C–H Activation

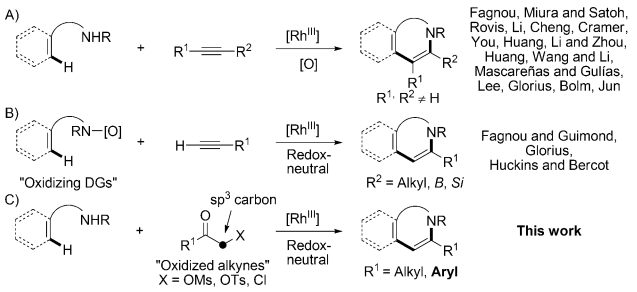
DOI: 10.1002/anie.201310272

α-MsO/TsO/Cl Ketones as Oxidized Alkyne Equivalents: Redox-Neutral Rhodium(III)-Catalyzed C–H Activation for the Synthesis of N-Heterocycles**

*Da-Gang Yu, Francisco de Azambuja, and Frank Glorius**

Dedicated to Professor Manfred T. Reetz on the occasion of his 70th birthday

Abstract: *α-Halo and pseudohalo ketones are used for the first time as C(sp^3)-based electrophiles in transition-metal-catalyzed C–H activation and as oxidized alkyne equivalents in Rh^{III}-catalyzed redox-neutral annulations to generate diverse N-heterocycles. This transformation is efficient and scalable. Due to the mild reaction conditions, a variety of functional groups could be tolerated.*



Scheme 1. Rh^{III}-catalyzed synthesis of diverse N-heterocycles. DG = directing group, MsO = methanesulfonate, TsO = *p*-toluenesulfonate.

N-Heterocycles are ubiquitous in natural products and play important roles in pharmaceutical and material chemistry.[1] Recently, transition-metal-catalyzed C–H activation has emerged to be one of the most powerful ways for their synthesis.[2] Rh^{III} catalysis is especially attractive due to its high efficiency, mild reaction conditions, and diverse reactions with a plethora of partners.[3]

Arguably, the annulation with alkynes is one of the most frequently applied methods to generate N-heterocycles through Rh^{III}-catalyzed directed C–H activation (Scheme 1A).[4] Often, stoichiometric oxidants, such as Cu^{II} and Ag^{I} salts, have to be used to regenerate the active Rh^{III} catalyst. The advent of oxidizing directing groups has emerged as a powerful alternative, allowing annulations under redox-neutral reaction conditions.[5,6] Notably, terminal alkynes, which were previously not applicable, also underwent the annulations efficiently and selectively (Scheme 1B).[6] However, the instability and limited variations of oxidizing directing groups call for new synthetic tools in this field. Since π bonds have been thoroughly studied, we decided to evaluate α-halo or pseudohaloketones, which are C(sp^3)-based electrophiles, as the equivalents of preoxidized alkynes. Herein, we report our efforts to efficiently use α-MsO/TsO/Cl ketones in Rh^{III}-catalyzed C–H activation to synthesize diverse N-heterocycles under mild and redox-neutral reaction conditions (Scheme 1C).

Ketones are common substrates in organic synthesis because of their ready accessibility and stability. Among them, α-(pseudo)halo ketones are widely applied as electrophiles in organic reactions,[7] including cross-couplings with organometallic reagents.[8] Although they have never been applied in transition-metal-catalyzed C–H activation,[9] we wondered if they would react with the in situ generated C(sp^2)–Rh intermediates. Recently, several groups have demonstrated that these species undergo Grignard-type additions to imines,[10] aldehydes,[11] isocyanates,[12] aziridines,[13] and even ketones[14] (Scheme 2A). Moreover, the alkenyl–Rh intermediates, which are generated by insertion of alkyne into the C–Rh bond, could also nucleophilically attack the ketone-,[15] imine-,[16] amide-, or ester-based directing groups[17] (Scheme 2B). All of this evidence suggested that C(sp^2)–Rh species show nucleophilic character to some extent and might attack the α-(pseudo)halo ketones to produce α-aryl- or alkenyl ketones. With a proper N-containing directing group, further condensation could generate the N-heterocycles with the assistance of the Rh^{III} catalyst (Scheme 2C).

