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

# Iron-Catalyzed Directed Alkylation of Aromatic and Olefinic Carboxamides with Primary and Secondary Alkyl Tosylates, Mesylates, and Halides

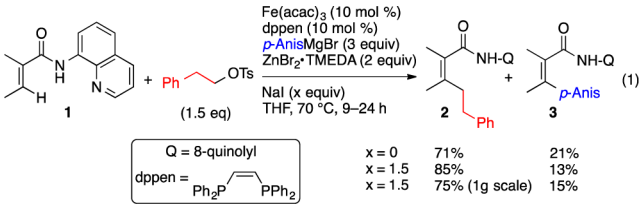
Laurean Ilies,* Tatsuaki Matsubara, Saki Ichikawa, Sobi Asako,† and Eiichi Nakamura*

Department of Chemistry, School of Science, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033, Japan

Supporting Information

**ABSTRACT:** Alkenes, arenes, and heteroarenes possessing an 8-quinolylamide group as the directing group are alkylated with primary and secondary alkyl tosylates, mesylate, and halides in the presence of $Fe(acac)_3$/diphosphine as a catalyst and ArZnBr as a base. The reaction proceeds stereospecifically for alkene substrates and takes place without loss of regiochemical integrity of the starting secondary tosylate, but with loss of the stereochemistry of the chiral center.

After extensive developments in the use of alkenes[1] and alkylmetal reagents[2] for directed C($sp^2$)−H functionalization of alkenes and arenes,[3] alkyl halides are receiving increasing attention as an alkyl donor[4] under palladium[5] and ruthenium catalysis,[6] and more recently under 3*d*-block transition metals, such as cobalt[7] and nickel.[8] However, the synthetic versatility of the alkyl halide approach is still limited[9] because of stereoisomerization of the olefins in the product,[8a] and the limitation of the alkyl donor mainly to alkyl halides. The use of alkanol derivatives as an alkyl donor has been illustrated only for the coupling of octyl tosylate with an acetophenone imine under cobalt catalysis.[7b] We report here that, under iron catalysis, alkyl tosylates, mesylate, and halides serve as effective alkyl donors for the alkylation of alkenes, arenes, and heteroarenes possessing an 8-aminoquinolyl carboxamide directing group[10] (eq 1). The




iron-catalyzed reaction of secondary alkyl tosylates proceeds with retention of regiochemical integrity,[8b] but with loss of the stereochemistry of the chiral center. The reaction tolerates the presence of a variety of functional groups, such as alkyl chloride, aryl halide, and ester, and can utilize an alcohol as an alkyl donor after *in situ* conversion into the corresponding mesylate (eq 2).

A typical reaction protocol is described first (eq 1): a solution of *p*-anisylmagnesium bromide (*p*-AnisMgBr) in THF (3 equiv) was added dropwise to a solution of the tiglamide **1** and $ZnBr_2$·TMEDA (2 equiv). Next, 2-phenethyl tosylate (1.2−1.5 equiv) in THF and a mixture of $Fe(acac)_3$ (10 mol %) and *cis*-1,2-bis(diphenylphosphino)ethylene (dppen, 10 mol %) in THF were added sequentially, and the reaction mixture was stirred at 70 °C for 9 h. Aqueous workup followed by silica-gel chromatography afforded the desired *β*-alkylated amide **2** in 71% yield together with a *Z*-arylated product[11] **3** in 21% yield (on a 0.4 mmol scale), both as a single isomer (eq 1). Addition of dry NaI to the reaction suppresses the arylation (13%) and afforded **2** in 85% yield. The reaction using 1.00 g of **1** gave **2** in 75% isolated yield. *p*-AnisMgBr was used to facilitate chromatographic removal of **3** and can be replaced with PhMgBr.

