Pivalophenone N–H imine as a benzonitrile surrogate for directed C–H bond functionalization†

Wengang Xu and Naohiko Yoshikai*

Pivalophenone N–H imine has been found to serve as a prominent substrate for directed C–H alkylation and arylation reactions with alkyl bromides and aryl chlorides, respectively, under cobalt–N-heterocyclic carbene (NHC) catalysis. Unlike the case of the parent pivalophenone imine, the increased steric bulk of the resulting ortho-substituted pivalophenone imines allows them to undergo clean imine-to-nitrile conversion under peroxide photolysis or aerobic copper catalysis conditions. Overall, these two-step transformations offer convenient synthetic methods for ortho-functionalized benzonitriles.

Introduction

Transition metal-catalyzed, directing group-assisted C–H bond activation represents a powerful means to transform C–H bonds into C–C and C–heteroatom bonds with predictable regioselectivity. The utility of such transformations should largely depend on the availability and the versatility of the directing group. In this context, a cyano group can potentially be a very useful directing group, owing to its presence in a large number of commercial chemicals as well as to its applicability to various synthetic transformations. Following the seminal report of Murai and coworkers on the Ru-catalyzed addition of benzonitrile to vinylsilane, several examples of ortho-functionalization of benzonitriles, such as Pd-catalyzed arylation, alkoxyla-

tion, halogenation, and Ru-catalyzed olefination, have been reported to date (Scheme 1a). However, expansion of the scope of such transformations appears nontrivial because of intrinsic competition between π- (side-on) and σ- (end-on) coordination modes of the cyano group, only the former being suitable for ortho C–H activation (Scheme 1b). As such, the development of a readily accessible and transformable directing group that functions as a cyano group equivalent would be attractive. This would be particularly the case for arene C–H alkylation using alkyl electrophiles, because, when compared to C–H arylation and olefination, directing groups for this reaction manifold are still limited regardless of the recent progress made by palladium, ruthenium, nickel, cobalt, and iron catalysts.

Recently, we demonstrated that aryl N–H imines, typically derived from the corresponding aryl nitriles and organolithium or Grignard reagents, smoothly participate in the cobalt-catalyzed directed hydroarylation of alkenes (Scheme 2a), which represents a rare example of N–H imine-directed C–H functionalization that results in the retention of the imine directing group. On our way to extend the utility of the N–H imine as a directing group for C–H functionalization, we became interested in the potential utility of the N–H imine functional group as a nitrile surrogate. In particular, our attention was attracted to the seminal work of Ingold on the reaction of N–H imines under peroxide photolysis conditions (Scheme 2b). Their study revealed that di-tert-butyl imine ([t-Bu]₂C = NH) undergoes facile fragmentation into pivalonitrile (t-BuCN) and tert-butyl radical, while sterically less hindered N–H imines undergo dimerization of the corresponding iminyl radicals to form azine derivatives.

Building on the above background, we have found that pivalophenone N–H imine serves as a benzonitrile surrogate for directed C–H functionalization reactions under cobalt conditions.

Scheme 1 Cyano group-directed arene C–H bond functionalizations: examples and intrinsic difficulty.
catalysis,\textsuperscript{19} which is reported herein. Thus, the tert-butyl N–H imine group smoothly directs cobalt-catalyzed C–H alkylation and arylation\textsuperscript{20} with the corresponding organic halides, and then readily undergoes fragmentation into a cyano group under peroxide photolysis or aerobic copper catalysis (Scheme 2c). Interestingly, the fragmentation step has proved to become feasible only after the installation of the ortho-substituent, which prevents the undesirable iminyl radical dimerization. The overall process offers a complementary and convenient route to a variety of ortho-substituted aryl nitriles, especially ortho-alkylated aryl nitriles, for which no direct preparative method from the corresponding aryl nitriles exists.