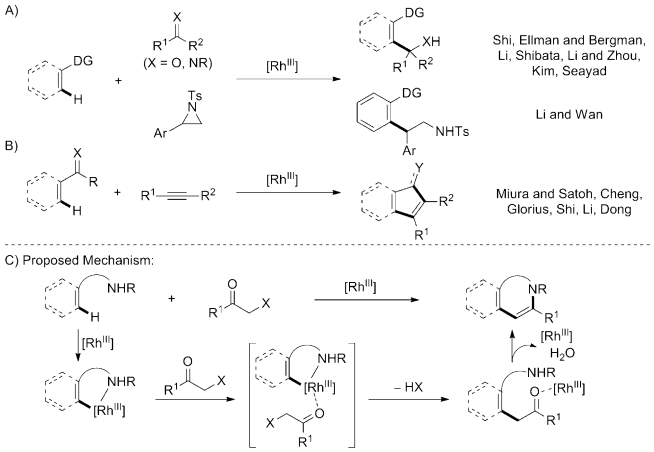
However, three major challenges have to be overcome:

(1) Selectivity. α-(Pseudo)halo ketones have two electrophilic sites and the in situ generated rhodacycle also has two nucleophilic sites. Thus it is challenging to achieve high regioselectivity.

[*] Dr. D.-G. Yu, F. de Azambuja, Prof. Dr. F. Glorius
Westfälische Wilhelms-Universität Münster
Organisch-Chemisches Institut
Corrensstrasse 40, 48149 Münster (Germany)
E-mail: glorius@uni-muenster.de
Homepage: http://www.uni-muenster.de/Chemie.oc/glorius/

[**] We thank Dr. Zhuangzhi Shi, Dr. Honggen Wang, Dr. Dongbing Zhao, and Corinna Nimphius for invaluable discussions and Jan Paulmann for preparation of some compounds (all WWU Münster). Generous financial support by the Alexander von Humboldt Foundation (D.-G.Y.), São Paulo Research Foundation (grant 2013/14209-9, F.deA.), the European Research Council (ERC) under the European Community's Seventh Framework Program ((FP7 2007–2013)/ERC grant agreement no. 25936), and the DFG (Leibniz award) are gratefully acknowledged.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.201310272.

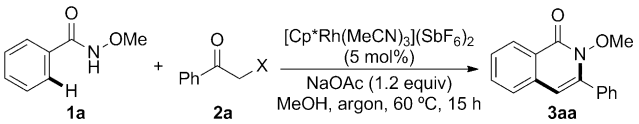


Scheme 2. Rh^{III}-catalyzed C–H activation and Grignard-type additions to different electrophiles.

(2) Inhibition of the catalyst by the leaving groups. In many cases, silver salts are typically required to remove the chloride from the rhodium coordination sphere in order to generate the cationic and highly active Rh^{III} catalyst and improve efficiency. The generated halides or pseudohalides may lower the reactivity of the catalyst.
(3) Compatibility of the two steps. On the basis of the right sequence, the reaction conditions, especially the pH, have to be suitable for both steps.

With this in mind, we started to explore the reaction (Table 1). We chose **1a** as the starting material due to its good directing ability and ease of condensation with carbonyl group.[18] While **2aa** furnished the desired product isoquinolone **3aa** in low yield, **2ab** showed much better reactivity and gave **3aa** in 62% yield (Table 1, entry 2). Notably, this is the first example in which halides serve as the leaving group in Rh^{III}-catalyzed C–C bond formation through C–H activation.[19] Besides, the C3-monoarylated product **3aa** could not be directly accessed, as disclosed here, in analogous annulations of terminal alkynes.[6] Due to the easy availability and similar reactivity, the tosylate **2ac** (Table 1, entry 3) and mesylate **2ad** (entry 4) were further tested and generated **3aa** in similarly excellent yields. However, the benzoate **2ae** showed no reactivity (Table 1, entry 5). Notably, the reaction also occurred under air in good yield (Table 1, entry 6). No **3aa** was observed in the absence of Rh^{III} catalyst (Table 1, entry 7). Other N-substituted amides (with H, Me, Ph, OPiv) and secondary mesylates were also tested, albeit with no success.

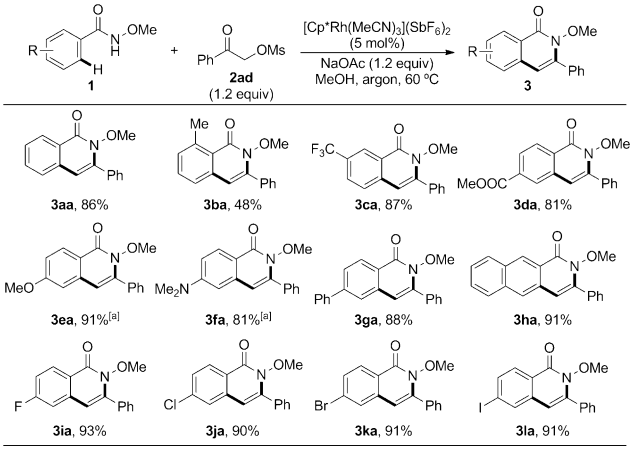
Table 1: Reaction condition optimization.[a]



Entry	X (**2a**)	Yield [%][b]
1	X = Br (**2aa**)	10[c]
2	X = Cl (**2ab**)	62
3	X = OTs (**2ac**)	86
4	**X = OMs (2ad)**	**86**
5	X = OBz (**2ae**)	0[c]
6[d]	X = OMs (**2ad**)	80
7[e]	X = OMs (**2ad**)	0[c]

[a] See **GP1** in the Supporting Information. [b] Yield of isolated product. [c] Yield determined by NMR spectroscopy. [d] Under air. [e] Without Rh^{III} catalyst.

