JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY
Communication
pubs.acs.org/JACS

A Molecular Iron Catalyst for the Acceptorless Dehydrogenation and Hydrogenation of N-Heterocycles

Sumit Chakraborty, William W. Brennessel, and William D. Jones*

Department of Chemistry, University of Rochester, Rochester, New York 14627, United States

Supporting Information

ABSTRACT: A well-defined iron complex (**3**) supported by a bis(phosphino)amine pincer ligand efficiently catalyzes both acceptorless dehydrogenation and hydrogenation of N-heterocycles. The products from these reactions are isolated in good yields. Complex **3**, the active catalytic species in the dehydrogenation reaction, is independently synthesized and characterized, and its structure is confirmed by X-ray crystallography. A *trans*-dihydride intermediate (**4**) is proposed to be involved in the hydrogenation reaction, and its existence is verified by NMR and trapping experiments.

Acceptorless catalytic dehydrogenation and hydrogenation of N-heterocycles are fundamentally important organic transformations. In addition, these reactions find potential applications in the field of organic hydrogen storage materials.[1] Although the dehydrogenation of N-heterocycles is a thermodynamically uphill process, experiments and computational studies have shown that the presence of the N atom decreases the endothermicity of the reaction when compared to cycloalkanes.[2] A large positive entropic contribution comes from releasing H_2 during the reaction.[2c] So far, heterogeneous catalysts have mostly been used for the dehydrogenation of N-heterocycles.[3] However, most of these heterogeneous systems require harsh conditions and show poor functional-group tolerance. In addition, rational tuning of catalysts is challenging because of the lack of mechanistic understanding.

On the other hand, well-defined homogeneous catalysts for the acceptorless dehydrogenation of N-heterocycles are rare in the literature, and advances have been primarily made with iridium-based precious metal catalysts.[4,5] Fujita and Yamaguchi first reported a [Cp*Ir(2-hydroxypyridine)] catalyst (Cp*: 1,2,3,4,5-pentamethyl cyclopentadienyl) capable of dehydrogenating tetrahydroquinoline derivatives in refluxing *p*-xylene.[4a] DFT studies have supported a ligand-promoted hydrogen abstraction from the substrate without changing the oxidation state of the metal.[4c] Noticeably, the same iridium complex can also serve as a catalyst for the hydrogenation of quinaldine, although a $[Cp^*Ir(Cl)(\mu\text{-}H)]_2$ complex has been shown to be the active intermediate. Xiao et al. have developed cyclometalated [Cp*IrCl(imino)] complexes as efficient dehydrogenation-hydrogenation catalysts for a broad range of N-heterocycles.[4e] Catalysis was performed with a low catalyst loading (0.1 mol %) in refluxing 2,2,2-trifluoroethanol (TFE, bp 78 °C). TFE appeared to play multiple roles in this reaction that include promoting halide dissociation and facilitating the H_2-release step. Recently, Fujita et al. have reported Cp*(L)Ir-(bipyridonate) catalysts (where L: neutral σ-donors) for perdehydrogenation and perhydrogenation of fused bicyclic N-heterocycles as well.[6]

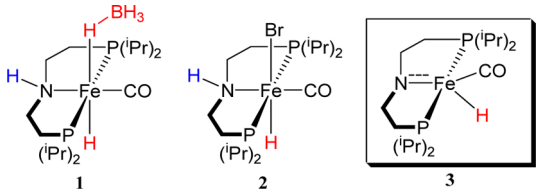


Figure 1. Fe catalysts employed in the current work.

