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

Bis(imino)pyridine Cobalt-Catalyzed Alkene Isomerization–Hydroboration: A Strategy for Remote Hydrofunctionalization with Terminal Selectivity

Jennifer V. Obligacion and Paul J. Chirik*

Department of Chemistry, Princeton University, Princeton, New Jersey 08544, United States

Supporting Information

ABSTRACT: Bis(imino)pyridine cobalt methyl complexes are active for the catalytic hydroboration of terminal, geminal, disubstituted internal, tri- and tetrasubstituted alkenes using pinacolborane (HBPin). The most active cobalt catalyst was obtained by introducing a pyrrolidinyl substituent into the 4-position of the bis(imino)pyridine chelate, enabling the facile hydroboration of sterically hindered substrates such as 1-methylcyclohexene, α-pinene, and 2,3-dimethyl-2-butene. Notably, these hydroboration reactions proceed with high activity and anti-Markovnikov selectivity in neat substrates at 23 °C. With internal olefins, the cobalt catalyst places the boron substituent exclusively at the terminal positions of an alkyl chain, providing a convenient method for hydrofunctionalization of remote C–H bonds.

The diverse and rich reaction chemistry associated with organoboron compounds inspires the discovery of efficient methods for their synthesis.[1] Transition metal-catalyzed alkene hydroboration, first described with Wilkinson's complex, $(Ph_3P)_3RhCl$,[2] has emerged as a versatile method for the preparation of alkylboronic esters and in some cases offers high chemo-, regio-, diastereo-, and enantioselectivity.[3] Group 4 metallocenes[4] and precious metal compounds[5] are the most well-studied catalysts for alkene hydroboration. Base metal catalysts, particularly those containing iron and cobalt, are attractive given the potential cost and environmental advantages associated with first-row transition metals.[6] Catalysis with these metals also offers the opportunity to discover new reactivity and overcome some of the limitations observed with established precious metal compounds.[7]

Ritter and co-workers reported a seminal example of iron-catalyzed hydroboration with the selective 1,4-addition of pinacolborane (HBPin) to conjugated dienes using an (imino)pyridine iron precatalyst activated with 2.5 equiv of Mg per iron.[8] Huang subsequently reported in situ activation of iron(II) halide complexes with $NaBEt_3H$ for the hydroboration of unactivated terminal olefins with HBPin.[9] Among these, an aryl-substituted bis(imino)pyridine[10] and Milstein's bipyridylphosphine ligand[11] provided improved activity and anti-Markovnikov selectivity over known precious metal catalysts. These catalyst mixtures required an excess of the alkene and were inactive for the hydroboration of internal olefins such as *trans*-3-octene and cyclooctene. Shortly thereafter, our laboratory reported that isolated bis(imino)pyridine iron dinitrogen complexes, such as $(^{iPr}PDI)Fe(N_2)_2$ and $[(^{Mes}PDI)Fe(N_2)]_2(\mu_2\text{-}N_2)$, are also excellent alkene hydroboration catalysts.[12] Notably, these reactions required no solvent or excess alkene. These iron catalysts provide exclusive anti-Markovnikov selectivity for the hydroboration of styrene, a challenging substrate for most precious metal catalysts.[3] Greenhalgh and Thomas have since described in situ activation of $(^{Et}PDI)FeCl_2$ with Grignard and alkyllithium reagents for the hydroboration of alkynes and terminal alkenes.[13] Haberberger and Enthaler have also reported iron-catalyzed alkyne hydroboration with HBPin upon thermal activation of $Fe_2(CO)_9$.[14]