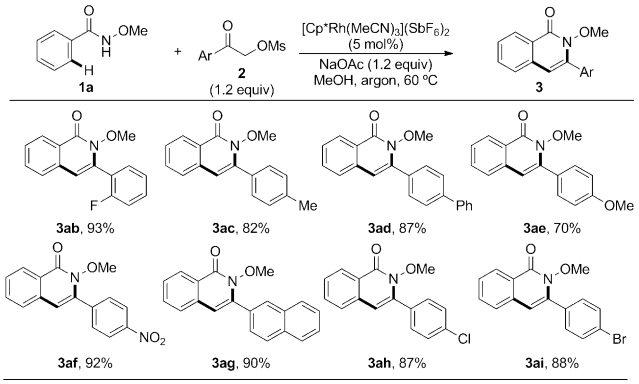
With the optimized reaction conditions in hand, we first explored the substrate scope of amides **1** (Scheme 3) with α-mesyloxyketone **2ad** due to its higher atom economy.[20] We



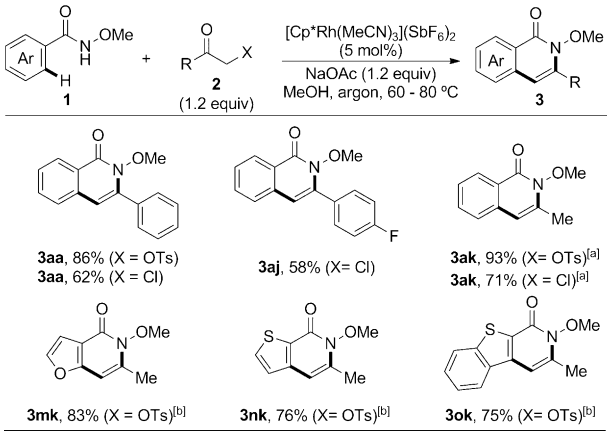
Scheme 3. Substrate scope: Variation of amides **1**. See **GP1** in the Supporting Information. [a] See **GP2** in the Supporting Information.

found that the reactions of the amides **1** were sensitive to steric hindrance (**3aa** and **3ba**) and the C–H functionalization took place selectively at the less hindered position (**3ca**). Interestingly, the electron density of **1** also played an important role in this transformation. The amides with electron-donating groups (EDGs, **1e** and **1f**) reacted slower than those with neutral groups (**1a** and **1g**). However, the desired isoquinolones **3ea** and **3fa** were still obtained in high yields after a reaction time of 24 h. On the other hand, those with electron-withdrawing groups (EWGs, **1c**, **1d**, and **1i**–**1l**) underwent alkylation faster with full conversion of **1** in 4–15 h, but the condensation step was very slow. Therefore, acid was added to speed up the condensation reactions and the desired isoquinolones were obtained in good yields after few minutes at room temperature. Due to the mild reaction conditions, this reaction tolerates many functional groups, such as MeO, NMe_2, CF_3, ester, and carbon–halide bonds. Substrate **1h** also showed good reactivity and selectivity and provided **3ha** in high yield.

Furthermore, various mesylates **2** were also tested (Scheme 4). We found that the steric hindrance of an *ortho*-fluoro substituent in substrate **2b** did not affect the reaction. The mesylates with electron-poor substituents (**2b**, **2f**, **2h**, and **2i**) showed higher reactivity than those with electron-rich substituents (**2c** and **2e**). Similarly, many functional groups were tolerated in this reaction. Moreover, 2-chloro-1-(4-fluorophenyl)ethanone (**2j**) also could afford the desired product **3aj** in moderate yield (Scheme 5).



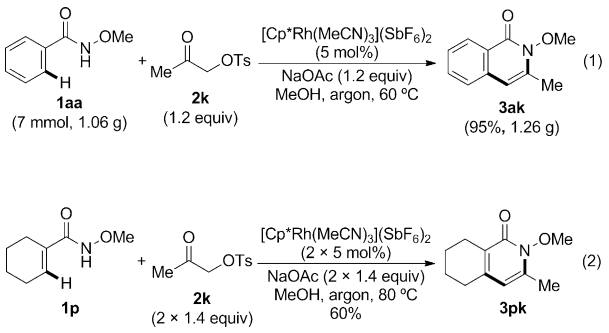
Scheme 4. Substrate scope: Variation of α-mesyloxyketones **2**. See **GP1** in the Supporting Information.