Despite the recent progress with these iridium-based catalysts, development of inexpensive, earth-abundant metal catalysts for the dehydrogenation and hydrogenation of N-heterocycles is highly desirable. In this context, iron fits well because of its low cost, low toxicity, high abundance, and isoelectronic (d^6 metal) nature with the aforementioned Ir(III) catalysts. Additionally, iron-based catalysts have been applied in dehydrogenation and hydrogenation reactions in recent years.[7] Therefore, we sought to carry out dehydrogenation of N-heterocycles with molecular iron catalysts. Recently, the Beller,[8] Schneider/Hazari,[9] and Guan[10] groups have independently reported bifunctional iron pincer complexes (**1**, **2**, and related chloride derivatives) supported by bis(phosphino)amine (PNP) ligands (Figure 1). Beller has demonstrated base-assisted catalytic dehydrogenation of methanol with these iron compounds.[8] Remarkably, ppm levels of catalyst loading could be employed, and catalysis could be performed at a relatively high temperature indicating the thermal stability of these iron complexes and related intermediates. On the other hand, Guan et al. carried out hydrogenation of unactivated esters with the same iron catalysts.[10] Encouraged by the dehydrogenation and hydrogenation activities shown by these iron complexes, we planned to explore their potential in catalytic dehydrogenation and hydrogenation of N-heterocycles. Herein, we report the acceptorless dehydrogenation and hydrogenation of N-heterocycles with a single molecular iron catalyst.

We initially tested the catalytic activity of complex **1** and **2** with a model substrate 1,2,3,4-tetrahydroquinaldine (**C**) (Table 1). When the dehydrogenation of **C** was carried out with 5 mol % of **1** in refluxing toluene while purging the solution slowly with nitrogen, only 10% conversion to the desired product was observed in 24 h (entry 1). Complex **2** in the presence of KO^{t}Bu

Received: May 6, 2014
Published: May 30, 2014

   dx.doi.org/10.1021/ja504523b | J. Am. Chem. Soc. 2014, 136, 8564−8567

Table 1. Catalytic Activities of Iron Complexes (1 and 2) for the Dehydrogenation of 1,2,3,4-Tetrahydroquinaldine

entry	catalyst (loading)	solvent	time (h)	conversion (%)
1	**1** (5 mol %)	toluene	24	10
2[a]	**2** (5 mol %)	THF	24	1
3	**1** (5 mol %)	xylene	24	82
4	**1** (3 mol %)	xylene	30	100
5	**1** (1 mol %)	xylene	48	45

[a]KO^{t}Bu (20 mol %) was added as an additive.

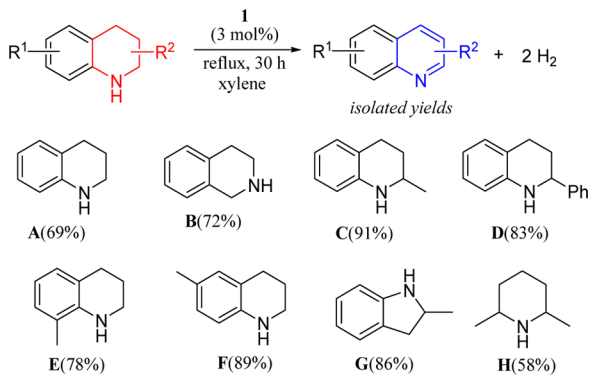


Figure 2. Acceptorless catalytic dehydrogenation of N-heterocycles. Conditions: **1** (25 μmol), N-heterocyclic substrate (0.83 mmol), xylene (1 mL), refluxed at 140 °C. Numbers in the parentheses represent isolated yields of the dehydrogenated N-heterocycles.

(20 mol %) afforded only 1% conversion after a day in THF (entry 2). However, gratifyingly, when xylene (avg bp 138.5 °C) was used instead of toluene or THF, 82% conversion of the starting material was observed with catalyst **1** (5 mol %) after 24 h (entry 3).[11] Moreover, under the same catalytic conditions, quantitative conversion was achieved in 30 h with an even lower catalyst loading (3 mol % of **1**, entry 4). An attempt to further decrease the amount of catalyst (1 mol %) led to an incomplete reaction even after a longer reaction time (entry 5). Control experiments without catalysts did not yield any product. Furthermore, the homogeneous nature of this system was indicated by performing a mercury-poisoning experiment[12] and an experiment with added PNP ligand.[13]

Having established the optimized reaction conditions for the catalytic dehydrogenation of **C**, we explored the substrate scope for this system using 3 mol % of **1** in refluxing xylene. As shown in Figure 2, several N-heterocyclic compounds (**A**–**H**) were dehydrogenated successfully under this oxidant-free condition, and the corresponding products were isolated in decent yields (58–91%). For all of the substrates, fully dehydrogenated products were isolated after the reaction. Partially dehydrogenated products were not observed. Positions of the -CH_3 groups in the N-heterocycles (**C**, **E**, and **F**) did not seem to be critical as all of these substrates gave quantitative conversions after 30 h. Apart from the tetrahydroquinoline derivatives, 2-methylindoline (**G**) and 2,6-dimethylpiperidine (**H**) were also successfully dehydrogenated. For substrate **H**, complete dehydrogenation led to the formation of the corresponding pyridine derivative. Remarkably, formation of quinoline or pyridine derivatives, potential ligands for iron, did not hamper the catalysis.

