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Direct Synthesis of Primary Anilines via Nickel-mediated C(sp^2)-H Aminations

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Abstract. An efficient and mild protocol for the direct conversion of arene C–H bonds to C–NH_2 without the need for extra deprotection step has been established, and to the best of our knowledge, this is the first time that the synthesis of primary anilines via nickel-mediated C(sp^2)-H activations has been reported. This approach utilizes 8-aminoquinoline as the directing group and sodium azide, a cheap and commercially available material, as the nitrogen source. In addition, the reaction is highly selective, affording the *mono*- *ortho*-aminated benzamides only. The reaction tolerates a broad range of substrates with diverse functional groups and the corresponding *ortho*-aminated benzamides were efficiently synthesized in 41-82% yields.

Keywords: C-H activation; primary aniline; nickel salt; sodium azide; anthranilic acid

The development of new ways for the synthesis of C-N bonds has always been a central topic in organic synthesis because C-N bonds are ubiquitous in organic compounds.[1] Among the various C-N bond containing compounds, anilines hold a special place due to their wide presence in natural products, pharmaceuticals, dyes, pigments and agrochemicals.[2] Traditionally, the synthesis of anilines has largely relied on the reduction of nitroarenes which themselves are produced through the classical electrophilic aromatic nitration reaction.[3] However, this method tends to suffer from problems such as producing large amount of toxic waste, harsh reaction conditions as well as selectivity issues. Alternatively, anilines can be efficiently constructed through transition metal catalyzed couplings such as Buchwald-Hartwig amination,[4] Ullmann-Goldberg coupling[5] and Chan-Lam reaction.[6] However, the need to use prefunctionalized starting materials and expensive catalysts and ligands make them less desirable. In light of above problems, chemists are searching for new ways to construct C-N bonds via C-H activation mode since a direct C-H bond amination approach would be much more concise and atom economical.

Indeed, C-N bond formation via C-H activation catalyzed or mediated by noble transition metals has long been known.[7] However, due to cost issues associated with expensive catalysts, recently chemists are beginning to develop C-H amination reactions using cheap transition metals as the promoter.[8-11] With suitable bidentate directing groups, considerable advances have been made in the area of arene C-H bond aminations and a variety of cheap metal promoters including Cu,[8] Ni,[9] Co[10] or Fe[11] salts have been shown to be competent catalysts or promoters for the C(sp^2)-H bond amination. For example, Daugulis group in 2013 was the first to report a copper-catalyzed selective *ortho*-amination of *N*-(quinolin-8-yl)benzamide with alkylamines under the assistance of 8-aminoquinoline.[8a] Shortly after that, Nakamura and Ilies reported that a similar *ortho*-amination reaction can take place with *N*-(quinolin-8-yl)benzamide using *N*-chloroamines as the amine source under Fe-catalysis.[11] Later on, Zhang and Liu disclosed a nickel-catalyzed version using silver salt as the oxidant.[9] In 2016, Zhang further demonstrated that cobalt catalyst can also be used to catalyze the same amination process.[10b] Besides 8-aminoquinoline,[12] other directing groups such as 2-aminophenyl oxazoline,[8b] 2-aminopyridine-1-oxide[10a] as well as 2-aminophenyl pyrazole[8j] have been shown to be viable auxiliaries for cheap transition metal promoted C(sp^2)-H aminations. Although numerous elegant works were reported in this field, most achievements of aromatic C−H bond aminations can only furnish a limited scope of aryl secondary or tertiary amines.[8-11] The direct conversion of aromatic C–H bonds to

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C–NH_2 promoted by cheap transition metal is actually rare.[13] Coincidentally, primary anilines are extremely useful because they can serve as precursors for many other functional groups, such as aryl diazonium salts, azoaryls, haloaryls as well as a broad scope of aryl secondary or tertiary amines.[14] Taking this into consideration and also in continuation of our efforts on the development of new reactions based on C−H activations,[15] we launched a study toward the synthesis of primary anilines. Herein, we disclose a novel route for the direct conversion of aromatic C–H bonds to C–NH_2 through nickel-mediated C−H activation using sodium azide, a cheap and commercially available material, as the nitrogen source under mild conditions. The reaction exhibits high *chemo*- and *mono*-selectivity in forming various primary anilines products, which can be easily converted into anthranilic acids, a critical scaffold in perfumes, agrochemicals and medicinal chemistry (Figure 1). [16]