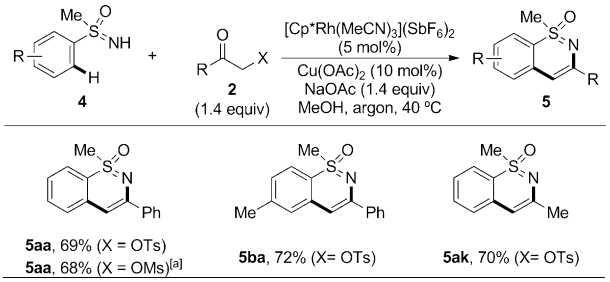


Scheme 5. Substrate scope: Reactions of different α-chloro- and α-tosyloxyketones. See **GP1** in the Supporting Information. [a] See **GP2** in the Supporting Information. [b] See **GP3** in the Supporting Information.

Besides the aryl ketones, we found that a dialkyl ketone derivative, 2-oxopropyl tosylate (**2k**), also worked efficiently (Scheme 5). In addition to **1a**, other heteroaryl amides, including furan **1m**, thiophene **1n**, and benzothiophene **1o**, also reacted with **2k** to generate the bisheterocycles in good yields. Notably, the condensations were more efficient than those with aryl ketone derivatives and thus no acid was necessary. In addition, this transformation is scalable and practical since a gram-scale reaction was equally efficient [Eq. (1)]. It is important to note that cyclohexenyl amide **1p** also participated in this reaction to generate highly substituted 2-pyridone **3pk** in a good yield through alkenyl C–H activation [Eq. (2)].

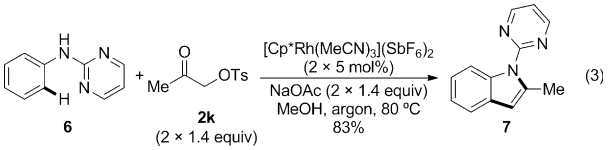
Besides the isoquinolones and 2-pyridones, we also applied this method to construct other important N-heterocycles with diverse directing groups. Recently, Bolm and coworkers disclosed the Rh^{III}-catalyzed oxidative annulation of sulfoximines with internal alkynes to generate 3,4-disubstituted 1,2-benzothiazines efficiently.[4p] Under slightly modified reaction conditions, sulfoximines (**4a** and **4b**) also showed good reactivity in the construction of 3-aryl- (**5aa** and **5ba**) and 3-methyl-substituted (**5ak**) 1,2-benzothiazines (Scheme 6), which are not easy to synthesize by other methods. Moreover, due to the high importance of indoles in natural products and drugs, many methods have been



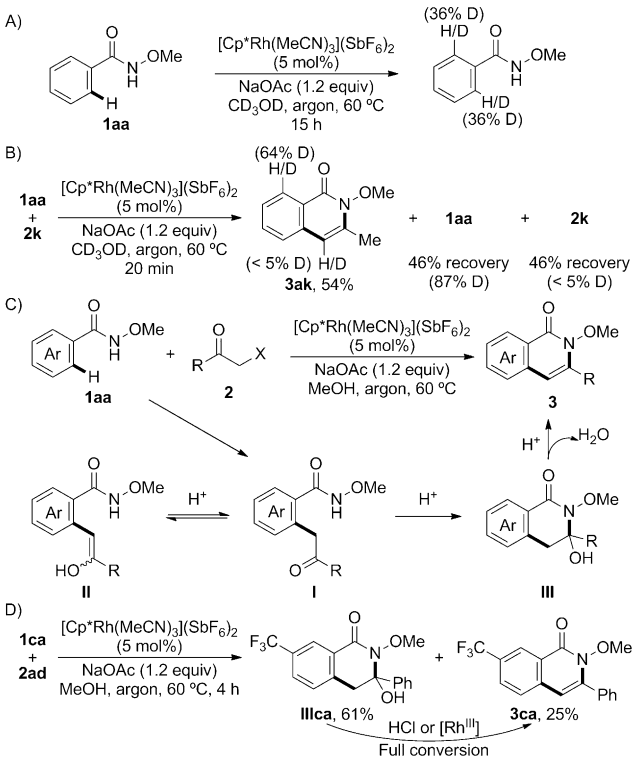


Scheme 6. Substrate scope: Reactions of sulfoximines. See **GP4** in the Supporting Information. [a] Yield determined by NMR spectroscopy.

developed to generate indoles from aniline derivatives and alkynes.[4,5] However, only 2,3-disubstituted indoles could be directly formed through Rh^{III}-catalyzed C–H activation. We were delighted to find that 2-phenylaminopyrimidine **6** generated 2-methylated indole **7** in good yield using this strategy [Eq. (3)].