In order to confirm the identity of the evolved gas from the dehydrogenation reaction, it was introduced into a separate reaction vessel containing cyclooctene, 5 mol % of $RhCl(PPh_3)_3$, and 3 mL of THF.[14] The later reaction was performed at 60 °C. Analysis of the product from the later reaction indicated a clean formation of cyclooctane (89% conversion by GC), demonstrating in turn H_2 being produced from the dehydrogenation reaction. In addition, the headspace gas analysis by GC unambiguously confirmed the formation of H_2 from the dehydrogenation reaction. In order to test the catalytic activity of the remaining iron species after the first catalytic run, a successive addition experiment was performed with a second batch of substrate **C**. Unfortunately, much lower conversion (~42% by NMR) was observed this time suggesting a significant amount of catalyst degradation after the first run. To test the thermal stability of the iron catalyst, two separate protio-xylene solutions of **1** were heated at 140 °C in the absence and presence of **C** (33 equiv with respect to **1**), and the reaction was monitored by ^{31}P NMR spectroscopy. Interestingly, for the reaction in the presence of **C**, a new pincer iron complex (**3**, located at 110.2 ppm) was found to be the major remaining species after 20 h, whereas the one without any substrate led to complete decomposition within 4 h (see Supporting Information, SI). These results suggest that the thermal decomposition of **1** is greatly suppressed when the substrate is present, but the same iron complex degrades much more rapidly in the absence of any substrate. This accounts for the much lower catalytic activity observed when the substrate was introduced for the second time.

Interestingly, when the dehydrogenation of **C** was performed in the presence of external H_2 (5 atm), a complete loss of catalytic activity was observed. This result suggested to us that perhaps the hydrogenation of unsaturated N-heterocycles[15] could also be performed utilizing the same iron catalysts. Gratifyingly, in the presence of **2** (3 mol %) and KO^{t}Bu (10 mol %), quinaldine (**K**) was quantitatively converted to the reduced product, 1,2,3,4-tetrahydroquinaldine (**C**), with only 5 atm of H_2 pressure in 24 h. THF was used as the solvent in this case, and the reaction was performed at 80 °C. The same reaction was also catalyzed by **1** (3 mol %) in toluene at 110 °C; however a lower conversion (89%) was achieved after the same reaction time. Under the best catalytic conditions, substrates **I**–**O** were successfully hydrogenated (Figure 3) under 5–10 atm of H_2 pressure, and the desired reduced products were obtained with good isolated yields (60–92%). Although most of the substrates (**I**–**M**) could be reduced with 5 atm of H_2, substrates **N** and **O** required higher

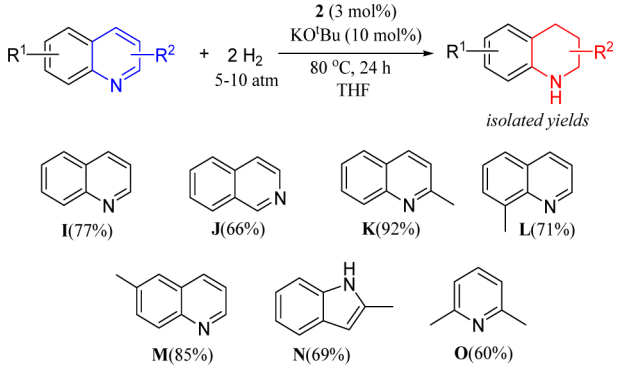
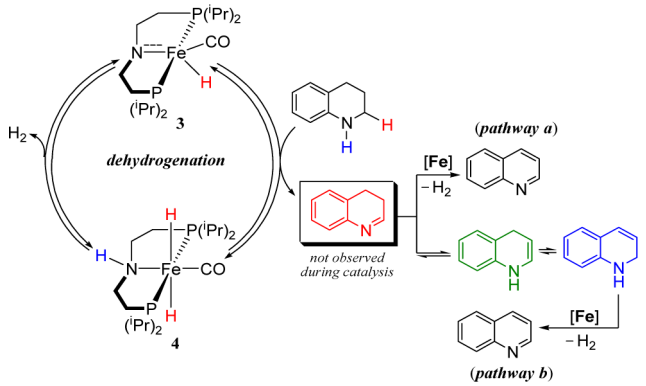