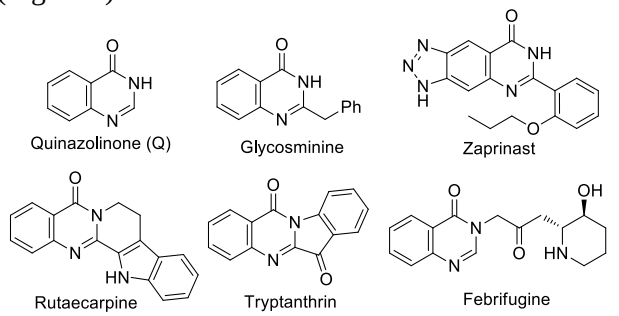
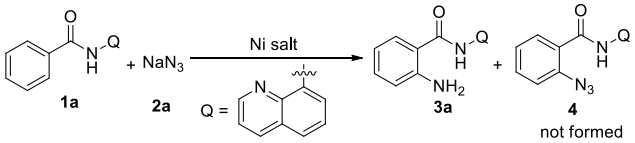


Figure 1. Biologically active anthranilic acid derivatives

Our original plan was to install an azide functionality on the aromatic ring through metal catalyzed 8-aminoquinoline assisted C(sp^2)-H activations since azides are very useful intermediates for transformations such as "Click chemistry".[17] However, much to our surprise, preliminary experimental results showed that actually a primary aniline derivative **3a** was obtained instead of the expected azide **4** when *N*-(quinolin-8-yl)benzamide **1a** was treated with 4 equiv of NaN_3 (**2a**), 2 equiv of $NiCl_2$ in the presence of 1 equiv of K_3PO_4 in DMSO at 100 °C under a nitrogen atmosphere (Table 1, entry 1). In order to optimize the reaction conditions, various bases, solvents, additives, nickel salts and oxidants were screened (Table 1). Tests revealed that K_2CO_3 was the optimal base while bases such as TEA, KOAc, and *t*-BuOK either gave inferior yields or failed completely (Table 1, entries 2-5). Surprisingly, better yields of **3a** were achieved with only 0.5 equiv of base. The use of more or less amount of base actually was detrimental to the reaction (not shown in Table 1). On the other hand, replacing solvent DMSO with DMAc, DMF, DCE or MeCN did not benefit the reaction (Table 1, entries 6-9). Subsequently, we further examined the possibility of using water and phase transfer catalyst as additives.[15g] Gratifyingly, we found that the yield of **3a** can be increased if a phase transfer catalysts such as tetrabutylammonium acetate (TBAA), tetrabutylammonium iodide (TBAI), or tetrabutyla-mmonium bromide (TBAB) was added into the reaction mixture, and the best yield of 59% was achieved with the addition of 2 equiv of TBAA (Table 1, entries 10-12). The yield of **3a** could be further elevated to 72% with appropriate amount of water was added into the reaction mixture (Table 1, entries 13-15). It is worthwhile to point out that the reaction is highly *mono*-selective and no diamination product is observed. After establishing TBAA and water as the optimal additives, we focused on investigating other nickel salts such as $NiBr_2$, NiI_2, $Ni(OTf)_2$ as promoter. Unfortunately, we did not see any improvement with all the other nickel salts tested (Table 1, entries 14, 16-18). It should be noted that in the absence of nickel salt, the reaction failed to deliver the desired products and all the starting materials were recovered from the reaction system (Table 1, entry 19). This indicated that nickel catalyst played an indispensable role in this reaction. Moreover, we found that the reaction did not proceed at all using a catalytic amount of nickel salt (5 mol%) using O_2 or Ag_2CO_3 as oxidant (Table 1, entry 20 and 21).

Table 1. Screening of the reaction conditions for the amination of **1a**[a]