Although the isolated bis(imino)pyridine iron dinitrogen complexes offer distinct advantages in selectivity and substrate scope, the challenge associated with preparing these compounds may detract from their ease of use. The in situ activation methods reported by Huang and later Thomas allow use of more easily accessed iron precursors but limits substrate scope and catalyst performance. By contrast, bis(imino)pyridine cobalt alkyl complexes, (PDI)CoR, are relatively straightforward to prepare, and significantly more examples are known than for the corresponding reduced iron compounds.[15] Previous studies from Gal and co-workers[16] and our laboratory[17] have demonstrated the utility of these compounds in alkene hydrogenation, inspiring investigation of their hydroboration activity. Cobalt-catalyzed alkene hydroboration remains rare. Zaidlewicz and Meller reported that bis(phosphine) cobalt(II) halide complexes produced modest (20–30%) yields for the hydroboration of 1-octene with catecholborane.[18] Complete conversion of isoprene was also observed with competing 1,2- and 1,4-addition under similar catalytic conditions.[19] Here we describe the catalytic, anti-Markovnikov selective hydroboration of sterically hindered, unactivated olefins with bis(imino)pyridine cobalt methyl complexes. With internal olefins, the boron fragment is placed exclusively at the terminus of the alkyl chain offering a convenient, base metal-catalyzed method for the remote hydrofunctionalization of unactivated C–H bonds.

Two bis(imino)pyridine cobalt methyl complexes, $(^{iPr}PDI)CoCH_3$ (**1**) and $(^{Mes}PDI)CoCH_3$ (**2**) (Figure 1), were initially evaluated. Standard conditions employed 1 mol% of the cobalt precursor in a neat, equimolar mixture of the alkene and HBPin. Each reaction was conducted at 23 °C, and the alkylboronic esters were identified by a combination of GC-MS,

Received: October 25, 2013
Published: December 13, 2013

dx.doi.org/10.1021/ja4108148 | J. Am. Chem. Soc. 2013, 135, 19107–19110

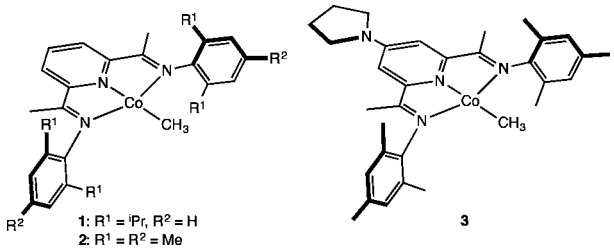
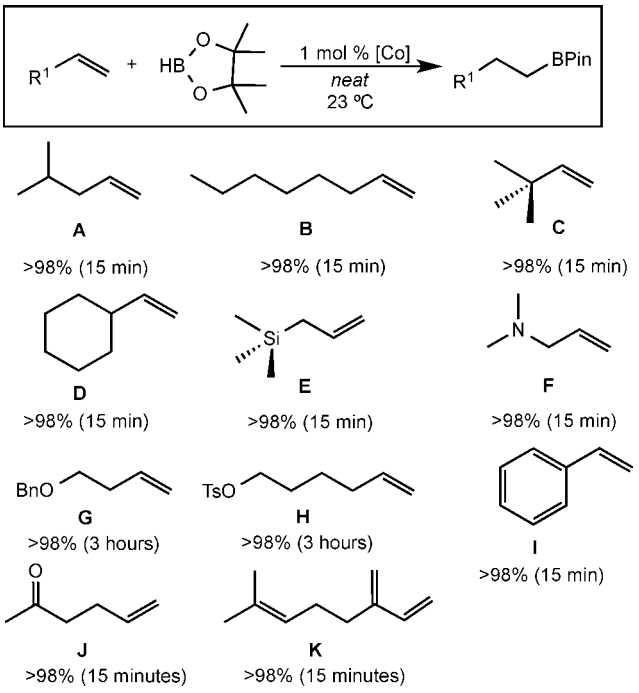


Figure 1. Bis(imino)pyridine cobalt methyl complexes used as precatalysts for alkene hydroboration.

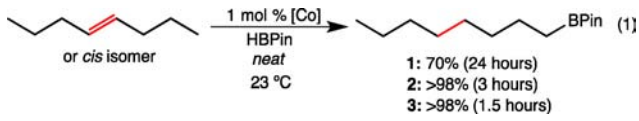
Scheme 1. Bis(imino)pyridine Cobalt-Catalyzed Hydroboration of Terminal Olefins with HBPin with 1 and 2[a]



[a]The reported times are the same for both cobalt precursors.