The use of *p*-anisylzinc bromide[12] generated from *p*-AnisMgBr and $ZnBr_2$ was found to effect cleanly 100% stereoselective coupling with phenethyl tosylate to afford **2**. This catalytic system utilizes 2.5 equiv of *p*-AnisMgBr and 1.5 equiv of $ZnBr_2$·TMEDA, where 2 equiv of the *p*-anisyl group are consumed to remove two hydrogens atoms from **1**, leaving 0.5 equiv of the *p*-anisyl moiety, probably staying as a stationary ligand on the iron atom. These conditions almost entirely suppress two undesirable side reactions of the aryl Grignard reaction: the Negishi-type cross-coupling with the tosylate (or halide)[13] to give 4-phenethylanisole and the homocoupling of the aryl group[14] to give 4,4′-bianisyl. The use of a slight excess of *p*-AnisMgBr (3 equiv, together with 2 equiv of $ZnBr_2$·TMEDA, as in eq 1) was often necessary to ensure reproducibility of the reaction because the *p*-anisyl group is partially consumed for the formation of **3** (which consumes 3 equiv/mol of the anisyl group).[11]

The effects of the directing group and the ligand are summarized in Figure 1 for alkylation of 3-methylbenzamide or tiglamide **1** with phenethyl tosylate. The 8-aminoquinoline directing group was essential, and a 2-methyl-8-aminoquinoline group was entirely ineffective, indicating sensitivity to steric hindrance. *N*-Phenylamide and pyridine directing groups resulted in recovery of the starting material. The reaction is also sensitive to the ligand, as shown in Figure 1b. The reaction took place most smoothly with a diphosphine possessing a *π*-bridge such as dppen and dppbz, but not with 1,2-ethylenediphosphine (dppe) lacking the *π*-bridge. Monophosphine and bipyridine ligands are ineffective.

Table 1 illustrates the stereospecific alkylation of *α*,*β*-unsaturated amides with alkyl tosylates and halides. All reactions resulted in quantitative conversion of the starting amide, accompanying the formation of 10−20% of the arylated product **3** (or congener). In no cases did we observe the homocoupling

**Received:** July 1, 2014
**Published:** July 17, 2014

   dx.doi.org/10.1021/ja5066015 | J. Am. Chem. Soc. 2014, 136, 13126−13129

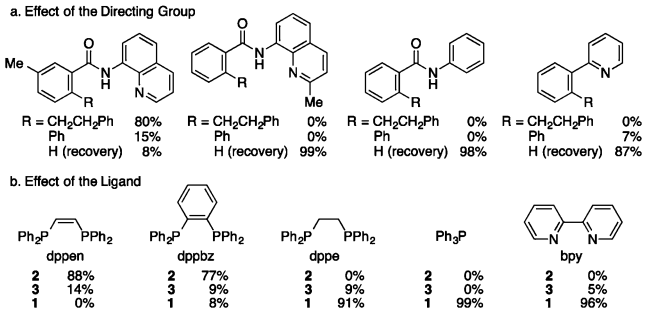



**Figure 1.** Effect of directing group and ligand. (a) Effects examined for the reaction of a benzamide substrate with phenethyl tosylate. R = $CH_2CH_2Ph$ refers to the yield of the desired product, R = Ph refers to the arylation side product (cf. **3** in eq 1), and R = H refers to the starting material. (b) Effects examined for alkene substrate **1** in eq 1.