Entry	Ni salt	Base	Solvent	Additive	Yield(%)[b]
1	$NiCl_2$	K_3PO_4	DMSO	-	21
2	$NiCl_2$	TEA	DMSO	-	0
3	$NiCl_2$	KOAc	DMSO	-	18
4[c]	$NiCl_2$	^{t}BuOK	DMSO	-	0
5	$NiCl_2$	K_2CO_3	DMSO	-	47
6	$NiCl_2$	K_2CO_3	DMAc	-	46
7	$NiCl_2$	K_2CO_3	DMF	-	44
8	$NiCl_2$	K_2CO_3	DCE	-	0
9	$NiCl_2$	K_2CO_3	MeCN	-	0
10	$NiCl_2$	K_2CO_3	DMSO	TBAI	53
11	$NiCl_2$	K_2CO_3	DMSO	TBAB	52
12	$NiCl_2$	K_2CO_3	DMSO	TBAA	59
13[c]	$NiCl_2$	K_2CO_3	DMSO	TBAA	67
14[d]	$NiCl_2$	K_2CO_3	DMSO	TBAA	72
15[e]	$NiCl_2$	K_2CO_3	DMSO	TBAA	70
16[d]	$NiBr_2$	K_2CO_3	DMSO	TBAA	64
17[d]	NiI_2	K_2CO_3	DMSO	TBAA	62
18[d]	$Ni(OTf)_2$	K_2CO_3	DMSO	TBAA	65
19[d]	-	K_2CO_3	DMSO	TBAA	0
20[f]	$NiCl_2$	K_2CO_3	DMSO	TBAA	0
21[g]	$NiCl_2$	K_2CO_3	DMSO	TBAA	0

[a]Reaction conditions: amide **1a** (0.2 mmol), **2** (0.8 mmol), Ni salt (0.4 mmol), Base (0.1 mmol), Additive (0.4 mmol), Solvent (4.0 mL), 100 °C under N_2 for 24 h. [b]Isolated yield. [c]Add 0.05 mL water as additive. [d]Add 0.10 mL water as additive. [e]Add 0.15 mL water as additive. [f]Ni salt (0.05 mmol) and under O_2. [g]Ni salt (0.05 mmol), Ag_2CO_3 (0.4 mmol).

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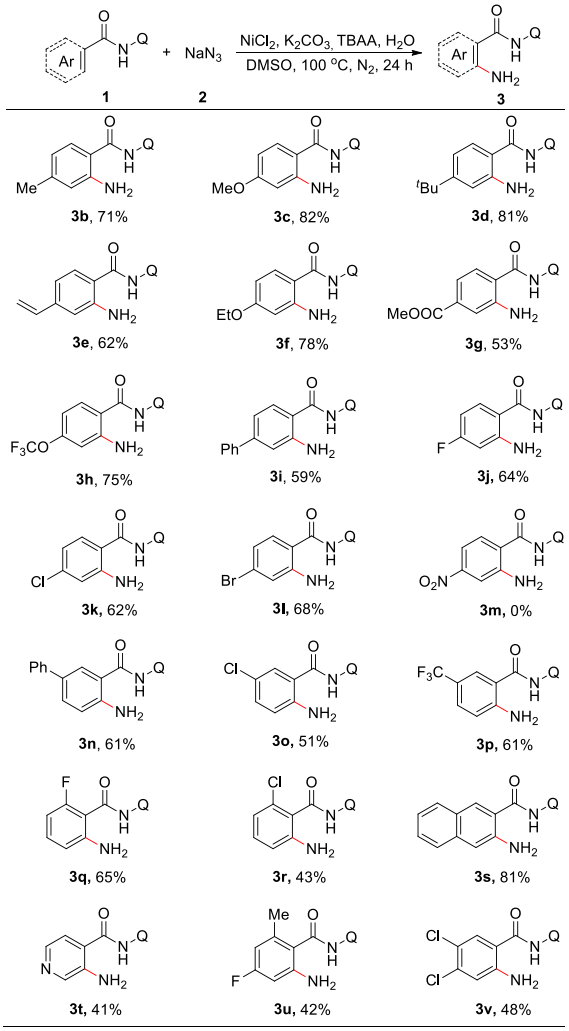
Experiments also showed that 2 equiv of $NiCl_2$ was necessary for the reaction to reach completion and further increasing the amount of $NiCl_2$ did not improve the yield. Based on the above results, we decided to set reacting **1a** with 4 equiv of **2a**, 2 equiv of $NiCl_2$, 2 equiv of TBAA and H_2O (0.50 mL/mmol) in the presence of 0.5 equiv of K_2CO_3 in DMSO at 100 °C as our standard conditions.

In order to explore the scope and limitation of this direct conversion of aromatic C–H bond to C–NH_2 reaction, various benzamides with diverse functional groups were tested under the established reaction conditions. We found that the reaction worked very well for a variety of substituted benzamides, affording the corresponding primary anilines in yields ranging from 41-82% and the results were summarized in Table 2. As illustrated in Table 2, this protocol was compatible with a wide range of functional groups such as alkyl, alkoxy, vinyl, fluoro, chloro, bromo, ester, aryl as well as trifluoromethyl

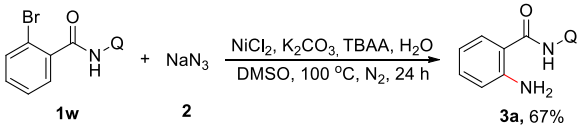
Table 2. Scope of the benzamides[a,b]



[a]Reaction conditions: amide **1a** (0.2 mmol), **2** (0.8 mmol), $NiCl_2$ (0.4 mmol), K_2CO_3 (0.1 mmol), TBAA (0.4 mmol), H_2O (0.1 mL), Solvent (4.0 mL), 100 °C under N_2 for 24 h. [b]Isolated yield.