^{1}H NMR, and ^{13}C NMR spectroscopies. Both cobalt compounds were effective for the anti-Markovnikov hydroboration of terminal olefins (Scheme 1).[9,12] Styrene (**I**) was rapidly (15 min) and exclusively converted to the terminal borane with no evidence for side products. For this class of substrates, the activity of the bis(imino)pyridine cobalt complexes is indistinguishable from that of the related iron dinitrogen compounds with the notable exception that cobalt derivative **2** maintains exclusive anti-Markovnikov selectivity for the hydroboration of styrene while $[(^{Mes}PDI)Fe(N_2)]_2(\mu_2\text{-}N_2)$ produces a mixture of products.[12] Myrcene (**K**) also underwent exclusive 1,2-hydroboration while hex-5-en-2-one (**J**) participated in predominantly C=C reduction.

The high activity and selectivity observed with terminal olefins prompted investigation of the hydroboration of more hindered alkenes. With **1**, α-methylstyrene reached 63% conversion in 24 h; >98% conversion was obtained in 15 min with **2**, an improvement over the most active bis(imino)-pyridine iron catalyst.[12] The hydroboration of *cis*- or *trans*-4-octene with **1** produced 70% conversion to the 1-octylboronic ester, a result of a net isomerization−hydroboration sequence that was selective for terminal functionalization (eq 1). Using the less hindered cobalt precursor, **2**, complete conversion to



the terminally functionalized product was observed in 3 h. Such a sequence involving *trans*-4-octene and HBPin was previously reported for rhodium with varied success[5,20,21] and was eventually traced to partially oxidized Wilkinson's complex.[22] Improved methods have appeared and include Rh catalysis in combination with Lewis acids,[23] microwave irradiation of Wilkinson's complex,[20] and use of $[Ir(COD)Cl]_2$ in combination with dppm ($Ph_2PCH_2PPh_2$).[5]

The cobalt-catalyzed tandem isomerization−hydroboration sequence was extended to more hindered tri- or tetrasubstituted alkenes such as α-pinene or 2,3-dimethyl-2-butene. With both **1** and **2**, <5% conversion to the desired alkylboranes was observed after prolonged reaction times. To overcome this challenge, the 4-pyrrolidinyl-substituted bis(imino)pyridine cobalt methyl complex, (4-pyrr-^{Mes}PDI)$CoCH_3$ (**3**, Figure 1), was prepared. This ligand modification was inspired by observations from iron catalyzed olefin hydrogenation[24] and hydrosilylation,[25] where introduction of electron-donating substituents into the 4-position of the pyridine ring in the bis(imino)pyridine chelate generated more active catalysts. The hydroboration−isomerization of *trans*-4-octene in the presence of 1 mol% of **3** reached >98% conversion to the terminal alkylboronic ester in 1.5 h in neat solution at 23 °C, establishing the improved performance associated with this cobalt precatalyst.

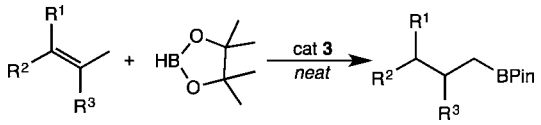
Using **3**, the isomerization−hydroboration of more sterically hindered olefins was evaluated. Results of these experiments are reported in Table 1. Trisubstituted alkenes bearing linear or branched alkyl substituents (entries 1 and 2) yielded the terminal alkylboronic ester over the course of 24 h in the presence of 1 mol% of the cobalt precursor, **3**. The methodology was also extended to include 2,3-dimethyl-2-butene (entry 3). At 50 °C, complete conversion to the terminal alkylborane was obtained. Introduction of the borane fragment of the remote methyl group demonstrates that the bis(imino)pyridine cobalt complex can access tertiary alkyl intermediates and "chain walk" to the preferred terminal position. By comparison, rhodium-phosphine catalysts reported by Baker and co-workers place the boron substituent at the 2-position of the alkyl chain.[26]