Figure 3. Hydrogenation of unsaturated N-heterocycles. Conditions: **2** (25 μmol), KO^{t}Bu (83 μmol), substrate (0.83 mmol), THF (2 mL). H_2 pressure: 5 atm (for **I**–**M**), 10 atm (for **N** and **O**). Numbers in the parentheses represent isolated yields of the hydrogenated N-heterocycles.

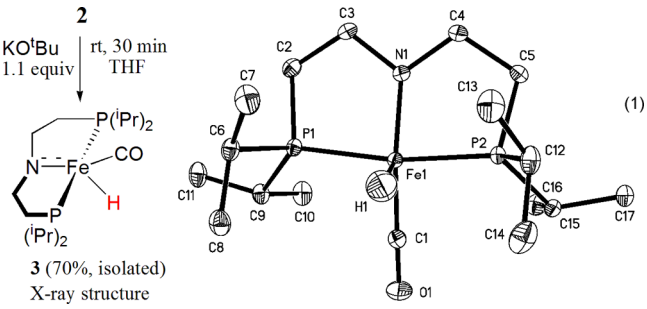
dx.doi.org/10.1021/ja504523b | J. Am. Chem. Soc. 2014, 136, 8564–8567

Scheme 1. Proposed Catalytic Pathway for the Dehydrogenation of N-Heterocycles



hydrogen pressure to fully convert. No products resulting from the over reduction of the aromatic ring were observed.

A proposed catalytic pathway for the dehydrogenation of N-heterocycles is outlined in Scheme 1. A penta-coordinated iron hydride species **3** is postulated to be the active catalytic intermediate in this reaction.[16] To verify its identity and involvement in the catalysis, complex **3** was independently synthesized by a reaction of **2** with KO^{t}Bu (eq 1). This complex

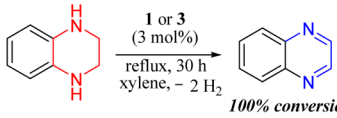


(1)

has been completely characterized by NMR, IR spectroscopy, elemental analysis, and X-ray crystallography. Complex **3** adopts a pseudotrigonal bipyramidal geometry in the solid state. Most noticeably, the Fe–N bond distance in **3** was found to be significantly shorter (1.86 Å) than other related octahedral iron complexes[8−10] (for example, 2.07 Å for **1**).[8]

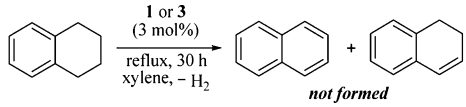
When **3** was used directly as the dehydrogenation catalyst, a very comparable catalytic activity was observed (TON of 33 in 30 h) under the same conditions. This result provides direct evidence that complex **3** is indeed an active intermediate in the dehydrogenation reaction of N-heterocycles.

Next, we examined the catalytic activity of **1** and **3** toward a cyclic secondary amine to probe the amine dehydrogenation step involved in the cycle. Consistent with our mechanistic hypothesis, when 1,2,3,4-tetrahydroquinoxaline was subjected to the catalytic conditions, the oxidized product quinoxaline was formed in quantitative amount (eq 2). In order to release the

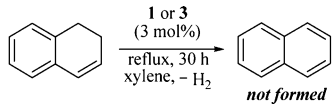


(2)

second equivalent of H_2 from substrate **A**, a C–H bond activation step must occur as no N–H bond remains in 3,4-dihydroquinoline. Two different pathways were considered (Scheme 1) that could lead to the final product: (a) a direct alkane dehydrogenation[17] by iron from the partially oxidized substrate (pathway a) and (b) isomerization of the initially formed C=N to a C=C, followed by the second dehydrogenation from the cyclic secondary amine fragment (pathway b).[4e] To test this hypothesis, we carried out dehydrogenation reactions of the following substrates: (i) 1,2,3,4-tetrahydronaphthalene, (ii) 1,2-dihydronaphthalene, and (iii) 3,4-dihydroisoquinoline. For the first two substrates, no dehydrogenation activity was observed with either **1** or **3** (eqs 3 and 4), suggesting