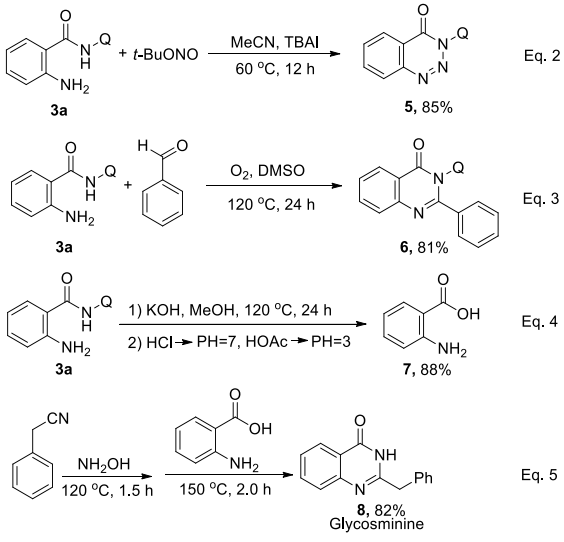
groups. Gratifyingly, a benzamide bearing a vinyl group on the *para*-position underwent the desired coupling to give the corresponding product **3e** in 62% yield, indicating that the vinyl group was not sensitive toward the reaction conditions. In contrast, the reaction of a nitro-substituted benzamide failed to deliver the desired product when it was subjected to the optimum reaction conditions, as decomposition of the starting material was observed (Table 2, entry **3m**). This suggested that the electron density on the phenyl ring is a critical factor for the reaction. It should be noted that a pyridine derived amide was also found to be a viable coupling partner, furnishing **3t** in 41% yield. In addition, even though 2-fluoro or 2-chloro substituted benzamide reacted normally to generate **3q** in 65% yield or **3r** in 43% yield respectively, what was obtained from the reaction of 2-bromobenzamides with sodium azide was actually **3a** (Scheme 1, Eq 1). We suspected that a nucleophilic aromatic substitution of the bromide took place before the C-H activation. We were disappointed to find that a 1-cyclohexene-1-carboxylic acid derived amide failed to react when it was subjected to the optimized conditions (not shown in Table 2).

Scheme 1. Nickel-mediated reaction of 2-bromo-benzamide with sodium azide.



The synthetic utility of this method was demonstrated by converting our products into several representative scaffolds. 1,2,3-benzotriazine-4-(3H)-one derivative **5** can be efficiently constructed with *tert*-butyl nitrite and **3a** in 85% yield (Scheme 2, Eq 2).[18] Meanwhile, quinazolin-4(3H)-one **6** can be

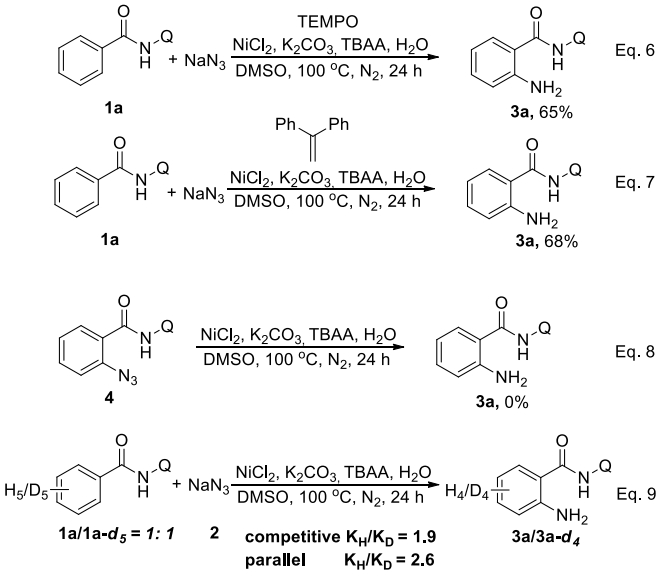
Scheme 2. Removal of the directing group and derivatization of the obtained products.



