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[Ir(cod)$_2$]BARF-Catalyzed C−H Bond Alkenylation and Alkylation of Ferrocenes

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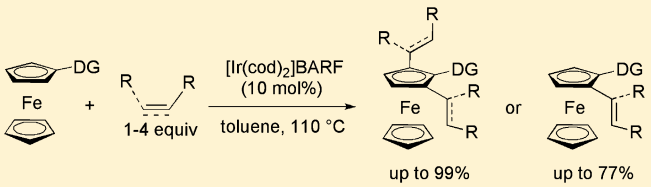
Supporting Information

ABSTRACT: [Ir(cod)$_2$]BARF [BARF = tetrakis(3,5-trifluoromethylphenyl)borate] catalyzed the directed alkenylation and alkylation of ferrocenes to form a variety of tri- and disubstituted ferrocenes. Mechanistic investigation revealed several putative intermediates along with the importance of COD (1,5-cyclooctadiene), as a diene ligand, and a possible catalyst deactivation pathway. On the basis of the mechanistic investigation, catalytic activity was further improved.



Ferrocene and its derivatives are among the most versatile organometallic compounds because of their unique structures, chemical and thermal stabilities, and redox properties.[1] These redox properties have found widespread application in fields such as material science and medicinal research.[2] Recent applications include use in nonvolatile organic memory,[3a] as an electrolyte for dye-sensitized solar cells,[3b] and as a reversible luminescence switch.[3c] Further, planar chiral ferrocenyl ligands are among the most successful chiral ligands in both academia and industry.[4] Ferrocene and its derivatives are usually functionalized using stoichiometric methods, such as electrophilic substitution, or lithiation of the cyclopentadienyl (Cp) ring(s);[1,4] however, these methods suffer from poor atom economy.

Functionalizations via transition-metal-catalyzed C−H activation of the Cp ring(s) are potentially more atom-efficient alternatives. However, only a few catalytic C−H activation reactions of ferrocenes have been reported to date.[5] Schmalz et al. reported the first catalytic C−H activation of ferrocenes using a Cu-catalyzed intramolecular carbene insertion into a Cp−H bond.[5a] However, this method is limited in terms of scope of substrates due to its intramolecular nature. Ir(I)-catalyzed C−H borylation of ferrocenes was also utilized for functionalizing ferrocenes, albeit with problematic regioselectivity.[5b] More recently, oxazoline-directed arylation of ferrocenes was reported using a Pd(II) complex. Most of the reactions in this report are, however, stoichiometric, and the yields of the catalytic reactions were generally low.[5c] There are a number of reports on stoichiometric directed C−H activation of ferrocenes via electrophilic substitution of electron-rich Cp ring(s).[6] In contrast, reports on stoichiometric directed C−H activation of ferrocenes via oxidative addition are scarce.[7]

We recently reported that a series of cationic [Ir(cod)$_2$]X (X = OTf, BF$_4$, BARF) complexes, combined with diphosphine, catalyzed the directed C−H activation of sp^2 C−H bonds.[8] Further, we reported that these catalysts could activate sp^3 C−H bonds.[9] With these highly active cationic Ir catalysts in hand, we report the first catalytic directed alkenylation and alkylation of ferrocenes.

Table 1 summarizes the result of catalyst screening using 2-ferrocenylpyridine (**1a**) and 2 equiv of diphenylacetylene (**2a**). Under the reaction conditions used for the activation of sp^3 C−H bonds,[9] disubstituted ferrocene **3a** formed in low yield due to the low conversion of **1a** (entry 1). Use of electron-rich or -poor phosphines did not significantly improve catalyst activity (entries 2 and 3). Unexpectedly, when conducted in the absence of phosphine ligands, the reaction was complete in 2 h to afford trisubstituted ferrocene **4a** in moderate yield (entry 4). There have been a few reports of C−H activation catalyzed by iridium diene complexes.[10] Neutral Ir(I) catalyst was inactive toward the reaction (entry 5).[8,9] Interestingly, although Rh(I) complexes are active toward the alkenylation and alkylation of arenes and olefins,[11] the Rh analogue, [Rh(cod)$_2$]BARF, did not catalyze the reaction at all (entry 6). An attempt to selectively form disubstituted ferrocene **3a** with 1 equiv of **2a** resulted in low selectivity, likely due to strong coordination of the pyridyl group (entry 7). The yield of **4a** was improved when the reaction was conducted in toluene at 110 °C (entry 8).