Results and discussion

The feasibility of the C–H alkylation of pivalophenone N–H imine (1a) was initially explored using n-octyl bromide (2a, 1.5 equiv.) as an alkylating agent. As a result of screening experiments (Table S1\textsuperscript{†}), a catalytic system comprising CoBr\textsubscript{2} (10 mol%), \(N,N'\)-diisopropylimidazolinium tetrafluoroborate (L\textsubscript{1} $HBF\textsubscript{4}, 10$ mol%), and \(\text{t-BuCH}_2\text{MgBr (2 equiv.), THF, rt, 12 h.} (\text{Table 1})\), was found to promote the desired reaction at room temperature, exclusively affording the monoalkylation product 3aa in 90% yield (Table 1). As was the case with previously reported cobalt-catalyzed C–H alkylation reactions,\textsuperscript{13b–e} the choice of the imidazol(in)ium salt as an N-heterocyclic carbene (NHC) precursor was crucial. The reaction using n-octyl chloride instead of 2a also afforded 3aa albeit in a modest yield.

Table 1 summarizes the scope of the present C–H alkylation. The reaction of 1a with various primary alkyl bromides afforded the corresponding monoalkylation products 3aa–3al in good yields, tolerating alkyl chloride (3ad), alkyl fluoride (3ae), olefin moieties (3af–3ah), and bulky substituents at the α-position (3ai–3al). Note that the reaction of 6-bromo-1-hexene exclusively afforded the simple alkylation product 3ag, while the analogous reaction using acetonophenone N-aryl imine was accompanied by a ring-closing alkylation (cyclopentylmethylolation) product.\textsuperscript{13d}

Cyclic and acyclic secondary alkyl bromides also reacted with 1a to afford the corresponding products 3am–3aq in moderate to good yields. A variety of substituted pivalophenone imines participated in the C–H alkylation using n-octyl bromide, tolerating substituents such as methoxy, trifluoromethoxy, methylthio, dimethylamino, fluoro, and trifluoromethyl groups (see 3da–3lh and 3ja). Imines bearing methyl, trifluoromethyl, or methoxy group at the \textit{meta} position and 2-naphthyl imine.

Table 1: ortho-Alkylation of pivalophenone N–H imines\textsuperscript{a}

| R     | Alkyl | LBF\textsubscript{4} | Product | Yield |
|-------|-------|-----------------------|---------|-------|
| t-Bu  | Me    | Co\textsubscript{2}  | 3aa     | 90%   |
| t-Bu  | Ph    | Co\textsubscript{2}  | 3ac     | 91%   |
| t-Bu  | Cl    | Co\textsubscript{2}  | 3ad     | (X = Cl) | 75% |
| t-Bu  | F     | Co\textsubscript{2}  | 3ae     | (X = F) | 80% |
| n-Oc  | Me    | Co\textsubscript{2}  | 3am     | 65%   |
| n-Oc  | Ph    | Co\textsubscript{2}  | 3ah     | 75%   |
| n-Oc  | Cl    | Co\textsubscript{2}  | 3ai     | (R = Ph) | 81% |
| n-Oc  | Cl    | Co\textsubscript{2}  | 3aj     | (R = t-C\textsubscript{6}H\textsubscript{4}Cl) | 90% |
| n-Oc  | Cl    | Co\textsubscript{2}  | 3ak     | (R = t-C\textsubscript{6}H\textsubscript{4}F) | 87% |
| n-Oc  | Cl    | Co\textsubscript{2}  | 3al     | (R = \text{tBu}) | 91% |
| n-Oc  | Me    | Co\textsubscript{2}  | 3an     | 87%   |
| n-Oc  | Me    | Co\textsubscript{2}  | 3ao     | 84%   |
| n-Oc  | Me    | Co\textsubscript{2}  | 3ap     | 51%   |
| n-Oc  | Me    | Co\textsubscript{2}  | 3aq     | 54%   |
| n-Oc  | Me    | Co\textsubscript{2}  | 3aa     | 90%   |
| n-Oc  | Me    | Co\textsubscript{2}  | 3ac     | 91%   |
| n-Oc  | Me    | Co\textsubscript{2}  | 3ad     | (X = Cl) | 75% |
| n-Oc  | Me    | Co\textsubscript{2}  | 3ae     | (X = F) | 80% |
| n-Oc  | Me    | Co\textsubscript{2}  | 3am     | 65%   |
| n-Oc  | Me    | Co\textsubscript{2}  | 3ah     | 75%   |
| n-Oc  | Me    | Co\textsubscript{2}  | 3ai     | (R = Ph) | 81% |
| n-Oc  | Me    | Co\textsubscript{2}  | 3aj     | (R = t-C\textsubscript{6}H\textsubscript{4}Cl) | 90% |
| n-Oc  | Me    | Co\textsubscript{2}  | 3ak     | (R = t-C\textsubscript{6}H\textsubscript{4}F) | 87% |
| n-Oc  | Me    | Co\textsubscript{2}  | 3al     | (R = \text{tBu}) | 91% |
| n-Oc  | Me    | Co\textsubscript{2}  | 3an     | 87%   |
| n-Oc  | Me    | Co\textsubscript{2}  | 3ao     | 84%   |
| n-Oc  | Me    | Co\textsubscript{2}  | 3ap     | 51%   |
| n-Oc  | Me    | Co\textsubscript{2}  | 3aq     | 54%   |
| n-Oc  | Me    | Co\textsubscript{2}  | 3aa     | 90%   |
| n-Oc  | Me    | Co\textsubscript{2}  | 3ac     | 91%   |
| n-Oc  | Me    | Co\textsubscript{2}  | 3ad     | (X = Cl) | 75% |
| n-Oc  | Me    | Co\textsubscript{2}  | 3ae     | (X = F) | 80% |
| n-Oc  | Me    | Co\textsubscript{2}  | 3am     | 65%   |
| n-Oc  | Me    | Co\textsubscript{2}  | 3ah     | 75%   |
| n-Oc  | Me    | Co\textsubscript{2}  | 3ai     | (R = Ph) | 81% |
| n-Oc  | Me    | Co\textsubscript{2}  | 3aj     | (R = t-C\textsubscript{6}H\textsubscript{4}Cl) | 90% |
| n-Oc  | Me    | Co\textsubscript{2}  | 3ak     | (R = t-C\textsubscript{6}H\textsubscript{4}F) | 87% |
| n-Oc  | Me    | Co\textsubscript{2}  | 3al     | (R = \text{tBu}) | 91% |
| n-Oc  | Me    | Co\textsubscript{2}  | 3an     | 87%   |
| n-Oc  | Me    | Co\textsubscript{2}  | 3ao     | 84%   |
| n-Oc  | Me    | Co\textsubscript{2}  | 3ap     | 51%   |
| n-Oc  | Me    | Co\textsubscript{2}  | 3aq     | 54%   |