obtained in 81% yield by treating **3a** with benzaldehyde under an oxygen atmosphere. (Scheme 2, Eq. 3).[19] Moreover, we were able to remove the directing group by simple hydrolysis in methanol and subsequent careful pH-adjustment. The resultant anthranilic acid was transformed into a biologically active compound glycosminine according to literature procedure in excellent yield (Scheme 2, Eq. 4 and 5).[20,21]

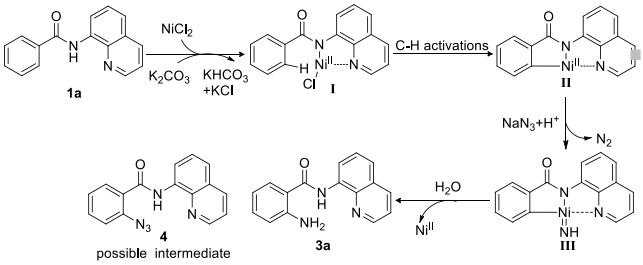
To gain insight into the mechanism of our reaction, a series of mechanistic experiments were performed (Scheme 3). First, radical inhibition experiments were implemented. We found that radical scavengers such as 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) and 1,1-diphenylethylene (DPE) did not affect the reaction efficiency under optimized conditions (Scheme 3, Eq. 6 and 7). These results suggested that the reaction may not involve radical process. A possible intermediate **4** was synthesized and subjected to the optimum conditions. However, no desired **3a** was formed and yet azide **4** was completely consumed. Kinetic isotopic effect (KIE) studies of this amination with sodium azide showed that intermolecular K_H/K_D of **1a** to **1a-d**$_5$ was 1.9 when a 1:1 mixture of **1a** and **1a-d**$_5$ was subjected to the optimized conditions in the same flask (Scheme 3, Eq. 9). On the other hand, K_H/K_D was determined to be around 2.6 if the reactions of **1a** and **1a-d**$_5$ were run parallelly. The competitive and parallel K_H/K_D values suggested that the cleavage of the *ortho* C-H bond may be involved in the rate-determining step.

Scheme 3. Mechanistic Studies



Although the exact mechanism is still not clear at present, based on the preliminary mechanistic experiments and literature precedents,[22] a plausible mechanism for the nickel-mediated C(sp^2)-H amination of benzamides is proposed and depicted in Scheme 4. The reaction is initiated by the complexation of benzamide **1a** with nickel salt to afford Ni(II)-complex **I**, which subsequently undergoes chelation-directed C-H activation to form intermediate **II**. Intermediate **II** next reacts with HN_3 generated in situ to form a Ni-nitrenoid intermediate **III**.[22f-h] Finally, intermediate **III** is transformed to **3a** after nitrene inserts into the C-Ni bond followed by protonolysis. Since not much is known about the reaction, other mechanisms could also operate here. For example, although the transformation of azide **4** to **3a** did not occur under the standard conditions, the formation of azide **4** as an intermediate couldn't be fully ruled out.

Scheme 4. Possible reaction mechanism



In conclusion, we have developed an efficient and mild protocol for the direct conversion of aromatic C-H bonds to C–NH_2 via 8-aminoquinoline assisted nickel-mediated C(sp^2)-H activations. Highly *mono*-selective *ortho*-amination of benzamides was achieved by treating various benzamides with sodium azide in the presence of simple Ni-salt. Compared with other known methods, our approach gives the primary anilines directly and utilizes cheap sodium azide as the nitrogen source. Notable features of the protocol include mild reaction conditions, excellent *mono*-selectivity and *ortho*-selectivity as well as good functional group compatibility. Preliminary study indicated that the reactions may go through a C-H activation process. Current efforts are directed towards making this reaction catalytic and the results will be reported in due course.

Experimental Section

Benzamide **1** (0.2 mmol), NaN_3 (52 mg, 0.8 mmol), $NiCl_2$ (52 mg, 0.4 mmol), K_2CO_3 (14 mg, 0.1 mmol), TBAA (120 mg, 0.4 mmol), H_2O (0.1 mL) and DMSO (4.0 mL) were added to a 35 mL Schlenk flask equipped with a high-vacuum PTFE valve-to-glass seal. Then the flask was sealed under N_2 and stirred at 100 °C for 24 h. After the reaction was quenched by addition of water, the mixture was extracted with dichloromethane, and the combined organic layer was dried over sodium sulfate. Concentration in vacuo followed by silica gel column purification with petroleum ether /ethyl acetate eluent gave the desired product **3**.