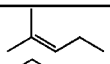
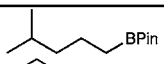
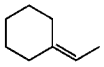
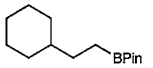
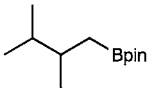
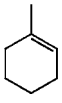
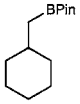
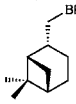
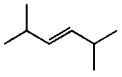
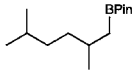
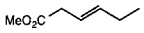
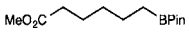
Endocyclic trisubstituted alkenes were also studied, as these substrates are challenging for known precious and base metal alkene hydroboration catalysts. Both 1-methylcyclohexene (entry 4) and α-pinene (entry 5) underwent bis(imino)-pyridine cobalt-catalyzed hydroboration to the terminal alkylboronic esters. Although diminished conversion and isolated yields were obtained at 23 °C, heating the catalytic reactions to 50 °C improved both conversions and isolated yields. The tandem cobalt-catalyzed isomerization−hydroboration sequence provides a convenient strategy for the selective hydrofunctionalization of remote, primary C−H bonds using readily available alkene substrates.

Alternative methods for selective hydrofunctionalization of primary C−H bonds in terminal alkenes have been reported using triple relay precious metal catalysts[27] and a dual precious

dx.doi.org/10.1021/ja4108148 | J. Am. Chem. Soc. 2013, 135, 19107−19110

Table 1. Hydroboration of Hindered Alkenes with 3



	Substrate	Product	T (°C)	% Conversion[a]
1			23[b]	>98 (75)
2			23[b]	>98 (74)
3			50[c]	>98 (55)
4			50[c]	70 (55)[e]
5			50[c]	>98 (67) (dr = 62:38)[f]
6			23[d]	>98
7			23[b]	88[g]

[a]Based on gas chromatography. Values in parentheses are isolated yields. [b]1 mol% **3** for 24 h. [c]5 mol% **3** for 72 h. [d]1 mol% for 72 h. [e]7% hydroboration of secondary positions observed. [f]Determined by oxidation with 30% H_2O_2 to the corresponding alcohol and analysis by quantitative ^{13}C NMR. [g]70% of the product is terminal alkylboranic ester; 30% alkene isomers.

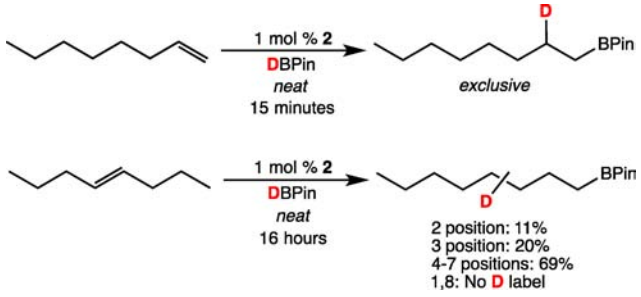
metal hydroformylation–hydrogenation sequence.[28] Palladium-catalyzed methods for the conversion of internal alkenes to internal ketones are also known.[29,30]

The hydroboration of 2,5-dimethyl-*trans*-3-hexene was also studied (entry 6). This substrate was of interest due the presence of a "blocked" alkene that would evaluate the ability of the cobalt catalyst to walk past tertiary carbon centers to reach the methyl positions. Performing the hydroboration with 1 mol % of **3** under neat conditions resulted in complete consumption of the alkene after 72 h and furnished the terminally functionalized compound as the major product. Minor byproducts from alkene hydrogenation (8%), dehydrogenative borylation (8%), and hydroboration in the 3-position of the chain (4%) were also observed. An increased purity of 92% was obtained when the reaction was performed in THF or toluene solution. Ester functionality (entry 7) was also tolerated, as the terminal alkylborane was identified as 70% of the product mixture. With α,β unsaturated ketones such as hex-4-en-3-one and 3-methylcyclohex-2-enone, predominant carbonyl reduction was observed (see SI).