\textsuperscript{a} Reaction conditions: imine 1 (0.2 mmol), alkyl bromide 2 (1.5 equiv.), Co\textsubscript{2} (10 mol%), L\textsubscript{1} $HBF\textsubscript{4} (10$ mol%), \text{t-BuCH}_2\text{MgBr (2 equiv.), THF, rt, 12 h.} \textsuperscript{†} The product was isolated in the form of ketone after acidic hydrolysis. \textsuperscript{‡} The major regioisomer is shown (r.r. = regioisomer ratio). The yield refers to the overall yield.
underwent exclusive or selective alkylation at the less hindered position (see 3ia–3ka and 3ma), whereas a 3,4-methylenedioxy group directed the reaction to take place preferentially at its proximity, albeit with modest regioselectivity (see 3la). Unfortunately, ortho-substituted pivalophenone imine failed to participate in the reaction. Cyclohexylation reactions were also successfully performed using several substituted imines (see 3bn, 3fn, and 3mn). Note that, under the present conditions, the ω-acylation reaction using valerophenone N-H imine instead of 1a took place rather sluggishly (<30% yield).

Next, we examined the feasibility of cobalt-catalyzed directed C–H arylation. Upon screening conditions for the coupling of imine 1a with 4-chloroanisole (4a), imidazolium salt L2-HBr featuring 2,6-diethylphenyl groups and cyclohexyl backbone emerged as an effective NHC precursor among others such as commercially available IMes and IPr derivatives (see Table S2 for detail). Furthermore, the use of $N,N',N''$-tetramethylethylenediamine (TMEDA) as an additive proved beneficial. Thus, a catalytic system comprised of these key components, Co(acac)$_2$ (10 mol%), L2-HBr (10 mol%), t-BuCH$_2$MgBr, and TMEDA (80 mol%), THF, rt, 12 h. Note that the imine bearing a 3,4-methylenedioxy group underwent arylation at the proximal ortho position (see 5la), in contrast to the modest regioselectivity observed for arylation of the same imine (see 3ia in Table 1). Also notable was the behavior of 2-naphthyl imine, which produced the arylation product 5ma as a regioisomeric mixture while undergoing exclusive arylation at the less hindered position (see 3ma and 3mn). As was the case with the C–H alkylation, ortho-substituted pivalophenone imine was reluctant to undergo the C–H arylation.