References

[1] a) J.-Q. Yu, Z. Shi, *Top. Curr. Chem.* **2010**, *292*, 347-378; b) Y. Park, Y. Kim, S. Chang, *Chem. Rev.* **2017**, *117*, 9247-9301; c) Y. Zhou, J. Yuan, Q. Yang, Q. Xiao, Y. Peng, *ChemCatChem.* **2016**, *8*, 2178-2192; d) J. Jiao, K. Murakami, K. Itami, *ACS Catal.* **2015**, *6*, 610-633; e) H. Kim, S. Chang, *ACS Catal.* **2016**, *6*, 2341-2351; f) H. Kim, S. Chang, *Acc. Chem. Res.* **2017**, *50*, 482-486; g) H. M. Davies, M. S. Long, *Angew. Chem. Int. Ed.* **2005**, *44*, 3518-3520; h) F. Collet, C. Lescot, P. Dauban, *Chem. Soc. Rev.* **2011**, *40*, 1926-1936; i) J. D. Bois, *Org. process. Res. Dev.* **2011**, *15*, 758-762.

[2] a) S. A. Lawrence, *Amines : Synthesis Properties and Applications*, Cambridge University Press, Cambridge, **2004**; b) U. Scholz, B. Schlummer, *Arylamines, in Science of Synthesis*, Georg Thieme, Stuttgart, **2007**; c) Z. Rappoport, *The Chemistry of Anilines*, Wiley-VCH, Weinheim, **2007**; d) A. Ricci, *Amino Group Chemistry*: *From Synthesis to the Life Sciences*, Wiley-VCH, Weinheim, **2008**.

[3] a) H. U. Blaser, U. Siegrist, H. Steiner, M. Studer, *Fine Chem. Heterog. Catal.* **2001**, 389; b) T. Mallat, A. Baiker, W. Kleist, K. Koehler, *Handbook of Heterogeneous Catalysis*, 2nd ed. **2008**, *7*, 3548.

[4] Buchwald-Hartwig reaction please see: a) F. Paul, J. Patt, J. F. Hartwig, *J. Am. Chem. Soc.* **1994**, *116*, 5969-5970; b) J. F. Hartwig, *Acc. Chem. Res.* **2008**, *41*, 1534-1544; c) D. S. Surry, S. L. Buchwald, *Angew. Chem. Int. Ed.* **2008**, *47*, 6338-6361.

[5] Ullmann-Goldberg condensation please see: a) F. Ullmann, *Ber. Dtsch. Chem. Ges*. **1903**, *36*, 2382-2384; b) I. Gold-berg, *Ber. Dtsch. Chem. Ges.* **1906**, *39*, 1691-1692.

[6] Chan-Lam coupling please see: a) D. M. T. Chan, K. L. Monaco, R. Wang, M. P. Winteres, *Tetrahedron Lett.* **1998**, *39*, 2933-2936; b) P. Y. S. Lam, C. G. Clark, S. Saubern, J. Adams, M. P. Winters, D. M. T. Chan, A. Combs, *Tetrahedron Lett*. **1998**, *39*, 2941-2944.

[7] a) W. C. P. Tsang, N. Zheng, S. L. Buchwald, *J. Am. Chem. Soc.* **2005**, *127*, 14560-14561; b) K. Inamoto, T. Saito, M. Katsuno, T. Sakamoto, K. Hiroya, *Org. Lett.* **2007**, *9*, 2931-2934; c) M. Wasa, J.-Q. Yu, *J. Am. Chem. Soc.* **2008**, *130*, 14058-14059; d) J. A. Jordan-Hore, C. C. C. Johansson, M. Gulias, E. M. Beck, M. J. Gaunt, *J. Am. Chem. Soc.* **2008**, *130*, 16184-16186; e) T.-S. Mei, X. Wang, J.-Q. Yu, *J. Am. Chem. Soc.* **2009**, *131*, 10806-10807.