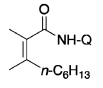
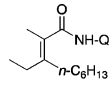
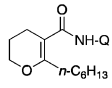
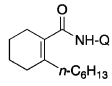
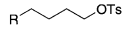
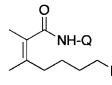
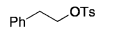
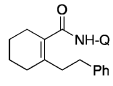
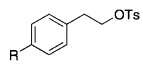
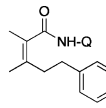
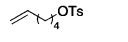
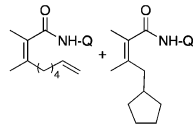
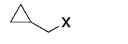
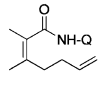
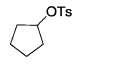
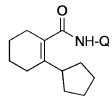
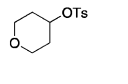
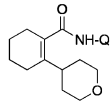
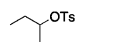
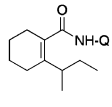
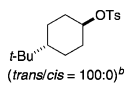
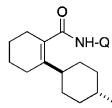
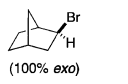
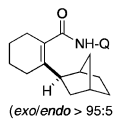
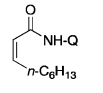
product of *p*-AnisMgBr.[14] Functionalization of olefinic C−H substrates with alkyl halides has so far been reported for the nickel-catalyzed reaction of an $\alpha,\beta$-unsaturated amide with alkyl bromide or chloride[8] that occurred with degradation of the olefin's stereochemistry.[8a] The 100% *Z*-stereoselective introduction of a hexyl group at the $\beta$-position was achieved by the use of 1-hexyl tosylate, and iodide, bromide, and chloride also reacted with equal ease (entries 1, 4−6). The reaction took place much faster at the tosyloxy group than at an alkyl chloride moiety (entry 7). Ester (entry 8), aryl chloride (entry 9), and aryl bromide (entry 10) groups remained entirely unaffected. The reaction of 5-hexenyl tosylate took place in 79% yield to give mainly a cyclized product (entry 13) without the olefin isomerization that was observed in cobalt catalysis,[7b] suggesting that metal hydride species are not involved. Cyclopropylmethyl bromide and tosylate reacted with complete opening of the cyclopropyl ring (entries 14 and 15), indicating that the alkyliron intermediate has a radical-like character.

The examples after entry 16 depict the reaction of alkenyl C−H substrates with secondary alkyl tosylates—an illustration of the advantage of iron catalysis over other catalytic systems so far reported. Cyclopentyl tosylate and tetrahydropyranyl tosylate reacted in modest to good yield (entries 16 and 17). 2-Butyl tosylate gave a 2-butylated product exclusively, and none of a 1-butylated product (entry 18).[7]

The stereochemistry of *trans*-4-*tert*-butylcyclohexyl tosylate decreased to 72:28 during the reaction (entry 19), while the *cis*-isomer gave none of the desired product, probably because of competitive $\beta$-eliminative loss of the axial tosyloxy group.[13e] The observed loss of the stereochemistry at the $sp^3$ center connected to the tosyloxy group suggests a radical-like character of the C−Fe bond in an intermediate that forms prior to the C−C bond formation.[13e] *Exo*-norbornyl bromide gave the less hindered *exo* product selectively (entry 20). Under these reaction conditions, tertiary alkyl halides such as *tert*-butyl bromide or chloride and adamantyl bromide did not produce the alkylated product at all, and the starting alkenecarboxamide was recovered together with 20%−30% of an arylated product (congener of **3**).

Trisubstituted acyclic or cyclic alkene substrates such as tiglamide (entries 1, 7, 8, 10−15), 3-ethyl-2-methylacrylamide (entry 2), cyclohexenamide (entries 4−6, 9, 16−20), or dihydropyranamide (entry 3) reacted well. By contrast, the reaction of acrylamide (entry 21) gave the desired (*Z*)-3-hexyl product only in 12% yield, giving predominantly a (*Z*)-3-anisylated product[11,15] (congener of **3**, 81% yield). A similar result was obtained for 2-methylacrylamide (Supporting