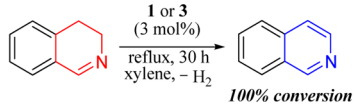
(3)



(4)

the direct alkane dehydrogenation pathway is unlikely to occur in this system. No dehydrogenation activity with 1,2-dihydronaphthalene indicates that having a relatively weak allylic C–H bond (~85 kcal/mol)[18] is not sufficient for the dehydrogenation with our iron catalysts.

However, when 3,4-dihydroisoquinoline was subjected to catalysis, the fully dehydrogenated product, isoquinoline (**J**), was formed as the sole product (eq 5). This result demonstrates that

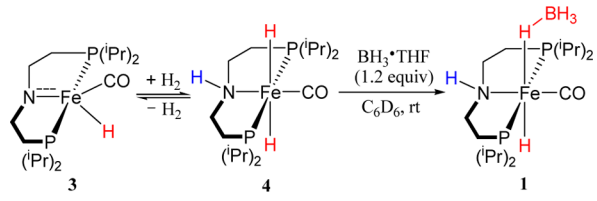


(5)

the presence of the N atom in cycloalkanes is critical for catalysis and also points to the second scenario involving a sequential isomerization-amine dehydrogenation process.

For the hydrogenation reaction, a *trans*-Fe(H)$_2$ species (**4**) is proposed to be the active intermediate. Guan et al. have proposed the same species as the active form of the catalyst in ester hydrogenation.[10] Although we could not isolate this species independently, its existence was supported by NMR spectroscopy and trapping experiments. Treatment of the independently synthesized complex **3** with H_2 (1 atm) generated the *trans*-dihydride intermediate at room temperature (Scheme 2). Compound **4** exhibited a multiplet resonance centered at −9.32 ppm for the two Fe-Hs in the ^{1}H NMR spectrum (see SI). In a separate reaction, it was also shown that the *trans*-dihydride intermediate readily loses H_2 under vacuum and is converted to **3**. These results are consistent with Guan's observation on the reactivity of the *in situ* formed complex **3**.[10] Nevertheless, complex **4** was trapped (Scheme 2) in the presence of a stoichiometric amount of BH_3·THF to form the iron hydrido-borohydride complex (**1**). As complex **4** could be

Scheme 2. NMR and Trapping Experiments to Support the Formation of the *trans*-Dihydride Intermediate



dx.doi.org/10.1021/ja504523b | J. Am. Chem. Soc. 2014, 136, 8564–8567

directly generated from **3** under H_2 pressure, we successfully carried out hydrogenation of quinaldine (**K**) using a catalytic amount of **3** (3 mol %). Therefore, complex **3** serves as the single molecular iron complex that can catalyze both dehydrogenation and hydrogenation of N-heterocycles. To the best of our knowledge, there is no report of a single first-row transition-metal-based catalyst capable of performing both of the reactions.

In summary, we have demonstrated reversible dehydrogenation−hydrogenation of N-heterocycles with earth-abundant iron-based molecular catalysts. Products from both the dehydrogenation and hydrogenation reactions were isolated in good yields. The penta-coordinated iron hydride species **3**, the proposed dehydrogenation intermediate, was isolated by an independent route, and its direct involvement in the catalysis was demonstrated. Substrate-driven mechanistic studies support the initial amine-dehydrogenation step and provide evidence against direct alkane dehydrogenation from the partially oxidized N-heterocycles. The presence of the N atom seems to be critical for a successful catalytic dehydrogenation. On the other hand, a *trans*-dihydride species (**4**) was invoked as the active catalyst for the hydrogenation of N-heterocycles. NMR and trapping experiments support the formation of such a species.

