2SiMe_3)_2$ with the appropriate chelate.[15] This method has been exploited by our laboratory as an alternative, high yielding route to **1-R$_2$** ($R = CH_2SiMe_3$) and other related bis(imino)pyridine iron dialkyls.[16]

For example, addition of the cyclohexyl-substituted bis(imino)pyridine to $(py)_2Fe(CH_2SiMe_3)_2$ furnished the desired iron dialkyl compound, **2-R$_2$**, as deep purple, air- and moisture-sensitive crystals in 83% yield (Figure 1). Notably, the ligand exchange procedure allowed straightforward isolation of alkyl- rather than aryl-substituted bis(imino)pyridine iron dialkyl complexes. Attempts to prepare **2-R$_2$** from direct alkylation of **2-Cl$_2$** with $LiCH_2SiMe_3$ also provided the desired product, albeit in lower yield and purity.

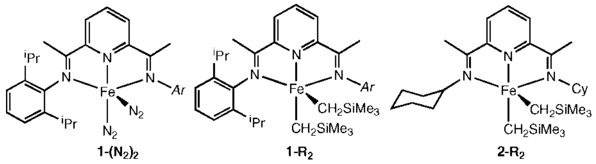

Figure 1. Bis(imino)pyridine iron precatalysts.

Paramagnetic **1-R$_2$** has been previously reported and fully characterized, including by X-ray crystallography.[17,18] The cyclohexyl-substituted bis(imino)pyridine iron alkyl complex, **2-R$_2$**, is also paramagnetic with a solution magnetic moment consistent with an $S = 2$ ground state. The solid-state structure (Figure 2) was determined by X-ray diffraction and establishes a distorted trigonal bipyramidal iron center where the two alkyl carbons and the pyridine nitrogen define the equatorial plane. The sum of these angles is 360.00(21)°. The imine nitrogens are axial and deviate from linearity due to the constraints of the chelate.

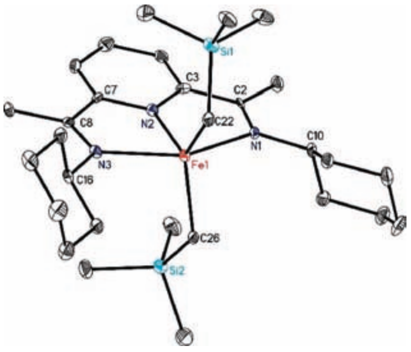

Figure 2. Molecular structure of **2-R$_2$** at 30% probability ellipsoids.

The two iron dialkyls, **1-R$_2$** and **2-R$_2$**, were assayed for the catalytic hydrosilylation of aldehydes and ketones at 23 °C (Table 1). Standard conditions involved stirring a 0.40 M toluene solution of substrate with either 1.0 (**1-R$_2$**) or 0.1 (**2-R$_2$**) mol % of iron in the presence of 2 equiv of Ph_2SiH_2. One equivalent of silane is also effective. The arylated bis(imino)pyridine iron dialkyl, **1-R$_2$**, required a higher catalyst loading (1 mol %) to achieve the same level of productivity as **2-R$_2$**. This difference is likely due to the greater moisture sensitivity of this specific iron dialkyl. The progress of the reaction was monitored by GC or ^{1}H NMR spectroscopy by analysis of either the silyl ether or the corresponding alcohol after treatment with NaOH.

$PhSiH_3$ was also effective for carbonyl hydrosilylation although the reactions were often exothermic and yielded products from multiple silane additions. These reactions also produced large amounts of dimer and oligomers derived from dehydrogenative coupling of the silane. Importantly, basic hydrolysis of the product mixtures obtained from these procedures cleanly yielded the desired alcohol. More hindered silanes such as Et_3SiH or PMHS produced no turnover even upon heating to 65 °C. The observed silane selectivity with the bis(imino)pyridine iron compounds is opposite to that described for $Fe(OAc)_2$-promoted aldehyde and ketone hydrosilylations where tertiary silanes are most effective.[9,10] Importantly, all of the iron compounds reported in this study are active catalysts for both aldehyde and ketone reduction at 23 °C without the need for an activator and with only 2 equiv of silane.