**Table 1. Iron-Catalyzed Reaction of Alkene Carboxamides with Various Primary and Secondary Alkyl Tosylates and Halides**[a]

| entry | alkyl-X | product | yield (%) |
|---|---|---|---|
| 1 | *n*-$C_6H_{13}$-OTs |  | 85 |
| 2 | *n*-$C_6H_{13}$-OTs |  | 87 |
| 3 | *n*-$C_6H_{13}$-OTs |  | 61 |
| 4<br>5<br>6 | *n*-$C_6H_{13}$-X |  | [89] (X = I)<br>[79] (X = Br)<br>[70] (X = Cl) |
| 7<br>8 |  |  | 89 (R = Cl)<br>83 (R = $CH_2CO_2Et$) |
| 9 |  |  | 93 |
| 10<br>11<br>12 |  |  | 85 [71] (R = H)<br>84 (R = Cl)<br>85 (R = Br) |
| 13 |  |  | 79<br>(12:88)[b] |
| 14<br>15 |  |  | 70 (X = Br)<br>26 (X = OTs) |
| 16 |  |  | 77 |
| 17 |  |  | 49 |
| 18 |  |  | 63[c] |
| 19 |  |  | 43<br>(*trans*/*cis* = 78:22)[b] |
| 20 |  |  | 56 |
| 21 | *n*-$C_6H_{13}$-I |  | 12[d] |

[a]The reaction was carried out using 0.4 mmol of amide, 3 equiv of *p*-AnisMgBr, 2 equiv of $ZnBr_2$·TMEDA, 1.2−1.5 equiv of an alkyl donor, $Fe(acac)_3$ (10 mol %) and dppen (10 mol %), and NaI (1.5 equiv) at 50−70 °C for 9−12 h in THF, as described in the text. The yield is based on a pure isolated product obtained by silica-gel chromatography, except in entries 4−6 and 15, where the yield was determined


dx.doi.org/10.1021/ja5066015 | *J. Am. Chem. Soc.* 2014, 136, 13126−13129

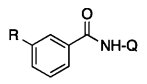
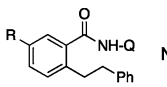
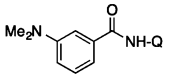
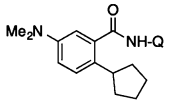
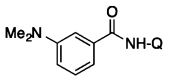
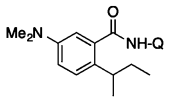
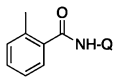
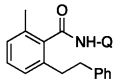
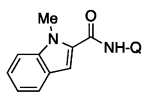
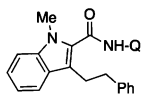
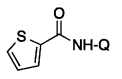
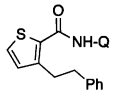
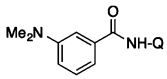
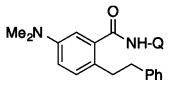
**Table 1. continued**

by GC or $^1$H NMR using an internal standard. The yields in brackets are for the reaction performed in the absence of NaI. See the Supporting Information for details. All reactions formed an arylation side product (an analogue of **3**) in 10−20% yield. [b]Ratio determined by $^1$H NMR. [c]The reaction produced 100% 2-butylated product and none of the 1-butylated product. [d]A 3-*p*-anisyl product was obtained in 81% yield.

Information (SI)). This competition between the two pathways suggests that a reactive iron intermediate bears both the alkyl and aryl groups on the iron atom.

In Table 2, we summarize the alkylation of aromatic and heteroaromatic carboxamides with alkyl tosylates and halides. For all substrates examined, the combined yield of the alkylation and arylation (*p*-anisylation) product was 80%−90%. A notable trend found in entries 1−6 for the reaction of 3-substituted benzamide with 2-phenethyl tosylate is that the yield of the alkylation decreases while that of the arylation increases,

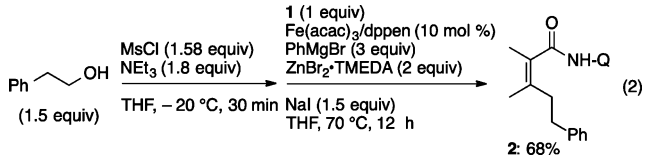
**Table 2. Iron-Catalyzed Alkylation of Aromatic and Heteroaromatic Carboxamides with Phenethyl, Cyclopentyl (entry 7), and 2-Butyl Tosylates (entry 8) and Phenethyl Halides (entries 12 and 13)[a]**