■ ASSOCIATED CONTENT

Supporting Information

Experimental details, characterization data, and X-ray crystallographic data for **3** (CCDC#1001232) are included. This material is free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

jones@chem.rochester.edu

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was funded by the Center for Electrocatalysis, Transport Phenomena, and Materials (CETM) for Innovative Energy Storage, an Energy Frontier Research Center funded by the U.S. Department of Energy, and the ESD NYSTAR program. S.C. thanks James Kovach (University of Rochester) for helpful discussion on the dehydrogenation mechanism.

■ REFERENCES

(1) (a) Eberle, U.; Felderhoff, M.; Schüth, F. *Angew. Chem., Int. Ed.* **2009**, *48*, 6608. (b) Sartbaeva, A.; Kuznetsov, V. L.; Wells, S. A.; Edwards, P. P. *Energy Environ. Sci.* **2008**, *1*, 79. (c) Makowski, P.; Thomas, A.; Kuhn, P.; Goettmann, P. *Energy Environ. Sci.* **2009**, *2*, 480. (d) Teichmann, D.; Arlt, W.; Wasserscheid, P.; Freymann, R. *Energy Environ. Sci.* **2011**, *4*, 2767. (e) Armaroli, N.; Balzani, V. *ChemSusChem* **2011**, *4*, 21. (f) Fukuzumi, S.; Suenobu, T. *Dalton Trans.* **2013**, *42*, 18.

(2) (a) Crabtree, R. H. *Energy Environ. Sci.* **2008**, *1*, 134 and references cited therein. (b) Jessop, P. *Nat. Chem.* **2009**, *1*, 350 and references cited therein. (c) Watson, L. A.; Eisenstein, O. J. *J. Chem. Educ.* **2002**, *79*, 1269.

(3) (a) Adkins, H.; Lundsted, L. G. *J. Am. Chem. Soc.* **1949**, *71*, 2964. (b) Lu, S. M.; Wang, Y. Q.; Han, X. W.; Zhou, Y. G. *Chin. J. Catal.* **2005**, *26*, 287. (c) Wang, Z.; Tonks, I.; Belli, J.; Jensen, C. M. *J. Organomet. Chem.* **2009**, *694*, 2854. (d) Mikami, K.; Ebata, K.; Mistudome, T.; Mizugaki, T.; Jitsukawa, K.; Kaneda, K. *Heterocycles* **2011**, *82*, 1371. (e) Sotoodeha, F.; Huberb, B. J. M.; Smith, K. J. *Appl. Catal., A* **2012**, *420*, 67.

(4) For homogeneous dehydrogenation and hydrogenation of tetrahydroquinolines and quinolines: (a) Yamaguchi, R.; Ikeda, C.; Takahashi, T.; Fujita, K.-I. *J. Am. Chem. Soc.* **2009**, *131*, 8410. (b) Li, H.; Jiang, J.; Lu, G.; Huang, F.; Wang, Z.-X. *Organometallics* **2011**, *30*, 3131. (c) Zhang, X.-B.; Xi, Z. *Phys. Chem., Chem. Phys.* **2011**, *13*, 3997. (d) Wu, J.; Talwar, D.; Johnston, S.; Yan, M.; Xiao, J. *Angew. Chem., Int. Ed.* **2013**, *52*, 6983. (e) Luca, O.; Huang, D. L.; Takase, M. K.; Crabtree, R. H. *New J. Chem.* **2013**, *37*, 3402.

(5) For catalytic dehydrogenation of other N-heterocycles: (a) Tsuji, Y.; Kotachi, S.; Huh, K. T.; Watanabe, Y. *J. Org. Chem.* **1990**, *55*, 580. (b) Hara, T.; Mori, K.; Mizugaki, T.; Ebitani, K.; Kaneda, K. *Tetrahedron Lett.* **2003**, *44*, 6207. (c) Dean, D.; Davis, B.; Jessop, P. G. *New J. Chem.* **2011**, *35*, 417.

(6) Fujita, K.-I.; Tanaka, Y.; Kobayashi, M.; Yamaguchi, R. *J. Am. Chem. Soc.* **2014**, *136*, 4829.