Finally, we investigated the mechanism of the reaction with amides **1**. The faster alkylation of amides bearing EWGs indicates that the C–H activation might proceed through a concerted metalation–deprotonation (CMD) mechanism.[21] The reactions of **1aa** in CD_3OD indicate that the C–H activation is reversible in the absence or presence of **2k** (Scheme 7A and B; see the Supporting Information for details). Moreover, the electron density of the arene affects the condensation of the ketone intermediates **I** (Scheme 7C). For electron-poor amides, the nucleophilicity of nitrogen is lower than for those substituted with EDGs. In addition, the acidity of the α-H of corresponding ketone intermediates **I** is expected to be higher and the enols **II** would be more favored, which will slow down the condensation. This may also explain why the reactions with **2k**, whose ketone intermediates **I** are



Scheme 7. Mechanistic studies and discussion.

preferred, are always cleaner than those with aryl ketone derivatives. When the reaction of **1ca** with **2ad** was not treated with acid, we were able to isolate intermediate **IIIca** in 61% yield along with **3ca** in 25% yield. More importantly, **IIIca** was fully converted to **3ca** in the presence of HCl or catalytic $[Cp^*Rh(MeCN)_3](SbF_6)_2$ (see the Supporting Information), which indicated that the cationic Rh^{III} catalyst not only catalyzed the C–H activation and addition to the α-(pseudo)halo ketones but also promoted the condensation (Scheme 7D).[18]

In conclusion, we have demonstrated that the α-halo and pseudohalo ketones could be utilized as oxidized alkyne equivalents in Rh^{III}-catalyzed redox-neutral annulation to efficiently generate diverse N-heterocycles. This seems to be the first time that α-halo and pseudohalo ketones have served as $C(sp^3)$-based electrophiles in transition-metal-catalyzed C–H activation. Various 3-aryl- and 3-alkyl-substituted isoquinolones and a 2-pyridone could be generated in moderate to excellent yields through aryl and alkenyl C–H activation, respectively. Notably, this transformation is efficient and scalable. Moreover, the generality of this method has been demonstrated by the efficient and selective synthesis of some C-monoarylated 1,2-benzothiazines and a C-monomethylated indole, which are not easy to obtain by other methods. Due to the mild reaction conditions, a variety of functional groups are compatible with this transformation, leaving the opportunity for potential further functionalization.

Received: November 26, 2013
Published online: February 2, 2014

Keywords: C–H activation · isoquinolones · ketones · N-heterocycles · rhodium catalysis

[1] T. Eicher, S. Hauptmann, H. Suschitzky, *The Chemistry of Heterocycles: Structure, Reactions, Syntheses and Applications*, Wiley, Hoboken, **2003**.

[2] Selected reviews: a) D. A. Colby, R. G. Bergman, J. A. Ellman, *Chem. Rev.* **2010**, *110*, 624; b) L. Ackermann, *Chem. Rev.* **2011**, *111*, 1315; c) T. Newhouse, P. S. Baran, *Angew. Chem.* **2011**, *123*, 3422; *Angew. Chem. Int. Ed.* **2011**, *50*, 3362; d) H. M. L. Davies, J. Du Bois, J.-Q. Yu, *Chem. Soc. Rev.* **2011**, *40*, 1855; e) L. McMurray, F. O'Hara, M. J. Gaunt, *Chem. Soc. Rev.* **2011**, *40*, 1885; f) O. Baudoin, *Chem. Soc. Rev.* **2011**, *40*, 4902; g) S. H. Cho, J. Y. Kim, J. Kwak, S. Chang, *Chem. Soc. Rev.* **2011**, *40*, 5068; h) C.-L. Sun, B.-J. Li, Z.-J. Shi, *Chem. Rev.* **2011**, *111*, 1293; i) D. Zhao, J. You, C. Hu, *Chem. Eur. J.* **2011**, *17*, 5466; j) C. S. Yeung, V. M. Dong, *Chem. Rev.* **2011**, *111*, 1215; k) J. Wencel-Delord, T. Dröge, F. Liu, F. Glorius, *Chem. Soc. Rev.* **2011**, *40*, 4740; l) B.-J. Li, Z.-J. Shi, *Chem. Soc. Rev.* **2012**, *41*, 5588; m) J. Yamaguchi, A. D. Yamaguchi, K. Itami, *Angew. Chem.* **2012**, *124*, 9092; *Angew. Chem. Int. Ed.* **2012**, *51*, 8960; n) S. R. Neufeldt, M. S. Sanford, *Acc. Chem. Res.* **2012**, *45*, 936; o) N. Kuhl, M. N. Hopkinson, J. Wencel-Delord, F. Glorius, *Angew. Chem.* **2012**, *124*, 10382; *Angew. Chem. Int. Ed.* **2012**, *51*, 10236; p) J. Wencel-Delord, F. Glorius, *Nat. Chem.* **2013**, *5*, 369; q) A. V. Gulevich, A. S. Dudnik, N. Chernyak, V. Gevorgyan, *Chem. Rev.* **2013**, *113*, 3084.