| entry | substrate | product | alkyln (%)[b] | aryln (%)[b] | recov (%)[b] |
|---|---|---|---|---|---|
| 1 |  |  | R = | | |
| 2 | | | Me: 82 | 2 | 0 |
| 3 | | | OMe: 87 | 2 | 2 |
| 4 | | | $NMe_2$: 93 | 5 | 0 |
| 5 | | | F: 75 | 13 | 4 |
| 6 | | | Cl: 60 | nd[c] | 5 |
| | | | Br: 53 | 25 | 10 |
| 7 |  |  | 89 | 5 | 0 |
| 8 |  |  | 83[d] | 9 | 4 |
| 9 |  |  | 70 | 27 | 3 |
| 10 |  |  | 81 | 14 | 5 |
| 11 |  |  | 41 | 35 | 2 |
| 12[e] |  |  | 84 | 14 | 0 |
| 13[f] | | | 72 | 24 | 0 |

[a]The reactions were performed under the same reaction conditions as used in Table 1. See the Supporting Information for details. [b]Yield (%) of the alkylation product is based on the isolated product, except entries 12 and 13, where it was determined by $^1$H NMR using an internal standard. Yields of the arylation product (introduction of the *p*-anisyl group) and recovery are based on either isolated product or GC. [c]Not determined. [d]The reaction produced 100% 2-butylated product and none of the 1-butylated product. [e]Phenethyl bromide was used as the starting material. [f]Phenethyl chloride was used as the starting material.

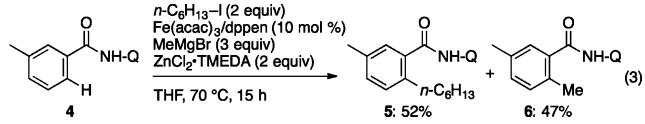
implying that both alkyl and aryl groups are attached to a high-valent iron intermediate responsible for C−H activation and/or C−C bond formation. These data also illustrate the functional group tolerance of the reaction. Secondary tosylates reacted cleanly, and 2-butyl tosylate gave a 2-butylated product uncontaminated by a 1-butylated product (entry 8). A 2-substituted amide reacted slower than the 3-substituted analogue and with much lower alkylation/arylation selectivity (entry 9). Indolecarboxamide (entry 10) gave the desired alkylated product in 81% yield, whereas thiophenecarboxamide (entry 11) gave a mixture of the alkylated and the arylated products in 41% and 35% yield, respectively. Phenethyl chloride and bromide served as a good alkyl donor (entries 12 and 13).

We can use an alcohol directly for the alkylation of the alkenecarboxamide **1** via one-pot *in situ* mesylation.[16] The reaction proceeded well to give the desired product **2** in 68% yield (eq 2).[17]




Several pieces of information relevant to the mechanism are summarized here. The present reaction retains the regiochemical integrity of a secondary tosylate (e.g., 2-butyl tosylate) as opposed to the cobalt-catalyzed reaction of alkyl halides,[7] indicating that $\beta$-elimination of an iron hydride does not interfere with the reaction. In addition to the data reported in the foregoing paragraphs, the ability of TEMPO to completely stop the reaction (Scheme S3 in SI) provides further support for the radical character of the organoiron intermediates.

The persistent formation of the *p*-anisyl side products suggests that an organoiron intermediate preceding the C−C bond formation carries both an alkyl group from alkyl-X and the *p*-anisyl group from *p*-AnisZnX and that there is a general preference for the alkyl group transfer except in Table 1, entry 21 where the *p*-anisyl transfer predominates. To further test this hypothesis, we reacted the benzamide **4** with hexyl iodide in the presence of MeZnX and obtained the hexylated (**5**) and the methylated products (**6**) in an almost 1:1 ratio (eq 3).