(7) For iron-based catalysts in hydrogenation and dehydrogenation: (a) *Iron Catalysis in Organic Chemistry: Reactions and Applications*; Plietker, B., Ed.; Wiley-VCH: Weinheim, 2008. (b) Nakazawa, H.; Itazaki, M. *Top. Organomet. Chem.* **2011**, *33*, 27 and references therein. (c) Darwish, M.; Wills, M. *Catal. Sci. Technol.* **2012**, *2*, 243 and references therein. (d) Morris, R. H. *Chem. Soc. Rev.* **2009**, *38*, 2282 and references therein.

(8) Alberico, E.; Sponholz, P.; Cordes, C.; Nielsen, M.; Drexler, H.-J.; Baumann, W.; Junge, H.; Beller, M. *Angew. Chem., Int. Ed.* **2013**, *52*, 14162.

(9) Koehne, I.; Schmeier, T. J.; Bielinski, E. A.; Pan, J. C.; Lagaditis, P. O.; Bernskoetter, W. H.; Takase, M. K.; Wurtle, C.; Hazari, N.; Schneider, S. *Inorg. Chem.* **2014**, *53*, 2133.

(10) Chakraborty, S.; Dai. H.; Bhattacharya, P.; Fairweather, N. T.; Gibson, M. S.; Krause, J. A.; Guan, H. *J. Am. Chem. Soc.* **2014**, *136*, ASAP, DOI: 10.1021/ja504034q. Provisional U.S. patent application with a serial number of 61/972927, 2014.

(11) Yamaguchi et al. have reported similar sharp increase in yields when they switched the solvent from toluene to *p*-xylene. See ref 4a.

(12) (a) Widegren, J. A.; Finke, R. G. *J. Mol. Catal. A: Chem.* **2003**, *198*, 317. (b) Crabtree, R. H. *Chem. Rev.* **2012**, *112*, 1536. It should be noted that Hg(l) does not always inhibit iron nanoparticle catalysts. See: (c) Sonnenberg, J. F.; Coombs, N.; Dube, P. A.; Morris, R. H. *J. Am. Chem. Soc.* **2012**, *134*, 5893−5899. (d) Bedford, R. B.; Betham, M.; Bruce, D. W.; Davis, S. A.; Frost, R. M.; Hird, M. *Chem. Commun.* **2006**, 1398. (e) Rangheard, C.; Fernández, C. J.; Phua, P.-H.; Hoorn, J.; Lefort, L.; de Vries, J. G. *Dalton Trans.* **2010**, *39*, 8464.

(13) When 5 mol% of free PNP ligand was added with 1 mol% of catalyst **1** (conditions of entry 5 in Table 1), 92% conversion of tetrahydroquinaldine was observed after 30 h. Without the added free ligand, only 34% conversion was achieved after 30 h under these conditions. If iron nanoparticles are being generated, one would not expect to see such a significant difference between these two experiments. Furthermore, a PMe_3 poisoning experiment was not conducted as complex **1** itself decomposed in the presence of excess of PMe_3, and therefore, the result from this experiment would be inconclusive.

(14) Yamaguchi et al. reported similar dual experiments in their studies. See refs 4a and 6.

(15) For hydrogenation of N-heterocycles: (a) Dobereiner, G. E.; Nova, A.; Schley, N. D.; Hazari, N.; Miller, S. J.; Eisenstein, O.; Crabtree, R. H. *J. Am. Chem. Soc.* **2011**, *133*, 7547 and references cited therein. (b) Wu, J.; Barnard, J. H.; Zhang, Y.; Talwar, D.; Robertson, C. M.; Xiao, J. *Chem. Commun.* **2013**, *49*, 7052 and references cited therein. For hydrogenation of imines: Lagaditis, P. O.; Sues, P. E.; Sonnenberg, J. F.; Wan, K. Y.; Lough, A. J.; Morris, R. H. *J. Am. Chem. Soc.* **2014**, *136*, 1367.

(16) Complex **3** was also proposed to be the active catalytic intermediate in Beller's methanol dehydrogenation chemistry (see ref 7), but no experimental evidence was provided.

(17) For a comprehensive review on alkane dehydrogenation: Choi, J.; MacArthur, A. H. R.; Brookhart, M.; Goldman, A. S. *Chem. Rev.* **2011**, *111*, 1761.

(18) Kerr, J. A. *Chem. Rev.* **1966**, *66*, 465.