To probe the feasibility of the imine-to-nitrile conversion, we initially subjected 1a to UV irradiation (254 nm) in di-tert-butyl peroxide. Not unexpectedly, the reaction mainly afforded azine 6 via dimerization of the iminyl radical, accompanied by only a trace amount of benzonitrile (Scheme 3a). In contrast, the ortho-alkylated imine 3ba quantitatively furnished 2-alkylbenzonitrile 7a under the same conditions (Scheme 3b). The ortho-alkylated imine 5aa also afforded 2-cyanobaryl 7b, albeit in somewhat lower yield (79%) due to the formation of 6-(tert-butyl)-3-methoxyphenanthridine as a byproduct via intramolecular cyclization of the iminyl radical.21 Furthermore, alternative conditions employing catalytic Cu(OAc)$_2$ under O$_2$

![Scheme 3](image-url)  
Scheme 3  Decomposition reactions of pivalophenone imines.
atmosphere, originally developed by Chiba for the conversion of 2-biaryl N–H imines to phenanthridines,\textsuperscript{22} proved equally effective for the conversion of 3aa and 5aa to 7a and 7b, respectively, presumably via fragmentation of a putative iminocopper species (Scheme 3c).

With the imine-to-nitrile conversion methods in hand, we explored two-step synthesis of ortho-alkylated or -arylated benzonitriles (Table 3). Thus, alkylation or arylation reactions of pivalophenone N–H imines were followed by submission of the crude products to the peroxide photolysis (A) or the aerobic copper catalysis (B). To our satisfaction, these protocols worked particularly well for the preparation of ortho-alkylbenzonitriles 7c–7p, many of which were obtained in yields close to the yields of the corresponding C–H alkylation products (Table 1). On the other hand, the yields of the ortho-arylbenzonitriles 7q–7v (ca. 60%) were apparently lower than that of the corresponding C–H arylation products (ca. 80%; Table 2), reflecting the lower efficiency of the second step.

Several experiments were performed to gain mechanistic insight into the present reactions (Scheme 4). A treatment of imine 1i in [D₈]-THF with excess t-BuCH₂MgBr caused a near complete disappearance of the N–H proton signal and a sizable chemical shift change of the C=N carbon in the ¹H and ¹³C NMR spectra (Fig. S1†), indicating formation of a magnesium alkylideneamide species (Scheme 4a). This suggests that the alkylideneamide anion, rather than the parent N–H imine,\textsuperscript{16,23} serves as the actual directing group for cobalt-mediated C–H activation, as is also the case for cobalt-catalyzed, secondary amide-directed C–H alkylation and arylation.\textsuperscript{13,19a,c} The superiority of this anionic directing group to an N-aryl imine directing group\textsuperscript{13b,20a} was demonstrated for both the alkylation and arylation reactions by competition experiments (Scheme 4b). The reaction of 1a with a mixture of n-octyl bromide and 4-chloroanisole exclusively afforded the alkylation product under the Co–L₁ system (Scheme 4c), which is consistent with the inability of L₁ to promote the C–H arylation reaction (Table S2†). By contrast, the same reaction under the Co–L₂ system produced none of the C–H functionalization products, presumably due to the interference of the C–H activation step by n-octyl bromide. The addition of TEMPO caused no apparent interference with the C–H alkylation using n-octyl bromide but substantially inhibited the reactions of cyclohexyl bromide and 4-chloroanisole (Scheme 4d). These observations suggest that, at least for the latter two cases, single electron transfer is involved in the carbon–halogen bond cleavage.\textsuperscript{13,19a–d}