Competition experiments using the standard *p*-AnisMgBr/$ZnBr_2$·TMEDA conditions showed that the order of reactivity for the leaving group is I > Br > OTs ≫ Cl (Scheme S4) and that a rapid conversion of the tosylate into the corresponding bromide occurs. The exchange of tosylate with bromide is faster than that with the iodide of NaI, in both the presence and absence of a substrate (Scheme S5). On the other hand, the use of a combination of PhMgCl and $ZnCl_2$·TMEDA for the reaction of hexyl tosylate and chloride gave the desired product in a much lower yield (21% and 31% yield, respectively, Scheme S6). We thus conclude that the halide groups on the magnesium and zinc atoms are active participants in the reaction.

In conclusion, we have developed a new protocol for coupling between an alkyl electrophile with alkene, arene, and heteroarene carboxamides under iron catalysis. Despite a variety of precious


dx.doi.org/10.1021/ja5066015 | J. Am. Chem. Soc. 2014, 136, 13126−13129

metal catalysts for C−H functionalization, the present method provides unique synthetic examples for the utilization of an alcohol and the corresponding tosylate and mesylate as an electrophile. Another feature of the reaction is the lack of regioisomerization in the reaction of a secondary tosylate and the lack of stereoisomerization of olefins in the product. Although the interest in iron catalysis[18,19] has so far been driven largely by its economic and environmental merits,[20] the present results suggest that iron catalysis may become more synthetically versatile than precious metal catalysis.[21]

## ■ ASSOCIATED CONTENT

### Supporting Information

Experimental procedures and physical properties of the compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

## ■ AUTHOR INFORMATION


### Corresponding Authors

laur@chem.s.u-tokyo.ac.jp
nakamura@chem.s.u-tokyo.ac.jp

### Present Address

[†]Division of Chemistry and Biotechnology, Graduate School of Natural Science and Technology, Okayama University, 3-1-1 Tsushimanaka, Kita-ku, Okayama 700-8530, Japan.


### Notes

The authors declare no competing financial interest.

## ■ ACKNOWLEDGMENTS

We thank MEXT for financial support (KAKENHI No. 22000008 to E.N. and Grant-in-Aid for Scientific Research on Innovative Areas No. 25105711 and Grant-in-Aid for Young Scientists (A) No. 26708011 for to L.I.). T.M. and S.A. thank the Japan Society for the Promotion of Science for Young Scientists for a Research Fellowship (No. 26-11422 and No. 23-8207, respectively). T.M. was supported by the Japan Society for the Promotion of Science through Program for Leading Graduate Schools (MERIT).

## ■ REFERENCES


(1) (a) Kakiuchi, F.; Murai, S. *Acc. Chem. Res.* **2002**, *35*, 826−834. (b) Colby, D. A.; Bergman, R. G.; Ellman, J. A. *Chem. Rev.* **2010**, *110*, 624−655. (c) Gao, K.; Yoshikai, N. *J. Am. Chem. Soc.* **2011**, *133*, 400−402. (d) Ilies, L.; Chen, Q.; Zeng, S.; Nakamura, E. *J. Am. Chem. Soc.* **2011**, *133*, 5221−5223.

(2) (a) Sun, C.-L.; Li, B.-J.; Shi, Z.-J. *Chem. Commun.* **2010**, *46*, 677−685. (b) Li, B.-J.; Shi, Z.-J. *Chem. Soc. Rev.* **2012**, *41*, 5588−5598. (c) Giri, R.; Thapa, S.; Kafle, A. *Adv. Synth. Catal.* **2014**, *356*, 1395−1411. (d) Chen, Q.; Ilies, L.; Yoshikai, N.; Nakamura, E. *Org. Lett.* **2011**, *13*, 3232−3234.

(3) Dyker, G., Ed.; *Handbook of C−H Transformations*; Wiley-VCH: Weinheim, Germany, 2005.

(4) Ackermann, L. *Chem. Commun.* **2010**, *46*, 4866−4877.