[3] a) T. Satoh, M. Miura, *Chem. Eur. J.* **2010**, *16*, 11212; b) D. A. Colby, A. S. Tsai, R. G. Bergman, J. A. Ellman, *Acc. Chem. Res.* **2011**, *44*, 814; c) F. W. Patureau, J. Wencel-Delord, F. Glorius, *Aldrichimica Acta* **2012**, *45*, 31; d) G. Song, F. Wang, X. Li, *Chem. Soc. Rev.* **2012**, *41*, 3651; e) S. Chiba, *Chem. Lett.* **2012**, *41*, 1554.

[4] Selected examples: a) D. R. Stuart, M. Bertrand-Laperle, K. M. N. Burgess, K. Fagnou, *J. Am. Chem. Soc.* **2008**, *130*, 16474; b) N. Guimond, K. Fagnou, *J. Am. Chem. Soc.* **2009**, *131*, 12050; c) T. Fukutani, N. Umeda, K. Hirano, T. Satoh, M. Miura, *Chem. Commun.* **2009**, 5141; d) K. Morimoto, K. Hirano, T. Satoh, M. Miura, *Org. Lett.* **2010**, *12*, 2068; e) T. K. Hyster, T. Rovis, *J. Am. Chem. Soc.* **2010**, *132*, 10565; f) X. Wei, M. Zhao, Z. Du, X. Li, *Org. Lett.* **2011**, *13*, 4636; g) J. Jayakumar, K. Parthasarathy, C.-H. Cheng, *Angew. Chem.* **2012**, *124*, 201; *Angew. Chem. Int. Ed.* **2012**, *51*, 197; h) M. V. Pham, B. Ye, N. Cramer, *Angew. Chem.* **2012**, *124*, 10762; *Angew. Chem. Int. Ed.* **2012**, *51*, 10610; i) G. Zhang, L. Yang, Y. Wang, Y. Xie, H. Huang, *J. Am. Chem. Soc.* **2013**, *135*, 8850; j) D. Zhao, Q. Wu, X. Huang, F. Song, T. Lv, J. You, *Chem. Eur. J.* **2013**, *19*, 6239; k) C. Wang, H. Sun, Y. Fang, Y. Huang, *Angew. Chem.* **2013**, *125*, 5907; *Angew. Chem. Int. Ed.* **2013**, *52*, 5795; l) N. Quiñones, A. Seoane, R. García-Fandiño, J. L. Mascareñas, M. Gulías, *Chem. Sci.* **2013**, *4*, 2874; m) J. Du, B. Zhou, Y. Yang, Y. Li, *Chem. Asian J.* **2013**, *8*, 1386; n) S. Park, B. Seo, S. Shin, J.-Y. Son, P. H. Lee, *Chem. Commun.* **2013**, *49*, 8671; o) D. Zhao, C. Nimphius, M. Lindale, F. Glorius, *Org. Lett.* **2013**, *15*, 4504; p) W. Dong, L. Wang, K. Parthasarathy, F. Pan, C. Bolm, *Angew. Chem.* **2013**, *125*, 11787; *Angew. Chem. Int. Ed.* **2013**, *52*, 11573; q) N. Wang, B. Li, H. Song, S. Xu, B. Wang, *Chem. Eur. J.* **2013**, *19*, 358; r) H. Lee, Y.-K. Sim, J.-W. Park, C.-H. Jun, *Chem. Eur. J.* **2014**, *20*, 323.

[5] For examples with internal alkynes, see: a) X. Zhang, D. Chen, M. Zhao, J. Zhao, A. Jia, X. Li, *Adv. Synth. Catal.* **2011**, *353*, 719; b) P. C. Too, T. Noji, Y. J. Lim, X. Li, S. Chiba, *Synlett* **2011**, 2789; c) T. K. Hyster, T. Rovis, *Chem. Commun.* **2011**, *47*, 11846; d) X. Xu, Y. Liu, C.-M. Park, *Angew. Chem.* **2012**, *124*, 9506; *Angew. Chem. Int. Ed.* **2012**, *51*, 9372; e) G. Liu, Y. Shen, Z. Zhou, X. Lu, *Angew. Chem.* **2013**, *125*, 6149; *Angew. Chem. Int. Ed.* **2013**, *52*, 6033; f) D. Zhao, Z. Shi, F. Glorius, *Angew. Chem.* **2013**, *125*,