The scope of substrates was examined under the reaction conditions of entry 8 in Table 1, using 4 equiv of an alkyne or alkenes **2** (Table 2). In entries 1−10, trisubstituted ferrocenes **4** were obtained as the major products with anti-Markovnikov selectivity. The reaction proceeded smoothly with a variety of terminal alkenes to form trisubstituted ferrocenes **4b−j** (entries 1−9). Functional groups such as ester, ketone, and boronic ester groups remained intact under the reaction conditions (entries 2, 3, and 5). The activated internal alkene **2k** formed the trisubstituted ferrocene **4k** as a diastereomeric mixture (major:minor = 9:1) (entry 10). The relative stereochemistry of

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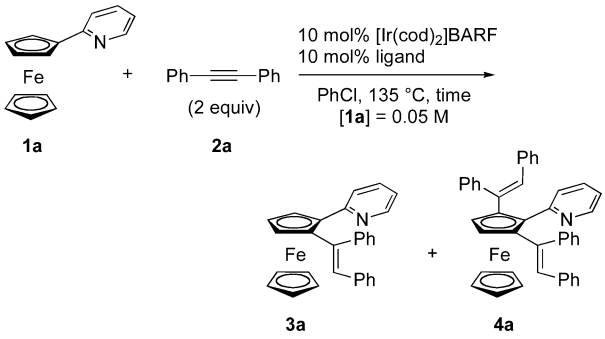
Table 1. Optimization of Reaction Conditions



entry	ligand	time (h)	3a (%)[a]	4a (%)[a]
1	*rac*-BINAP	12	7	0
2	DBPFc[b]	25	14	1
3[c]	$P(4\text{-}FC_6H_4)_3$	24	19	8
4	none	2	0	59[d]
5[e]	none	24	trace	0
6[f]	none	29	0	0
7[g]	none	3	40	31
8[h]	none	2	trace	77[d]

[a]NMR yields. [b]1,1′-Bis(di-*tert*-butylphosphino)ferrocene. [c]$P(4\text{-}FC_6H_4)_3$ (20 mol %) was used. [d]Isolated yields. [e]$[Ir(cod)Cl]_2$ (5 mol %) was used in place of $[Ir(cod)_2]BARF$. [f]$[Rh(cod)_2]BARF$ was used in place of $[Ir(cod)_2]BARF$. [g]One equiv of **2a** was used. [h]In toluene, at 110 °C.

the major isomer of **4k** was determined to be *meso* by X-ray crystallography (see Supporting Information). A nonactivated internal alkene and a terminal alkyne were inactive toward the reaction (entries 11 and 12).[11,12]

Next, the scope of the directing groups was examined under the reaction conditions used in Table 2 (Figure 1). The reaction between 1-octene (**2j**) and *N*-phenylmethylferrocenyl imine formed the trisubstituted ferrocene **4n**. Use of an isoquinolyl directing group resulted in the formation of a racemic mixture of planar chiral disubstituted ferrocene **3o** in high selectivity due to steric repulsion within **3o**.[13] Diphenylphosphine oxide was also used as a directing group to form planar chiral ferrocenyl phosphine oxide **3p**, albeit in low yield. The results in Table 2 and Figure 1 demonstrate the versatility and high regioselectivity that have not been achieved previously in the catalytic C−H activation of ferrocene derivatives.

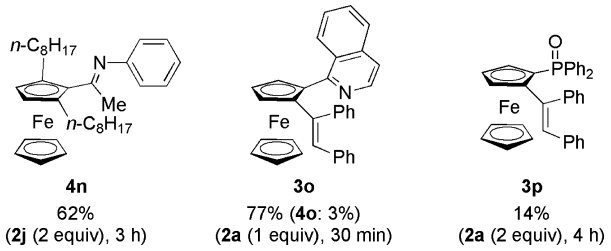
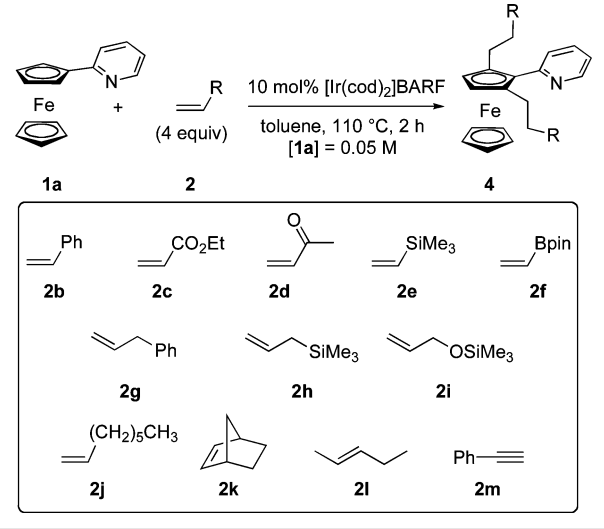


Figure 1. Scope of directing groups.