\begin{table}[h]
\centering
\caption{Two-step synthesis of ortho-substituted benzonitriles\textsuperscript{a}}
\begin{tabular}{lll}
\hline
| Reaction Conditions | Products |
\hline
\textbf{A} | hv (254 nm) | t-BuOOH-t-Bu, 12 h |
\textbf{B} | Cu(DMP)₂ (10 mol%) | O₂ (1 atm) | DMF, 80 °C, 12 h |
\hline
1 | R=Ph, R'=t-Bu | 7a, 81% (B) |
2 | R=n-Oct, R'=t-Bu | 7b, 78% (A) |
3 | R=n-Oct, R'=t-Bu | 7c, 82% (A) |
4 | R=n-Oct, R'=t-Bu | 7d, 78% (A) |
5 | R=n-Oct, R'=t-Bu | 7e, 82% (A) |
6 | R=n-Oct, R'=t-Bu | 7f, 77% (B) |
7 | R=n-Oct, R'=t-Bu | 7g, 79% (A) |
8 | R=n-Oct, R'=t-Bu | 7h, 71% (A) |
9 | R=n-Oct, R'=t-Bu | 7i, 77% (B) |
10 | R=n-Oct, R'=t-Bu | 7j, 77% (B) |
11 | R=n-Oct, R'=t-Bu | 7k, 75% (A) |
12 | R=n-Oct, R'=t-Bu | 7l, 71% (A) |
13 | R=n-Oct, R'=t-Bu | 7m, 77% (B) |
14 | R=n-Oct, R'=t-Bu | 7n, 77% (B) |
15 | R=n-Oct, R'=t-Bu | 7o, 71% (A) |
16 | R=n-Oct, R'=t-Bu | 7p, 75% (A) |
\hline
\end{tabular}
\textsuperscript{a} See the ESI for the detailed procedure. The yields refer to overall yields based on 1.
\end{table}

\begin{scheme}
\caption{Mechanistic experiments (PMP = p-methoxyphenyl). The yields in Scheme 4b–d were determined by GC using n-tridecane as an internal standard.}
\centering
\includegraphics[width=\textwidth]{Scheme4.png}
\end{scheme}
Conclusions

In summary, we have demonstrated that pivalophenone N–H imine serves as an excellent substrate for the cobalt-catalyzed directed C–H alkylation and amination reactions with alkyl bromides and aryl chlorides, respectively. Owing to the added steric bulk in the ortho position, the resulting unpurified ortho-alkylated or -amylated pivalophenone imines undergo clean fragmentation of the imine functionality to afford the corresponding ortho-functionalized aryl nitriles. The present two-step protocol would be particularly attractive for the preparation of ortho-alkylated aryl nitriles, which have not been directly accessed from the corresponding aryl nitriles via C–H activation. We anticipate that pivalophenone N–H imine could be exploited as a benzonitrile surrogate not only for cobalt catalysis but also for other transition metal-catalyzed C–H functionalization reactions under mild conditions. Studies in this direction are ongoing in our laboratory.

Acknowledgements

This work was supported by the Singapore Ministry of Education, Nanyang Technological University (RG 5/14, RG 114/15), and JST, CREST. We thank Dr Pin-Sheng Lee for the preparation of NHC precursors including L2·HBr.

Notes and references

1 For selected reviews, see: (a) D. A. Colby, R. G. Bergman and J. A. Ellman, Chem. Rev., 2010, 110, 624; (b) T. W. Lyons and M. S. Sanford, Chem. Rev., 2010, 110, 1147; (c) L. Ackermann, Chem. Rev., 2011, 111, 1315; (d) K. M. Engle, T. S. Mei, M. Wasa and J. Q. Yu, Acc. Chem. Res., 2012, 45, 788; (e) P. B. Arockiam, C. Bruneau and P. H. Dixneuf, Chem. Rev., 2012, 112, 5879; (f) D. A. Colby, A. S. Tsai, R. G. Bergman and J. A. Ellman, Acc. Chem. Res., 2012, 45, 814; (g) L. Ackermann, Acc. Chem. Res., 2014, 47, 281.

2 F. Kakiechi, M. Sonoda, T. Tsujimoto, N. Chatani and S. Murali, Chem. Lett., 1999, 1083.

3 (a) W. Li, Z. Xu, P. Sun, X. Jiang and M. Fang, Org. Lett., 2011, 13, 1286; (b) J.-C. Wan, J.-M. Huang, Y.-H. Jhan and J.-C. Hsieh, Org. Lett., 2013, 15, 2742.