Additional experiments were conducted with **2** to gain insight into the mechanism of turnover. No reaction was observed upon addition of 1-octene to a benzene-d_6 solution of **2**, establishing the role of HBPin in catalyst activation. Accordingly, treatment of a benzene-d_6 solution of (^{Mes}PDI)-$CoCH_2CH_3$[31] with HBPin under a dinitrogen atmosphere resulted in immediate formation of (^{Mes}PDI)CoN_2 along with CH_3CH_2BPin. The bis(imino)pyridine cobalt ethyl complex was selected to facilitate characterization of the organic products. We also note that it is well-established[32] that bis(imino)pyridine cobalt hydride complexes readily convert to the corresponding dinitrogen compounds with loss of H_2 under an N_2 atmosphere implicating formation of (^{Mes}PDI)-CoH following treatment with HBPin.

Cobalt-catalyzed deuterioboration experiments were also conducted with DBPin. The deuterated borane was readily synthesized by exposure of neat HBPin to 4 atm of D_2 for 24 h with 1 mol% of **2**. Stirring a neat mixture of 1-octene and DBPin in the presence of 1 mol% of **2** for 15 min at 23 °C exclusively furnished the 1-octylboronate ester with the deuterium located solely in the 2-position of the product as determined by ^2H and ^{13}C NMR spectroscopies (Scheme 2).

Scheme 2. Catalytic Hydroboration of 1- and 4-Octene with DBPin in the Presence of 2



Repeating the deuterium labeling experiment with 4-octene as the substrate and analysis of the product mixture by ^2H NMR spectroscopies established a majority of the isotopic label in the interior (4–7) positions of the octyl chain in the alkylboronic ester. Detectable amounts of deuterium were also located in the 2 (11%) and 3 (20%) positions. Notably, no deuterium was detected at either terminus (1 or 8 positions) of the chain.

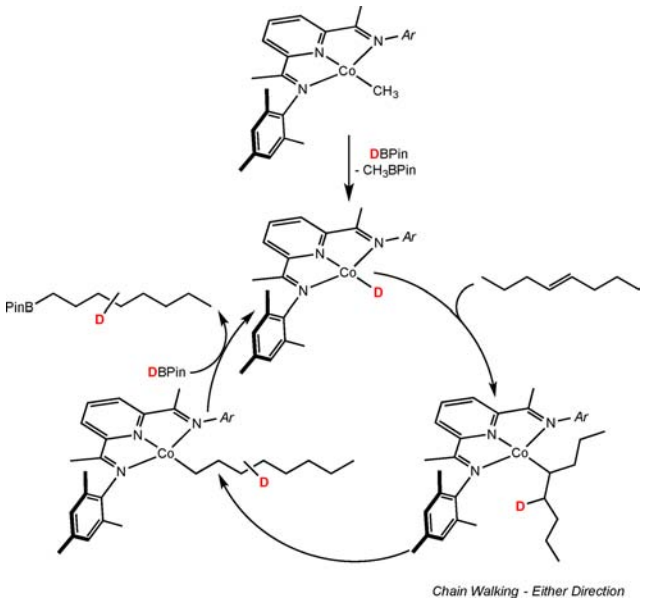
Based on these observations, a mechanism for bis(imino)-pyridine cobalt-catalyzed alkene hydroboration is proposed (Scheme 3). An example with DBPin and *trans*-4-octene is provided to illustrate the observed chain walking process. Entry into the catalytic cycle proceeds by reaction of the bis(imino)-pyridine cobalt methyl complex with DBPin to liberate the alkylboric ester and generate a bis(imino)pyridine cobalt deuteride. In the case of α-olefins (not shown), 1,2-insertion is likely facile[16] with no competition from β-H elimination and chain walking. Subsequent reaction with DBPin, either via σ-bond metathesis or oxidative addition-reductive elimination furnishes the observed alkylboronic ester with the isotopic label exclusively in the 2-position of the product.