Table 2. Scope of an Alkyne and Alkenes



entry	2	4 (%)[a]	entry	2	4 (%)[a]
1	**2b**	79	7[e]	**2h**	58
2	**2c**	87	8[f]	**2i**	71
3[b]	**2d**	52	9	**2j**	83
4	**2e**	84	10	**2k**	>99
5[b,c]	**2f**	61	11[g]	**2l**	0
6[d]	**2g**	74	12[d]	**2m**	0

[a]Isolated yields. [b]3 h. [c]Yield after converting Bpin into OH. [d]Two equiv of **2g** or **2m** was used. [e]5 h. [f]Yield after converting $OSiMe_3$ into OH. [g]16 h.

We carried out a mechanistic investigation using variable-temperature NMR analyses: we used $[Ir(cod)_2]BF_4$ in place of $[Ir(cod)_2]BARF$ in order to simplify NMR spectra and submitted it to the reaction of a 2-ferrocenylpyridine (**1a**) or 2-phenylpyridine (**1q**) as an analogue of **1a**, with ethyl acrylate (**2c**). $CDCl_3$ was chosen as a solvent due to the low solubility of $[Ir(cod)_2]BF_4$ in toluene-d_8. The reaction between $[Ir(cod)_2]BF_4$ and 1 equiv of **1a** or **1q** proceeded on mixing at −40 °C to form bispyridine complex **5a** or **5q** with concomitant release of 1,5-cyclooctadiene (COD) and unreacted $[Ir(cod)_2]BF_4$ in a ratio of about 1:1:1 (Scheme 1).[14] The structures of **5a** and **5q** were characterized using ^1H, ^{13}C, gCOSY, and gHMQC NMR experiments. Similar coordination of substrate was not observed when $[Ir((R)\text{-binap})(cod)]BF_4$ and **1a** were mixed at 23 °C. Thus, the nonlabile COD ligand is likely one of the factors that decreases the catalytic activity of $[Ir(phosphine)_2(cod)]BF_4$ complexes, as seen in Table 1, entries 1−3. We also noted that the Ir center in $[Ir(cod)_2]BF_4$ is more electron-poor than that of $[Ir((R)\text{-binap})(cod)]BF_4$ based on ^1H and $^{13}C\{^1H\}$ NMR.[14] This electronic difference will also affect the activity of these complexes toward the catalytic reaction.

Upon the addition of 1 equiv of ethyl acrylate (**2c**) to the mixture of **5a**, $[Ir(cod)_2]BF_4$, and COD, the reaction proceeded at 0 °C to form a mixture of several species that could not be identified. In contrast, the reaction of **2c** with the mixture of **5q**, $[Ir(cod)_2]BF_4$, and COD was complete in about 10 min at 23 °C to form the Ir-ester complex **6** almost exclusively along with COD and its isomerized products (Scheme 1). All methylene protons in **6** appeared as nonequivalent signals in the ^1H NMR spectrum due to the conformational rigidity of the ethylene tether. The ^{13}C signal of the carbonyl carbon appeared at 196 ppm, shifted downfield by 23 ppm from the signal for the free pyridine-ester product.[15] This downfield shift indicates η^1-coordination of the carbonyl oxygen.[16]