4 W. Li and P. Sun, J. Org. Chem., 2012, 77, 8362.

5 B. Du, X. Jiang and P. Sun, J. Org. Chem., 2013, 78, 12280.

6 M. C. Reddy and M. Jeganmohan, Chem. Commun., 2015, 51, 10738.

7 For the use of a cyano group as an end-on directing group for meta- or para-selective C–H activation, see: (a) D. Leow, G. Li, T.-S. Mei and J.-Q. Yu, Nature, 2012, 486, 518; (b) R.-Y. Tang, G. Li and J.-Q. Yu, Nature, 2014, 507, 215; (c) G. Yang, P. Lindowksa, D. Zhu, J. Kim, P. Wang, R.-Y. Tang, M. Movassaghi and J.-Q. Yu, J. Am. Chem. Soc., 2014, 136, 10807; (d) S. Bag, T. Patra, A. Modak, A. Deb, S. Maiti, U. Dutta, A. Dey, R. Kancherla, A. Maji, A. Hazra, M. Bera and D. Maiti, J. Am. Chem. Soc., 2015, 137, 11888; (e) S. Li, L. Cai, H. Ji, L. Yang and G. Li, Nat. Commun., 2016, 7, 10443; (f) T. Patra, S. Bag, R. Kancherla, A. Mondal, A. Dey, S. Pimparkar, S. Agasti, A. Modak and D. Maiti, Angew. Chem., Int. Ed., 2016, 55, 7751.

8 X. Yang, X. Jin and C. Wang, Adv. Synth. Catal., 2016, 358, 2436.

9 For selected reviews, see: (a) D. Albericio, M. E. Scott and M. Lautens, Chem. Rev., 2007, 107, 174; (b) L. Ackermann, R. Vicente and A. R. Kapdi, Angew. Chem., Int. Ed., 2009, 48, 9792; (c) J. Le Bras and J. Muzart, Chem. Rev., 2011, 111, 1170; (d) C. S. Yeung and V. M. Dong, Chem. Rev., 2011, 111, 1215; (e) C. Liu, J. Yuan, M. Gao, S. Tang, W. Li, R. Shi and A. Lei, Chem. Rev., 2015, 115, 12138; (f) Y. Segawa, T. Maekawa and K. Itami, Angew. Chem., Int. Ed., 2015, 54, 66.

10 (a) Y.-H. Zhang, B.-F. Shi and J.-Q. Yu, Angew. Chem., Int. Ed., 2009, 48, 6097; (b) D. Shabashov and O. Daugulis, J. Am. Chem. Soc., 2010, 132, 3965; (c) Y. Zhao and G. Chen, Org. Lett., 2011, 13, 4850; (d) E. T. Nadres, G. I. F. Santos, D. Shabashov and O. Daugulis, J. Org. Chem., 2013, 78, 9689; (e) B. Xiao, Z.-J. Liu, L. Liu and Y. Fu, J. Am. Chem. Soc., 2013, 135, 616; (f) R.-Y. Zhu, J. He, X.-C. Wang and J.-Q. Yu, J. Am. Chem. Soc., 2014, 136, 13194; (g) S.-Y. Zhang, Q. Li, G. He, W. A. Nack and G. Chen, J. Am. Chem. Soc., 2015, 137, 531.

11 (a) L. Ackermann, P. Nowak, R. Vicente and N. Hofmann, Angew. Chem., Int. Ed., 2009, 48, 6045; (b) L. Ackermann, N. Hofmann and R. Vicente, Org. Lett., 2011, 13, 1875.

12 (a) Y. Aihara and N. Chatani, J. Am. Chem. Soc., 2013, 135, 5308; (b) W. Song, S. Lackner and L. Ackermann, Angew. Chem., Int. Ed., 2014, 53, 2477; (c) Z. Ruan, S. Lackner and L. Ackermann, Angew. Chem., Int. Ed., 2016, 55, 3153.

13 (a) Q. Chen, L. Ilies and E. Nakamura, J. Am. Chem. Soc., 2011, 133, 428; (b) K. Gao and N. Yoshikai, J. Am. Chem. Soc., 2013, 135, 9279; (c) B. Punji, W. Song, G. A. Shevchenko and L. Ackermann, Chem.–Eur. J., 2013, 19, 10605; (d) K. Gao, T. Yamakawa and N. Yoshikai, Synthesis, 2014, 46, 2024; (e) R. Mei and L. Ackermann, Adv. Synth. Catal., 2016, 358, 2443.