For internal alkenes, insertion into the bis(imino)pyridine cobalt deuteride yields a secondary cobalt alkyl which undergoes a sequence of rapid β-hydrogen elimination–olefin reinsertion steps that account for observed scrambling of the isotopic label en route to selective formation of the terminal octylboronic ester. We note that interception of the secondary cobalt alkyl intermediates with HBPin is not competitive with alkyl isomerization, as no secondary products were observed. Once the cobalt reaches the end of the octyl chain, reaction with the borane liberates the observed product. Thus for internal olefins, it is likely that the net isomerization sequence is the turnover limiting step in the catalytic cycle.

In summary, aryl-substituted bis(imino)pyridine cobalt methyl complexes are effective precatalysts for the hydroboration of alkenes with pinacolborane. The base metal catalysts offer improved activity and unique selectivity over

dx.doi.org/10.1021/ja4108148 | J. Am. Chem. Soc. 2013, 135, 19107–19110

Scheme 3. Proposed Mechanism for Bis(imino)pyridine Cobalt-Catalyzed Alkene Hydroboration with DBPin Accounting for the Observed Preference for Terminal Selectivity



precious metal catalysts for hindered tri- and tetrasubstituted olefins and proceed rapidly in the absence of organic solvent. For internal olefins, isomerization to the terminal position of the alkyl chain is observed providing a convenient method for the selective hydrofunctionalization of remote C−H bonds.

■ ASSOCIATED CONTENT

Supporting Information

Complete experimental details, characterization data of hydroboration products, and crystallographic data for **3** in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

pchirik@princeton.edu

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank Princeton University for financial support, Iraklis Pappas for solving the X-ray structure of **3**, and Dr. Crisita Atienza for experimental assistance and suggestions.