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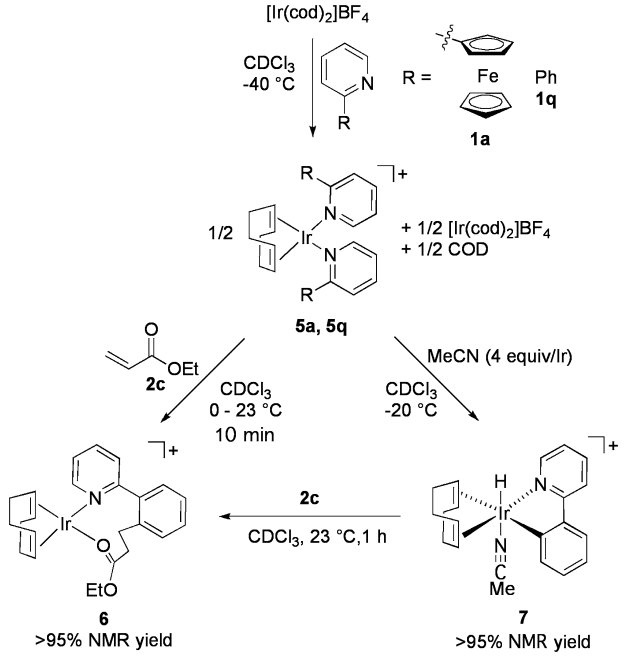
Scheme 1. Reaction between $[Ir(cod)_2]BF_4$, 1a or 1q, and 2c

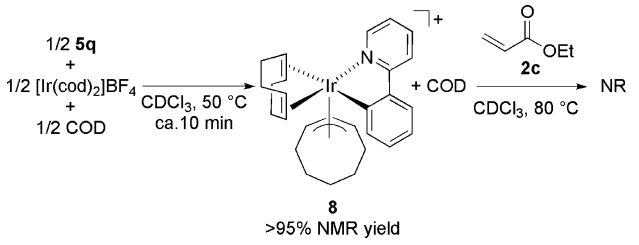


Observation of the Ir-hydride species that may form via oxidative addition of **1q** was attempted using MeCN (4 equiv/Ir) as a trapping agent. Indeed, in the presence of MeCN, stable Ir-hydride species **7** formed when the mixture of **5q**, $[Ir(cod)_2]BF_4$, and COD was reacted at −20 °C (Scheme 1). The COD ligand in **7** was intact in the presence of hydride ligand at 23 °C.[17] The ^{1}H signals of Ir−H and Ir−NCMe were observed at −15.6 and 2.31 ppm, respectively. The stereochemistry of complex **7** was deduced based on the Ir−H chemical shifts of analogous complexes.[17] The Ir-hydride **7** reacted with alkene **2c** at 23 °C to form the Ir-ester complex **6** with concomitant release of MeCN. The putative Ir-alkyl-aryl complex that may form via insertion of **2c** into the Ir−H bond could not be detected due to rapid reductive elimination and subsequent formation of **6**. Results of these stoichiometric reactions indicate that the catalytic reaction using ferrocenyl substrates most likely proceeds via oxidative addition of the Cp ring.[7]

Oxidative addition of **1q** was faster in the presence of MeCN (started at −20 °C) than in the absence (started at 0 °C), most likely due to MeCN-assisted faster dissociation of **1q** from the bispyridine complex **5q**. This assumption was successfully applied to improve the catalytic activity. Thus, the reaction between **1a** and **2j** conducted using 5 mol % of $[Ir(cod)_2]$-BARF (in toluene, 110 °C, 19.5 h) slowly formed the disubstituted product **3j** and the trisubstituted product **4j** in 12% and 4% yield, respectively. However, in the presence of MeCN (10 equiv/Ir), the same reaction was complete in 6 h to form **4j** in 82% yield, which means nearly 26-fold increase of TOF. Detailed kinetic studies will enable us to confirm the origin of the rate acceleration.