14 (a) E. R. Fruchey, B. M. Monks and S. P. Cook, J. Am. Chem. Soc., 2014, 136, 13130; (b) L. Ilies, T. Matsubara, S. Ichikawa, S. Asako and E. Nakamura, J. Am. Chem. Soc., 2014, 136, 13126; (c) B. M. Monks, E. R. Fruchey and S. P. Cook, Angew. Chem., Int. Ed., 2014, 53, 11065; (d) G. Cera, T. Haven and L. Ackermann, Angew. Chem., Int. Ed., 2016, 55, 1484.

15 For a recent review on C–H alkylation using olefins as alkylation agents, see: Z. Dong, Z. Ren, S. J. Thompson and G. Dong, Chem. Rev., 2017, DOI: 10.1021/acs.chemrev.6b00574.

16 W. Xu and N. Yoshikai, Angew. Chem., Int. Ed., 2016, 55, 12731.

17 For N–H imine-directed C–H activation/annulation reactions, see: (a) T. Fukutani, N. Umeda, K. Hirano, T. Satoh and M. Miura, Chem. Commun., 2009, 5141; (b) Z.-M. Sun, S.-P. Chen and P. Zhao, Chem.–Eur. J., 2010, 16, 2619; (c) D. N. Tran and N. Cramer, Angew. Chem., Int. Ed., 2010, 49, 8181; (d) D. N. Tran and N. Cramer, Angew. Chem., Int. Ed., 2011, 50, 11098; (e) D. N. Tran and...
N. Cramer, Angew. Chem., Int. Ed., 2013, 52, 10630; (f) J. Zhang, A. Ugrinov and P. Zhao, Angew. Chem., Int. Ed., 2013, 52, 6681; (g) R. He, Z.-T. Huang, Q.-Y. Zheng and C. Wang, Angew. Chem., Int. Ed., 2014, 53, 4950; (h) T. Jia, C. Zhao, R. He, H. Chen and C. Wang, Angew. Chem., Int. Ed., 2016, 55, 5268; (i) J. H. Kim, S. Gressies and F. Glorius, Angew. Chem., Int. Ed., 2014, 53, 4950; (j) T. Jia, C. Zhao, R. He, H. Chen and C. Wang, Angew. Chem., Int. Ed., 2016, 55, 5268; (k) S. Gupta, J. Han, Y. Kim, S. W. Lee, Y. H. Rhee and J. Park, J. Org. Chem., 2014, 79, 9094.

18 D. Griller, G. d. Mendenha, W. Vanhoof and K. U. Ingold, J. Am. Chem. Soc., 1974, 96, 6068.

19 (a) L. Ackermann, J. Org. Chem., 2014, 79, 8948; (b) K. Gao and N. Yoshikai, Acc. Chem. Res., 2014, 47, 1208; (c) N. Yoshikai, Bull. Chem. Soc. Jpn., 2014, 87, 843; (d) M. Moselage, J. Li and L. Ackermann, ACS Catal., 2016, 6, 498; (e) P. Gandeepan and C.-H. Cheng, Acc. Chem. Res., 2015, 48, 1194; (f) D. Wei, X. Zhu, J.-L. Niu and M.-P. Song, ChemCatChem, 2016, 8, 1242.

20 (a) K. Gao, P.-S. Lee, C. Long and N. Yoshikai, Org. Lett., 2012, 14, 4234; (b) W. Song and L. Ackermann, Angew. Chem., Int. Ed., 2012, 51, 8251; (c) J. Li and L. Ackermann, Chem.–Eur. J., 2015, 21, 5718.

21 R. T. McBurney, A. M. Z. Slawin, L. A. Smart, Y. Yu and J. C. Walton, Chem. Commun., 2011, 47, 7974.

22 L. Zhang, G. Y. Ang and S. Chiba, Org. Lett., 2010, 12, 3682.

23 H.-F. Klein, S. Camadanli, R. Beck, D. Leukel and U. Flörke, Angew. Chem., Int. Ed., 2005, 44, 975.

24 (a) J. Wencel-Delord, T. Droge, F. Liu and F. Glorius, Chem. Soc. Rev., 2011, 40, 4740; (b) T. Gensch, M. N. Hopkinson, F. Glorius and J. Wencel-Delord, Chem. Soc. Rev., 2016, 45, 2900.