Iron-catalyzed hydrosilylation with **1-R$_2$** and **2-R$_2$** exhibits a broad functional group tolerance. Substituted acetophe-

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(13) Bart, S. C.; Lobkovsky, E.; Chirik, P. J. *J. Am. Chem. Soc.* **2004**, *126*, 13794.

(14) Trovitch, R. J.; Lobkovsky, E.; Bill, E.; Chirik, P. J. *Organometallics* **2008**, *27*, 1470.

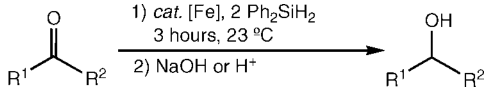
(15) Cámpora, J.; Naz, A. M.; Palma, P.; Álvarez, E.; Reyes, M. L. *Organometallics* **2005**, *24*, 4878.

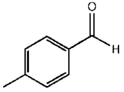
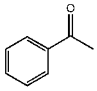
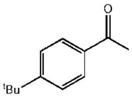
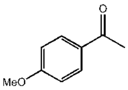
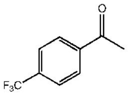
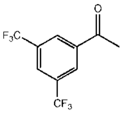
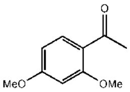
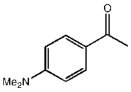
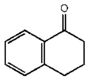
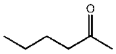
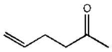
(16) Fernández, I.; Trovitch, R. J.; Lobkovsky, E.; Chirik, P. J. *Organometallics* **2008**, *27*, 109.

(17) Bouwkamp, M. W.; Bart, S. C.; Hawrelak, E. J.; Trovitch, R. J.; Lobkovsky, E.; Chirik, P. J. *Chem. Commun.* **2005**, 3406.

(18) Scott, J.; Gambarotta, S.; Korobkov, I.; Budzelaar, P. H. M. *J. Am. Chem. Soc.* **2005**, *127*, 13019.

Table 1. Catalytic Hydrosilylation of Aldehydes and Ketones with **1-R$_2$** and **2-R$_2$** and Ph_2SiH_2 (Percent Conversions Are Reported)

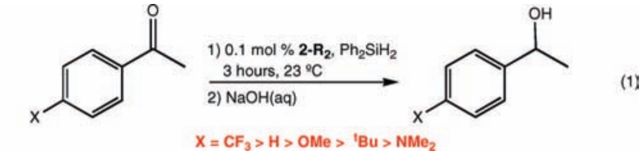


entry	substrate	1-R$_2$^{a}	2-R$_2$^{b}
1		> 99	> 99
2		> 99	> 99
3		> 99	> 99
4		> 99	> 99
5		> 99	> 99
6		21	68
7		57	94
8		27	95
9		27	82
10		> 99	58
11		75	54

^{a} 1 mol % of **1-R2**. ^{b} 0.1 mol % of **2-R2**.

nones, with the exception of 3,5- and 2,4-disubstituted examples (entries 6 and 7), are quantitatively reduced in 3 h. Alkyl-substituted ketones are more sluggish (entries 9−11), although longer reaction times, typically 12 h, produced complete conversion with little evidence for catalyst decomposition. The iron-catalyzed hydrosilylation reactions were easily adapted to preparative scale. For example, the **2-R$_2$**-catalyzed reduction of acetophenone on a 0.600 g scale yielded 97% of isolated silyl ether and 90% of 1-phenylethanol.