12652; *Angew. Chem. Int. Ed.* **2013**, *52*, 12426; g) B. Liu, C. Song, C. Sun, S. Zhou, J. Zhu, *J. Am. Chem. Soc.* **2013**, *135*, 16625; h) S.-C. Chuang, P. Gandeepan, C.-H. Cheng, *Org. Lett.* **2013**, *15*, 5750; i) X.-C. Huang, X.-H. Yang, R.-J. Song, J.-H. Li, *J. Org. Chem.*, DOI: 10.1021/jo402497v. For recent examples with other compounds, see: j) X. Huang, J. Huang, C. Du, X. Zhang, F. Song, J. You, *Angew. Chem.* **2013**, *125*, 13208; *Angew. Chem. Int. Ed.* **2013**, *52*, 12970; k) F. Hu, Y. Xia, F. Ye, Z. Liu, C. Ma, Y. Zhang, J. Wang, Angew. Chem., DOI: 10.1002/ange.201309650; *Angew. Chem. Int. Ed.*, DOI: 10.1002/anie.201309650.

[6] a) N. Guimond, S. I. Gorelsky, K. Fagnou, *J. Am. Chem. Soc.* **2011**, *133*, 6449; b) H. Wang, C. Grohmann, C. Nimphius, F. Glorius, *J. Am. Chem. Soc.* **2012**, *134*, 19592; c) J. R. Huckins, E. A. Bercot, O. R. Thiel, T.-L. Hwang, M. M. Bio, *J. Am. Chem. Soc.* **2013**, *135*, 14492.

[7] N. De Kimpe, R. Verhé, *α-Haloketones, α-Haloaldehydes and α-Haloimines*, Wiley, New York, **1988**, p. 1.

[8] a) M. Yasuda, S. Tsuji, Y. Shigeyoshi, A. Baba, *J. Am. Chem. Soc.* **2002**, *124*, 7440; b) C. F. Malosh, J. M. Ready, *J. Am. Chem. Soc.* **2004**, *126*, 10240; c) C. Liu, C. He, W. Shi, M. Chen, A. Lei, *Org. Lett.* **2007**, *9*, 5601; d) X. Dai, N. A. Strotman, G. C. Fu, *J. Am. Chem. Soc.* **2008**, *130*, 3302; e) P. M. Lundin, J. Esquivias, G. C. Fu, *Angew. Chem.* **2009**, *121*, 160; *Angew. Chem. Int. Ed.* **2009**, *48*, 154; f) P. M. Lundin, G. C. Fu, *J. Am. Chem. Soc.* **2010**, *132*, 11027; g) K. Huang, G. Li, W.-P. Huang, D.-G. Yu, Z.-J. Shi, *Chem. Commun.* **2011**, *47*, 7224.

[9] For the C–H activation with α-halo amides and esters, see: a) E. J. Hennessy, S. L. Buchwald, *J. Am. Chem. Soc.* **2003**, *125*, 12084; b) A. Nakatani, K. Hirano, T. Satoh, M. Miura, *Chem. Eur. J.* **2013**, *19*, 7691; c) C. Liu, D. Liu, W. Zhang, L. Zhou, A. Lei, *Org. Lett.* **2013**, *12*, 6166.

[10] a) Y. Li, B.-J. Li, W.-H. Wang, W.-P. Huang, X.-S. Zhang, K. Chen, Z.-J. Shi, *Angew. Chem.* **2011**, *123*, 2163; *Angew. Chem. Int. Ed.* **2011**, *50*, 2115; b) A. S. Tsai, M. E. Tauchert, R. G. Bergman, J. A. Ellman, *J. Am. Chem. Soc.* **2011**, *133*, 1248; c) M. E. Tauchert, C. D. Incarvito, A. L. Rheingold, R. G. Bergman, J. A. Ellman, *J. Am. Chem. Soc.* **2012**, *134*, 1482; d) K. D. Hesp, R. G. Bergman, J. A. Ellman, *Org. Lett.* **2012**, *14*, 2304; e) Y. Li, X.-S. Zhang, H. Li, W.-H. Wang, K. Chen, B.-J. Li, Z.-J. Shi, *Chem. Sci.* **2012**, *3*, 1634; f) Y. Li, X.-S. Zhang, Q.-L. Zhu, Z.-J. Shi, *Org. Lett.* **2012**, *14*, 4498; g) B. Zhou, Y. Yang, S. Lin, Y. Li, *Adv. Synth. Catal.* **2013**, *355*, 360; h) Y. Lian, T. Huber, K. D. Hesp, R. G. Bergman, J. A. Ellman, *Angew. Chem.* **2013**, *125*, 657; *Angew. Chem. Int. Ed.* **2013**, *52*, 629.