(5) (a) Tremont, S. J. *J. Am. Chem. Soc.* **1984**, *106*, 5759−5760. (b) Zhang, Y.-H.; Shi, B.-F.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2009**, *48*, 6097−6100. (c) Shabashov, D.; Daugulis, O. *J. Am. Chem. Soc.* **2010**, *132*, 3965−3972. (d) Nadres, E. T.; Santos, G. I. F.; Shabashov, D.; Daugulis, O. *J. Org. Chem.* **2013**, *78*, 9689−9714. (e) Zhao, Y.; Chen, G. *Org. Lett.* **2011**, *13*, 4850−4853. (f) Xiao, B.; Liu, Z.-J.; Liu, L.; Fu, Y. *J. Am. Chem. Soc.* **2013**, *135*, 616−619.

(6) (a) Ackermann, L.; Novák, P.; Vicente, R.; Hofmann, N. *Angew. Chem., Int. Ed.* **2009**, *48*, 6045−6048. (b) Ackermann, L.; Novák, P. *Org. Lett.* **2009**, *11*, 4966−4969. (c) Ackermann, L.; Hofmann, N.; Vicente, R. *Org. Lett.* **2011**, *13*, 1875−1877. (d) Hofmann, N.; Ackermann, L. *J. Am. Chem. Soc.* **2013**, *135*, 5877−5884.

(7) (a) Chen, Q.; Ilies, L.; Nakamura, E. *J. Am. Chem. Soc.* **2011**, *133*, 428−429. (b) Gao, K.; Yoshikai, N. *J. Am. Chem. Soc.* **2013**, *135*, 9279−9282. (c) Song, W.; Ackermann, L. *Angew. Chem., Int. Ed.* **2012**, *51*, 8251−8254.

(8) (a) Chatani, N.; Aihara, Y. *J. Am. Chem. Soc.* **2013**, *135*, 5308−5311. (b) Song, W.; Lackner, S.; Ackermann, L. *Angew. Chem., Int. Ed.* **2014**, *53*, 2477−2480.

(9) Heck-type reactions: (a) Firmansjah, L.; Fu, G. C. *J. Am. Chem. Soc.* **2007**, *129*, 11340−11341. (b) Liu, C.; Tang, S.; Liu, D.; Yuan, J.; Zheng, L.; Meng, L.; Lei, A. *Angew. Chem., Int. Ed.* **2012**, *51*, 3638−3641. (c) Nishikata, T.; Noda, Y.; Fujimoto, R.; Sakashita, T. *J. Am. Chem. Soc.* **2013**, *135*, 16372−16375. (d) Harris, M. R.; Konev, M. O.; Jarvo, E. R. *J. Am. Chem. Soc.* **2014**, *136*, 7825−7828. (e) McMahon, C. M.; Alexanian, E. J. *Angew. Chem., Int. Ed.* **2014**, *53*, 5974−5977. (f) Zou, Y.; Zhou, J. *Chem. Commun.* **2014**, *50*, 3725−3728.

(10) (a) Zaitsev, V. G.; Shabashov, D.; Daugulis, O. *J. Am. Chem. Soc.* **2005**, *127*, 13154−13155. (b) Rouquet, G.; Chatani, N. *Angew. Chem., Int. Ed.* **2013**, *52*, 11726−11743. (c) Shang, R.; Ilies, L.; Matsumoto, A.; Nakamura, E. *J. Am. Chem. Soc.* **2013**, *135*, 6030−6032.

(11) Ilies, L.; Asako, S.; Nakamura, E. *J. Am. Chem. Soc.* **2011**, *133*, 7672−7675.

(12) (a) Asako, S.; Ilies, L.; Nakamura, E. *J. Am. Chem. Soc.* **2013**, *135*, 17755−17757. (b) Asako, S.; Norinder, J.; Ilies, L.; Yoshikai, N.; Nakamura, E. *Adv. Synth. Catal.* **2014**, *356*, 1481−1485.