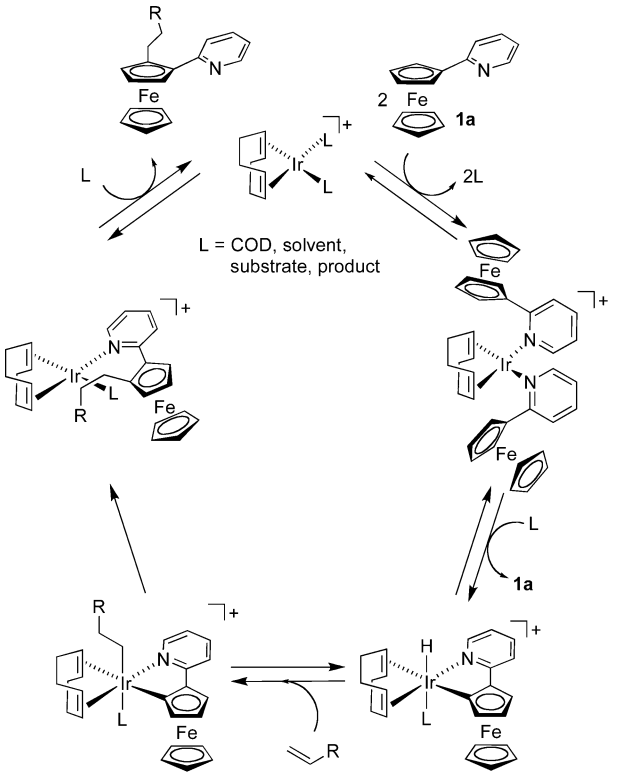
When the mixture of **5q**, $[Ir(cod)_2]BF_4$, and COD was heated to 50 °C in the absence of **2c**, the Ir-π-allyl complex **8** formed (Scheme 2). Complex **8** did not react with alkene **2c** even at 80 °C. Thus, the formation of **8** is likely one of the catalyst deactivation pathways. Indeed, when an Ir complex possessing only a COD as a ligand was used, which was prepared from 2.5 mol % of $[Ir(cod)Cl]_2$ and 5 mol % of

Scheme 2. Formation of the Ir-π-Allyl Complex 8



NaBARF, the reaction of **1a** with **2j** in toluene at 110 °C concluded within 3 h, and the trisubstituted product **4j** was obtained in 91% yield. This corresponds to a nearly 56-fold increase of TOF compared to the same reaction using 5 mol % of $[Ir(cod)_2]$BARF. On the basis of these mechanistic investigations, we proposed a catalytic cycle that proceeds via an oxidative addition/reductive elimination pathway (Scheme 3).

Scheme 3. Proposed Catalytic Cycle



In conclusion, this communication presents the first directed alkenylation and alkylation of ferrocenes catalyzed by $[Ir(cod)_2]$BARF. A variety of alkenes and directing groups were successfully employed to selectively form trisubstituted ferrocenes and disubstituted ferrocenes. The mechanistic investigation revealed that the reaction likely proceeds via a directed oxidative addition of the Cp ring to the $[Ir(cod)(L)_2]^+$ species. The COD ligand was intact at least under the stoichiometric condition. Further, a possible catalyst deactivation pathway was proposed. These mechanistic investigations were utilized to logically improve the catalyst activity. We are currently investigating the enantioselective version of the reaction.

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■ ASSOCIATED CONTENT

Supporting Information

The experimental procedure and physical properties of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) *Ferrocenes: Homogeneous Catalysis/Organic Synthesis/Materials Science*; Togni, A.; Hayashi, T., Eds.; Wiley-VCH: Weinheim, 1995. (b) *Ferrocenes: Ligands, Materials and Biomolecules*; Štěpnička, P., Ed.; Wiley & Sons Ltd: Chichester, England, 2008.

(2) (a) Fouda, M. F. R.; Abd-Elzaher, M. M.; Abdelsamaia, R. A.; Labib, A. A. *Appl. Organomet. Chem.* **2007**, *21*, 613. (b) Amer, W. A.; Wang, L.; Amin., A. M.; Ma, L.; Yu, H. *J. Inorg. Organomet. Polym. Mater.* **2010**, *20*, 605.

(3) (a) Choi, T.-L.; Lee, K.-H.; Joo, W.-J.; Lee, S.; Lee, T.-W.; Chae, M. Y. *J. Am. Chem. Soc.* **2007**, *129*, 9842. (b) Daeneke, T.; Kwon, T.-H.; Holmes, A. B.; Duffy, N. W.; Bach, U.; Spiccia, L. *Nat. Chem.* **2011**, *3*, 211. (c) Tropiano, M.; Kilah, N. L.; Morten, M.; Rahman, H.; Davis, J. J.; Beer, P. D.; Faulkner, S. *J. Am. Chem. Soc.* **2011**, *133*, 11847.

(4) (a) Arrayás, R. G.; Adrio, J.; Carretero, J. C. *Angew. Chem., Int. Ed.* **2006**, *45*, 7674. (b) *Chiral Ferrocenes in Asymmetric Catalysis*; Dai, L.-X.; Hou, X.-L., Eds.; Wiley-VCH: Weinheim, 2009.

(5) (a) Siegel, S.; Schmalz, H.-G. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2456. (b) Datta, A.; Köllhofer, A.; Plenio, H. *Chem. Commun.* **2004**, 1508. (c) Xia, J.-B.; You, S.-L. *Organometallics* **2007**, *26*, 4869.