Because many of the substituted acetophenones were completely converted after 3 h, competition experiments were conducted to delineate substituent effects. Each experiment involved hydrosilylation of an equimolar mixture of the two substrates with 0.5 equiv of Ph_2SiH_2 (1 equiv of ketone **1**/1 equiv of ketone **2**/0.5 equiv of Ph_2SiH_2) using 0.1 mol % of **2-R$_2$** followed by analysis of the resulting silyl ether by GC (eq 1). Overall, the relative rate of ketone hydrosilylation increases with electron-withdrawing groups in the para position,[19,20] where the most electron-deficient substrates, p-CF_3 and p-H, are reduced the most rapidly while those with electron-donating groups, p-NMe_2 and p-^tBu, are the most sluggish. While electron-withdrawing groups are known to slow Ru transfer hydrogenation catalysts, a trend similar to that reported here has been observed by Morris and coworkers with ferrous dications.[11]



The iron-catalyzed hydrosilylation of α,β-unsaturated ketones was also examined (Figure 3). Previous work from our laboratory has established that addition of this class of substrates to **1-(N$_2$)$_2$** results in immediate decomposition of the iron compound.[14] Thus, iron dialkyl compounds were explored as alternatives. Hydrosilylation of cyclohexenone or isophorone with Ph_2SiH_2 in the presence of 0.1 mol % of **2-R$_2$** occurred smoothly over the course of 12 h at 23 °C. The corresponding alcohols, with no evidence for alkene reduction, were obtained exclusively following basic hydrolysis. Replacing the secondary silane with the more reactive $PhSiH_3$ also resulted in complete conversion to product with exclusive selectivity.

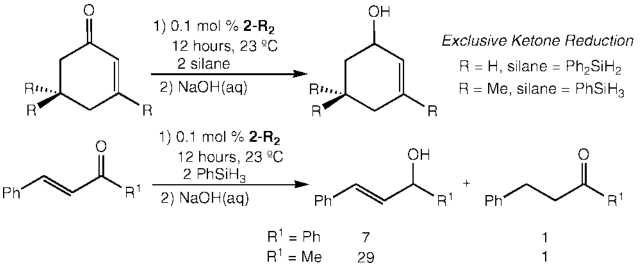


Figure 3. Hydrosilylation of α,β-unsaturated ketones with **2-R$_2$**.

Iron-catalyzed hydrosilylation of chalcone or benzylidene acetone with 2 equiv of $PhSiH_3$ and 0.1 mol % of **2-R$_2$** resulted in predominantly 1,2-addition (carbonyl) reduction with detectable amounts of 1,4-addition products (Figure 3). The selectivities exhibited by **2-R$_2$** are superior to those observed with the Shvo-type iron hydrogenation catalyst reported by Casey where mixtures of the product from 1,2-addition and complete reduction were observed.[8]

Deuterium-labeling studies were also performed to confirm the selectivity for 1,2-addition. Deuterosilylation of cyclo-

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[19] Anslyn, E. V.; Dougherty, D. A. *Modern Physical Organic Chemistry*; University Science Books: Sausalito, CA, 2006; p 446.

[20] (a) Hansch, C.; Leo, A.; Taft, R. W. *Chem. Rev.* **1991**, *91*, 165. (b) Hashiguchi, S.; Fujii, A.; Takehara, J.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1995**, *117*, 7562.

hexenone with $PhSiD_3$ and **2-R$_2$** produced a single peak in the ^2H NMR spectrum corresponding to the alcohol methine position following basic hydrolysis. In contrast, deuterosilylation of chalcone in the presence of 0.1 mol % of **2-R$_2$** and $PhSiD_3$ confirmed the 7:1 ratio of 1,2- versus 1,4-addition of the silane as deuteration was observed both in the methine (1,2) and benzylic positions.

In summary, readily accessed bis(imino)pyridine iron dialkyl complexes are efficient precatalysts for the hydrosilylation of aldehydes and ketones using $PhSiH_3$ and Ph_2SiH_2. This method exhibits broad functional group tolerance and high activities at 23 °C. Further investigations into the scope, mechanism, and enantioselectivity of these reactions are a continuing area of investigation in our laboratory.

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Supporting Information Available: Complete experimental procedures and full characterization data including the crystallographic data for **2-R$_2$**. This material is available free of charge via the Internet at http://pubs.acs.org.

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