[11] a) J. Park, E. Park, A. Kim, Y. Lee, K.-W. Chi, J. H. Kwak, Y. H. Jung, I. S. Kim, *Org. Lett.* **2011**, *13*, 4390; b) Y. Li, X.-S. Zhang, K. Chen, K.-H. He, F. Pan, B.-J. Li, Z.-J. Shi, *Org. Lett.* **2012**, *14*, 636; c) S. Sharma, E. Park, J. Park, I. S. Kim, *Org. Lett.* **2012**, *14*, 906; d) Y. Yang, B. Zhou, Y. Li, *Adv. Synth. Catal.* **2012**, *354*, 2916; e) X. Shi, C.-J. Li, *Adv. Synth. Catal.* **2012**, *354*, 2933; f) Y. Lian, R. G. Bergman, J. A. Ellman, *Chem. Sci.* **2012**, *3*, 3088; g) Y. Lian, R. G. Bergman, L. D. Lavis, J. A. Ellman, *J. Am. Chem. Soc.* **2013**, *135*, 7122; h) P. W. Tan, N. A. B. Juwaini, J. Seayad, *Org. Lett.* **2013**, *15*, 5166; See also Ref. [10h].

[12] a) K. D. Hesp, R. G. Bergman, J. A. Ellman, *J. Am. Chem. Soc.* **2011**, *133*, 11430; b) S. Takebayashi, T. Shizuno, T. Otani, T. Shibata, *Beilstein J. Org. Chem.* **2012**, *8*, 1844; c) W. Hou, B. Zhou, Y. Yang, H. Feng, Y. Li, *Org. Lett.* **2013**, *15*, 1814.

[13] X. Li, S. Yu, F. Wang, B. Wan, X. Yu, *Angew. Chem.* **2013**, *125*, 2637; *Angew. Chem. Int. Ed.* **2013**, *52*, 2577.

[14] X.-S. Zhang, Q.-L. Zhu, F.-X. Luo, G. Chen, X. Wang, Z.-J. Shi, *Eur. J. Org. Chem.* **2013**, 6530.

[15] a) F. W. Patureau, T. Besset, N. Kuhl, F. Glorius, *J. Am. Chem. Soc.* **2011**, *133*, 2154; b) K. Muralirajan, K. Parthasarathy, C.-H. Cheng, *Angew. Chem.* **2011**, *123*, 4255; *Angew. Chem. Int. Ed.* **2011**, *50*, 4169.

[16] a) Z. Qi, M. Wang, X. Li, *Org. Lett.* **2013**, *15*, 5440; b) Y. Chen, F. Wang, W. Zhen, X. Li, *Adv. Synth. Catal.* **2013**, *355*, 353; c) L. Dong, C.-H. Qu, J.-R. Huang, W. Zhang, Q.-R. Zhang, J.-G. Deng, *Chem. Eur. J.* **2013**, *19*, 16537; See also Ref. [4c].

[17] B.-J. Li, H.-Y. Wang, Q.-L. Zhu, Z.-J. Shi, *Angew. Chem.* **2012**, *124*, 4014; *Angew. Chem. Int. Ed.* **2012**, *51*, 3948.

[18] a) Z. Shi, C. Grohmann, F. Glorius, *Angew. Chem.* **2013**, *125*, 5503; *Angew. Chem. Int. Ed.* **2013**, *52*, 5393. For recent examples with other compounds, see: b) R. Zeng, J. Ye, C. Fu, S. Ma, *Adv. Synth. Catal.* **2013**, *355*, 1963; c) R. Zeng, S. Wu, C. Fu, S. Ma, *J. Am. Chem. Soc.* **2013**, *135*, 18284; d) T. A. Davis, T. K. Hyster, T. Rovis, *Angew. Chem.* **2013**, *125*, 14431; *Angew. Chem. Int. Ed.* **2013**, *52*, 14181; e) B. Ye, P. A. Donets, N. Cramer, *Angew. Chem.* **2014**, *126*, 517; *Angew. Chem. Int. Ed.* **2014**, *53*, 507; f) Z. Shi, M. Boultadakis-Arapinis, D. C. Koester, F. Glorius, *Chem. Commun.* **2014**, DOI: 10.1039/C4CC00029C.

[19] For Rh^{III}-catalyzed C–H amination with halides as leaving groups, see: a) K.-H. Ng, Z. Zhou, W.-Y. Yu, *Org. Lett.* **2012**, *14*, 272; b) C. Grohmann, H. Wang, F. Glorius, *Org. Lett.* **2012**, *14*, 656; c) K.-H. Ng, Z. Zhou, W.-Y. Yu, *Chem. Commun.* **2013**, *49*, 7031; d) R.-J. Tang, C.-P. Luo, L. Yang, C.-J. Li, *Adv. Synth. Catal.* **2013**, *355*, 869.

[20] For the definition of the term atom economy, see: a) B. M. Trost, *Science* **1991**, *254*, 1471; for cross-couplings of mesylates, see: b) C. M. So, F. Y. Kwong, *Chem. Soc. Rev.* **2011**, *40*, 4963.

[21] D. Lapointe, K. Fagnou, *Chem. Lett.* **2010**, *39*, 1118.