■ REFERENCES

(1) (a) Brown, H. C. *Organic Synthesis via Organoboranes*; Wiley Interscience: New York, 1975. (b) Mikhailov, B. M.; Bubnov, Y. N. *Organoboron Compounds in Organic Synthesis*; Harwood Academic: Amsterdam, 1983. (c) Hartwig, J. F. *Acc. Chem. Res.* **2012**, *45*, 864.
(2) Männing, D.; Nöth, H. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 878.
(3) (a) Burgess, K.; Ohlmeyer, M. J. *Chem. Rev.* **1991**, *91*, 1179. (b) Miyaura, N. In *Catalytic Heterofunctionalization—From Hydroboration to Hydrozirconation*; Togni, A., Grützmacher, H., Eds.; Wiley-VCH Verlang: Weinheim, 2001. (c) Crudden, C. M.; Edwards, D. *Eur. J. Org. Chem.* **2003**, 4695. (d) Thomas, S. P.; Aggarwal, V. K. *Angew. Chem., Int. Ed.* **2009**, *48*, 1896.
(4) (a) Xe, H.; Hartwig, J. F. *J. Am. Chem. Soc.* **1996**, *118*, 1696. (b) Hartwig, J. F.; Muhoro, C. N. *Organometallics* **2000**, *19*, 30.
(5) Yamamoto, Y.; Fujikawa, R.; Umemoto, T.; Miyaura, N. *Tetrahedron* **2004**, *60*, 10695 and references therein.
(6) (a) Sherry, B. D.; Fürstner, A. *Acc. Chem. Res.* **2008**, *41*, 1500. (b) Chirik, P. J. *Catalysis Without Precious Metals*; Bullock, R. M., Ed.; Wiley-VCH: Weinheim, 2010; pp 83−110. (c) Junge, K.; Schroder, M.; Beller, M. *Chem. Commun.* **2011**, *47*, 4849. (d) Morris, R. H. *Chem. Soc. Rev.* **2009**, *38*, 2282. (e) Nakazawa, H.; Itazaki, M. *Top. Organomet. Chem.* **2011**, *33*, 27.
(7) Chirik, P. J.; Wieghardt, K. W. *Science* **2010**, *327*, 794.
(8) Wu, J. Y.; Moreau, B.; Ritter, T. *J. Am. Chem. Soc.* **2009**, *131*, 12915.
(9) Zhang, L.; Peng, D.; Leng, X.; Huang, Z. *Angew. Chem., Int. Ed.* **2013**, *52*, 3676.
(10) Gibson, V. C.; Redshaw, C.; Solan, G. A. *Chem. Rev.* **2007**, *107*, 1745.
(11) Balaraman, E.; Gnanaprakasm, B.; Shimon, L. J. W.; Milstein, D. *J. Am. Chem. Soc.* **2010**, *132*, 16756.
(12) Obligacion, J. V.; Chirik, P. J. *Org. Lett.* **2013**, *15*, 2680.
(13) Greenhalgh, M. D.; Thomas, S. P. *Chem. Commun.* **2013**, *49*, 11230.
(14) Haberberger, M.; Enthaler, S. *Chem. Asian J.* **2013**, *8*, 50.
(15) Gibson, V. C.; Humphries, M. J.; Tellmann, K. P.; Wass, D. F.; White, A. J. P.; Williams, D. J. *Chem. Commun.* **2001**, 2252.
(16) Knijnenburg, Q.; Horton, A. D.; van der Heijden, H.; Kooistra, T. M.; Hetterscheid, D. G. H.; Smits, J. M. M.; de Bruin, B.; Budzelaar, P. H. M.; Gal, A. W. *J. Mol. Catal.* **2005**, *232*, 151.
(17) Monfette, S.; Turner, Z. R.; Semproni, S. P.; Chirik, P. J. *J. Am. Chem. Soc.* **2012**, *134*, 4561.
(18) Zaidlewicz, M.; Meller, J. *Tetrahedron Lett.* **1997**, *38*, 7279.
(19) Zaidlewicz, M.; Meller, J. *J. Main Group Metal Chem.* **2000**, *23*, 765.
(20) Srebnik, M.; Pereira, S. *J. Am. Chem. Soc.* **1996**, *118*, 909.
(21) Tucker, C. E.; Davidson, J.; Knochel, P. *J. Org. Chem.* **1992**, *57*, 3482.
(22) Hadebe, S. W.; Robinson, R. S. *Tetrahedron Lett.* **2006**, *47*, 1299.
(23) Lata, C. J.; Crudden, C. M. *J. Am. Chem. Soc.* **2010**, *132*, 131.
(24) Yu, R. P.; Darmon, J. M.; Hoyt, J. M.; Margulieux, G. W.; Turner, Z. R.; Chirik, P. J. *ACS Catal.* **2012**, *2*, 1760.
(25) Atienza, C. C. H.; Tondreau, A. M.; Weller, K. J.; Lewis, K. M.; Cruse, R. W.; Nye, S. A.; Boyer, J. L.; Delis, J. G. P.; Chirik, P. J. *ACS Catal.* **2012**, *2*, 2169.
(26) Westcott, S. A.; Blom, H. P.; Marder, T. B.; Baker, R. T. *J. Am. Chem. Soc.* **1992**, *114*, 8863.
(27) Dong, G.; Teo, P.; Wickens, Z. K.; Grubbs, R. H. *Science* **2011**, *333*, 1609.
(28) Takahashi, K.; Yamashita, M.; Nozaki, K. *J. Am. Chem. Soc.* **2012**, *134*, 18746.
(29) Mitsudome, T.; Mizumoto, K.; Mizugaki, T.; Jitsukawa, K.; Kaneda, K. *Angew. Chem., Int. Ed.* **2010**, *49*, 1238.
(30) Morandi, B.; Wickens, Z. K.; Grubbs, R. H. *Angew. Chem., Int. Ed.* **2013**, *52*, 2944.
(31) Tellmann, K. P.; Humphries, M. J.; Rzepa, H. S.; Gibson, V. C. *Organometallics* **2004**, *23*, 5503.
(32) Bowman, A. C.; Milsmann, C.; Atienza, C. C. H.; Lobkovsky, E.; Wieghardt, K.; Chirik, P. J. *J. Am. Chem. Soc.* **2010**, *132*, 1676.