[8] a) L. D. Tran, J. Roane, O. Daugulis, *Angew. Chem. Int. Ed.* **2013**, *52*, 6043-6046; b) M. Shang, S. Z. Sun, H. X. Dai, J. Q. Yu, *J. Am. Chem. Soc.* **2014**, *136*, 3354-3357; c) B. K. Singh, A. Polley, R. Jana, *J. Org. Chem.* **2016**, *81*, 4295-4303; d) C. Yamamoto, K. Takamatsu, K. Hirano, M. Miura, *J. Org. Chem.* **2016**, *81*, 7675-7684; e) N. T. T. Tran, Q. H. Tran, T. Truong, *J. Catal.* **2014**, *320*, 9-15; f) P. Sadhu, T. Punniyamurthy, *Chem. Commun.* **2016**, *52*, 2803-2806; g) J. Roane, O. Daugulis, *J. Am. Chem. Soc.* **2016**, *138*, 4601-4607; h) S. Pradhan, P. B. De, T. Punniyamurthy, *J. Org. Chem.* **2017**, *82*, 4883-4890; i) Q. Li, S.-Y. Zhang, G. He, Z. Ai, W. A. Nack, G. Chen, *Org. Lett.* **2014**, *16*, 1764-1767; j) W. C. Lee, Y. Shen, D. A. Gutierrez, J. J. Li, *Org. Lett.* **2016**, *18*, 2660-2663.

[9] Q. Yan, Z. Chen, W. Yu, H. Yin, Z. Liu, Y. Zhang, *Org. Lett.* **2015**, *17*, 2482-2485.

[10] a) L.-B. Zhang, S.-K. Zhang, D. Wei, X. Zhu, X.-Q. Hao, J.-H. Su, J.-L. Niu, M.-P. Song, *Org. Lett.* **2016**, *18*, 1318-1321; b) Q. Yan, T. Xiao, Z. Liu, Y. Zhang, *Adv. Synth. Catal.* **2016**, *358*, 2707-2711; c) C. Du, P.-X. Li, X. Zhu, J.-N. Han, J.-L. Niu, M.-P. Song, *ACS Catal.* **2017**, *7*, 2810-2814.

[11] T. Matsubara, S. Asako, L. Ilies, E. Nakamura, *J. Am. Chem. Soc.* **2014**, *136*, 646-649.

[12] For selected examples of C-H activation under the assistance of 8-aminoquinoline: a) J. Liu, G. Chen, Z. Tan, *Adv. Synth. Catal.* **2016**, *358*, 1174-1194; b) G. Rouquet, N. Chatani, *Angew. Chem. Int. Ed.* **2013**, *52*, 11726-11743; c) W.-H. Rao, B.-F. Shi, *Org. Chem. Front.* **2016**, *3*, 1028-1047; d) V. Prakash Reddy, R. Qiu, T. Iwasaki, N. Kambe, *Org. Biomol. Chem.* **2015**, *13*, 6803-6813; e) X. Wang, P. Xie, R. Qiu, L. Zhu, T. Liu, Y. Li, T. Iwasaki, C.-T. Au, X. Xu, Y. Xia, S.-F. Yin, N. Kambe, *Chem. Commun.* **2017**, *53*, 8316-8319; f) J. Liu, Z. Xue, Z. Zeng, Y. Chen, G. Chen, *Adv. Synth. Catal.* **2016**, *358*, 3694-3699; g) G. Chen, X. Zhang, Z. Zeng, W. Peng, Q. Liang, J. Liu, *ChemistrySelect* **2017**, *2*, 1979-1982.

[13] a) C. Grohmann, H. Wang, F. Glorius, *Org. Lett.* **2013**, *15*, 3014-3017; b) J. Peng, M. Chen, Z. Xie, S. Luo, Q. Zhu, *Org. Chem. Front.* **2014**, *1*, 777-781.

[14] a) H. J. Lucas, E. R. Kennedy, *Organic Syntheses* **1939**, *19*, 55; b) M. D. Bochare, M. S. Degani, *ACS Sustainable Chem. Eng.* **2017**, *5*, 3716-3720; c) S. Gomez, J. A. Peters, T. Maschmeyer, *Adv. Synth. Catal.* **2002**, *344*, 1037-1057; d) T. T. Dang, P. Ramalingam, A. M. Seayad, *ACS Catal.* **2015**, *5*, 4082-4088.