(13) Selected examples: (a) Tamura, M.; Kochi, J. K. *J. Organomet. Chem.* **1971**, *31*, 289−309. (b) Nakamura, M.; Matsuo, K.; Ito, S.; Nakamura, E. *J. Am. Chem. Soc.* **2004**, *126*, 3686−3687. (c) Nagano, T.; Hayashi, T. *Org. Lett.* **2004**, *6*, 1297−1299. (d) Nakamura, M.; Ito, S.; Matsuo, K.; Nakamura, E. *Synlett* **2005**, 1794−1798. (e) Ito, S.; Fujiwara, Y.-I.; Nakamura, E.; Nakamura, M. *Org. Lett.* **2009**, *11*, 4306−4309.

(14) (a) Cahiez, G.; Chaboche, C.; Mahuteau-Betzer, F.; Ahr, M. *Org. Lett.* **2005**, *7*, 1943−1946. (b) Nagano, T.; Hayashi, T. *Org. Lett.* **2005**, *7*, 491−493.

(15) (a) Norinder, J.; Matsumoto, A.; Yoshikai, N.; Nakamura, E. *J. Am. Chem. Soc.* **2008**, *130*, 5858−5859. (b) Yoshikai, N.; Matsumoto, A.; Norinder, J.; Nakamura, E. *Angew. Chem., Int. Ed.* **2009**, *48*, 2925−2928. (c) Yoshikai, N.; Asako, S.; Yamakawa, T.; Ilies, L.; Nakamura, E. *Chem.—Asian J.* **2011**, *6*, 3059−3065. (d) Ilies, L.; Konno, E.; Chen, Q.; Nakamura, E. *Asian J. Org. Chem.* **2012**, *1*, 142−145.

(16) Do, H.-Q.; Chandrashekar, E. R. R.; Fu, G. C. *J. Am. Chem. Soc.* **2013**, *135*, 16288−16291.

(17) We thank a reviewer for suggesting this reaction to us.

(18) Selected reviews: (a) Bolm, C.; Legros, J.; Le Paih, J.; Zani, L. *Chem. Rev.* **2004**, *104*, 6217−6254. (b) Plietker, B., Ed.; *Iron Catalysis in Organic Chemistry*; Wiley-VCH: Weinheim, Germany, 2008. (c) Enthaler, S.; Junge, K.; Beller, M. *Angew. Chem., Int. Ed.* **2008**, *47*, 3317−3321. (d) Sherry, B. D.; Fürstner, A. *Acc. Chem. Res.* **2008**, *41*, 1500−1511. (e) Czaplik, W. M.; Mayer, M.; Cvengros, J.; Jacobi von Wangelin, A. *ChemSusChem* **2009**, *2*, 396−417. (f) Sun, C.-L.; Li, B.-J.; Shi, Z.-J. *Chem. Rev.* **2011**, *111*, 1293−1314.

(19) (a) Nakamura, E.; Yoshikai, N. *J. Org. Chem.* **2010**, *75*, 6061−6067. (b) Ilies, L.; Nakamura, E. Iron-Catalyzed Cross-Coupling Reactions. In *The Chemistry of Organoiron Compounds*; Marek, I., Rappoport, Z., Eds.; John Wiley & Sons, Ltd.: Chichester, U.K., 2014. (c) Nakamura, E.; Hatakeyama, T.; Ito, S.; Ishizuka, K.; Ilies, L.; Nakamura, M. Iron-Catalyzed Cross-Coupling Reactions. In *Organic Reactions*; Denmark, S. E., Ed.; Vol. *83*; John Wiley & Sons: 2014.

(20) Nakamura, E.; Sato, K. *Nat. Mater.* **2011**, *10*, 158−161.

(21) Matsubara, T.; Asako, S.; Ilies, L.; Nakamura, E. *J. Am. Chem. Soc.* **2014**, *136*, 646−649.