(6) Recent examples: (a) Moyano, A.; Rosol, M.; Moreno, R. M.; López, C.; Maestro, M. A. *Angew. Chem., Int. Ed.* **2005**, *44*, 1865. (b) Hijazi, A.; Djukic, J.-P.; Allouche, L.; de Cian, A.; Pfeffer, M. *Organometallics* **2007**, *26*, 4180. (c) Xu, C.; Wang, Z.-Q.; Zhang, Y.-P.; Dong, X.-M.; Hao, X.-Q.; Fu, W.-J.; Ji, B.-M.; Song, M.-P. *Eur. J. Inorg. Chem.* **2011**, 4878.

(7) (a) Farrington, E. J.; Viviente, E. M.; Williams, B. S.; van Koten, G.; Brown, J. M. *Chem. Commun.* **2002**, 308. (b) Kuklin, S. A.; Sheloumov, A. M.; Dolgushin, F. M.; Ezernitskaya, M. G.; Peregudov, A. S.; Petrovskii, P. V.; Koridze, A. A. *Organometallics* **2006**, *25*, 5466.

(8) (a) Tsuchikama, K.; Kasagawa, M.; Hashimoto, Y.; Endo, K.; Shibata, T. *J. Organomet. Chem.* **2008**, *693*, 3939. (b) Tsuchikama, K.; Hashimoto, Y.; Endo, K.; Shibata, T. *Adv. Synth. Catal.* **2009**, *351*, 2850.

(9) (a) Tsuchikama, K.; Kasagawa, M.; Endo, K.; Shibata, T. *Org. Lett.* **2009**, *11*, 1821. (b) Pan, S.; Endo, K.; Shibata, T. *Org. Lett.* **2011**, *13*, 4692. (c) Shibata, T.; Hirashima, H.; Kasagawa, M.; Tsuchikama, K.; Endo, K. *Synlett* **2011**, 2171.

(10) (a) Esteruelas, M. A.; Oliván, M.; Oro, L. A.; Tolosa, J. I. *J. Organomet. Chem.* **1995**, *487*, 143. (b) Fischer, C.; Carreira, E. M. *Org. Lett.* **2001**, *3*, 4319. (c) Sakaguchi, S.; Kubo, T.; Ishii, Y. *Angew. Chem., Int. Ed.* **2001**, *40*, 2534. (d) Sakaguchi, S.; Mizuta, T.; Furuwan, M.; Kubo, T.; Ishii, Y. *Chem. Commun.* **2004**, 1638. (e) Song, G.; Li, Y.; Chen, S.; Li, X. *Chem. Commun.* **2008**, 3558. (f) Onodera, G.; Kato, M.; Kawano, R.; Kometani, Y.; Takeuchi, R. *Org. Lett.* **2009**, *11*, 5038.

(11) Colby, D. A.; Bergman, R. G.; Ellman, J. A. *Chem. Rev.* **2010**, *110*, 624.

(12) (a) Kakiuchi, F.; Murai, S. *Acc. Chem. Res.* **2002**, *35*, 826. (b) Ritleng, V.; Sirlin, C.; Pfeffer, M. *Chem. Rev.* **2002**, *102*, 1731.

(13) Lim, Y.-G.; Lee, K.-H.; Koo, B. T.; Kang, J.-B. *Tetrahedron Lett.* **2001**, *42*, 7609.

(14) (a) Crabtree, R. H.; Morris, G. E. *J. Organomet. Chem.* **1977**, *135*, 395. (b) Uson, R.; Oro, L. A.; Carmona, D.; Esteruelas, M. A. *Inorg. Chim. Acta* **1983**, *73*, 275.

(15) Kuninobu, Y.; Nishina, Y.; Okaguchi, K.; Shouho, M.; Takai, K. *Bull. Chem. Soc. Jpn.* **2008**, *81*, 1393.

(16) (a) Schobert, R.; Pfab, H.; Mangold, A.; Hampel, F. *Inorg. Chim. Acta* **1999**, *291*, 91. (b) Daley, C. J. A.; Bergens, S. H. *J. Am. Chem. Soc.* **2002**, *124*, 3680.

(17) Martín, M.; Sola, E.; Torres, O.; Plou, P.; Oro, L. A. *Organometallics* **2003**, *22*, 5406.