[15] a) J. Liu, S. Zhuang, Q. Gui, X. Chen, Z. Yang, Z. Tan, *Adv. Synth. Catal.* **2015**, *357*, 732-738; b) J. Liu, L. Yu, S. Zhuang, Q. Gui, X. Chen, W. Wang, Z. Tan, *Chem. Commun.* **2015**, *51*, 6418-6421; c) Q. Gui, X. Chen, L. Hu, D. Wang, J. Liu, Z. Tan, *Adv. Synth. Catal.* **2016**, *358*, 509-514; d) X. Chen, Z. Tan, Q. Gui, L. Hu, J. Liu, J. Wu, G. Wang, *Chem. Eur. J.* **2016**, *22*, 6218-6222; e) L. Hu, X. Chen, Q. Gui, Z. Tan, G. Zhu, *Chem. Commun.* **2016**, *52*, 6845-6848; f) L. Hu, Q. Gui, X. Chen, Z. Tan, G. Zhu, *Org. Biomol. Chem.* **2016**, *14*, 11070-11075; g) L. Yu, H. Huang, X. Chen, L. Hu, Y. Yu, Z. Tan, *Chem. Commun.* **2017**, *53*, 4597-4600; h) J. Wu, D. Wang, X. Chen, Q. Gui, H. Li, Z. Tan, G. Huang, G. Wang, *Org. Biomol. Chem.* **2017**, *15*, 7509-7512. (i) L. Hu, X. Chen, L. Yu, Y. Yu, Z. Tan, G. Zhu, Q. Gui, *Org. Chem. Front*. **2017**, DOI: 10.1039/c7qo00717e.

[16] a) Y. Takase, T. Saeki, N. Watanabe, H. Adachi, S. Souda, I. Saito, *J. Med. Chem.* **1994**, *37*, 2106-2111; b); H. Kikuchi, K. Yamamoto, S. Horoiwa, S. Hirai, R. Kasahara, N. Hariguchi, M. Matsumoto, Y. Oshima, *J. Med. Chem.* **2006**, *49*, 4698-4706; c) X. Liu, H. Fu, Y. Jiang, Y. Zhao, *Angew. Chem. Int. Ed.*

2009, *48*, 348-351; d) T. Abe, K. Kida, K. Yamada, *Chem. Commun.* **2017**, *53*, 4362-4365.

[17] a) W. G. Lewis, L. G. Green, F. Grynszpan, Z. Radic , P. R. Carlier, P. Taylor, M. G. Finn, K. B. Sharpless, *Angew. Ch*em. *Int. Ed.* **2002**, *41*, 1053-1057; b) V. V. Rostovtsev, L. G. Green, V. V. Fokin, K. B. Sharpless, *Angew. Chem. Int. Ed.* **2002**, *41*, 2596-2599; c) Y. Bourne, H. C. Kolb, Z. Radic, K. B. Sharpless, P. Taylor, P. Marchot, *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 1449-1454; d) L. Zhang, X. Chen, P. Xue, H. H. Y. Sun, I. D. Williams, K. B. Sharpless, V. V. Fokin, G. Jia, *J. Am. Chem. Soc.* **2005**, *127*, 15998-15999.

[18] Y. Yan, H. Li, B. Niu, C. Zhu, T. Chen, Y. Liu, *Tetrahedron Lett.* **2016**, *57*, 4170-4173.

[19] a) N. Y. Kim, C.-H. Cheon, *Tetrahedron Lett.* **2014**, *55*, 2340-2344; b) W. Phakhodee, S. Wangngae, M. Pattarawarapan, *J. Org. Chem.* **2017**, *82*, 8058-8066.

[20] B. Khan, R. Kant, D. Koley, *Adv. Synth. Catal.* **2016**, *358*, 2352-2358.

[21] M. Adib, S. Ansari, A. Mohammadi, H. R. Bijanzadeh, *Tetrahedron Lett.* **2010**, *51*, 30–32.

[22] a) S.-Y. Yan, Y.-J. Liu, B. Liu, Y.-H. Liu, B.-F. Shi, *Chem. Commun.* **2015**, *51*, 4069-4072; b) T. Kubo, N. Chatani, *Org. Lett.* **2016**, *18*, 1698-1701; c) J. Peng, Z. Xie, M. Chen, J. Wang, Q. Zhu, *Org. Lett.* **2014**, *16*, 4702-4705; d) T. Maejima, M. Ueda, J. Nakano, Y. Sawama, Y. Monguchi, H. Sajiki, *J. Org. Chem.* **2013**, *78*, 8980-8985; e) M. Li, Y. Yang, D. Zhou, D. Wan, J. You, *Org. Lett.* **2015**, *17*, 2546-2549; f) D. J. Mindiola, G. L. Hillhouse, *J. Am. Chem. Soc.* **2001**, *123*, 4623-4624; g) R. Waterman, G. L. Hillhouse, *J. Am. Chem. Soc.* **2008**, *130*, 12628-12629; h) D. E. Herbert, N. C. Lara, T. Agapie, *Chem. Eur. J.* **2013**, *19*, 16453-16460.

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