ChemPubSoc Europe

DOI: 10.1002/chem.201600229

CHEMISTRY
A European Journal
Communication

Organic Synthesis

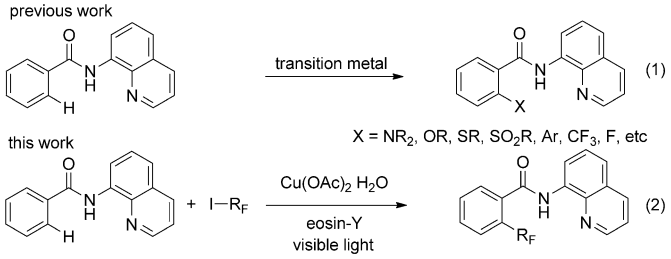
Photocatalytic/Cu-Promoted C–H Activations: Visible-light-Induced *ortho*-Selective Perfluoroalkylation of Benzamides

Xiang Chen,[a] Ze Tan,*[a] Qingwen Gui,[a] Liang Hu,[a] Jidan Liu,[a] Jing Wu,[a, b] and Guangwei Wang*[b]

Abstract: A visible-light-induced and copper-promoted perfluoroalkylation of benzamides was successfully developed under the assistance of an 8-aminoquinoline directing group. It provides a straightforward method for the synthesis of *ortho*-perfluoroalkyl-substituted benzoic acid derivatives. The reaction employs a cheap organic dye eosin Y as the photoredox catalyst and is run under the irradiation of a 26 W fluorescent LED light bulb.

Recently, the development of new methods for the formation of C–C and C–X bonds by transition-metal catalyzed or promoted functionalization of C–H bonds has been area of intensive research.[1] Since Daugulis' pioneering work,[2] 8-aminoquinoline has emerged as one of the most powerful and versatile directing groups for transition-metal catalyzed or -promoted functionalization of C–H bonds, as exemplified by the huge number of recent publications in this area.[2–9] Cu-,[2a–d,3c,4] Pd-,[5] Ni-,[6,3d] Co-,[2e–h,7] and Fe-catalyzed[8] or -mediated chelation-assisted C–H bond activations to construct C–C and C–X bonds (X = S, O, N, F) [Eq. (1)] with the aid of an 8-aminoquinoline directing group have been developed by the groups of Daugulis,[2] Hirano, and Miura,[3c,4a–e] Ge,[4g,h,6j] Kuninobu and Kanai,[4i,j,5f] Stahl,[4f] Chatani,[3b,d,6a–d] and others.[5a–e,6e–i] Ours and other groups also independently developed the selective *ortho*-sulfonylation and nitration of benzamides bearing the 8-aminoquinoline group.[9] Besides the 8-aminoquinoline group, a 2-aminophenyloxazoline group developed by Yu and Dai, and a (pyridine-2-yl)isopropylamine group developed by Shi are also powerful bidentate directing groups for transition-metal-catalyzed or -promoted C–H activations.[10]

Fluoroalkylated molecules are widely exploited in applications, such as materials, agrochemicals, pharmaceuticals, and many other areas of research due to their unique physical, chemical, and biological properties. Among these organofluorine compounds, those bearing trifluoromethyl and perfluoroalkyl (R_F) groups have been receiving significant interest because of their metabolic stability, lipophilicity and electron-withdrawing properties.[11] One of the most common ways of introducing trifluoromethyl or perfluoroalkyl groups involves the generation of trifluoromethyl and perfluoroalkyl radicals.[12] For example, when perfluoroalkyl iodides are treated with dithionite, perfluoroalkyl radicals are generated and can react further to form new C–C bonds.[13] When copper salt was reacted with Togni reagent, it is believed that a trifluoromethyl radical was generated in the process.[14] Interestingly, perfluoroalkyl radicals can also be generated from R_F–I in the presence of a photoredox catalyst under visible light.[15] Though there are numerous transformations developed by the reaction of these trifluoromethyl and perfluoroalkyl radicals with various functionalities, few involve the activation of C–H bonds.[15h,i,16] In continuation of our research efforts on the development of new C–C and C–X bond-formation processes by C–H cleavage,[9a,b] we have launched a study into the introduction of trifluoromethyl and perfluoroalkyl groups on arenes by C–H activation and herein we report that benzamides bearing an 8-aminoquinoline group can be selectively *ortho*-perfluoroalkylated in the presence of simple copper salt and a catalytic amount of photoredox catalyst under visible light (Scheme 1, [Eq. (2)]).



Scheme 1. 8-Aminoquinoline-assisted C–C and C–X bond-formation reactions with benzamide derivatives.

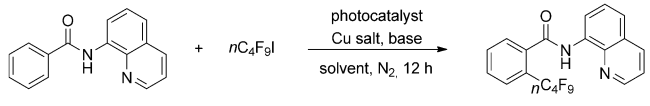
We commenced our study by choosing the reaction of *N*-(quinolin-8-yl)benzamide (**1a**) with *n*-C_4F_9I (**2a**) as the model reaction. When **1a** was treated with five equivalents of *n*-C_4F_9I in the presence of 5% mmol of $[Ru(bpy)_3Cl_2]\cdot 6H_2O$ (bpy = 2,2′-bipyridine),[15a,b,g,h,17] 1.5 equiv of $Cu(OAc)_2$, and 1 equiv of

[a] X. Chen, Prof. Dr. Z. Tan, Q. Gui, L. Hu, J. Liu, J. Wu
State Key Laboratory of Chemo/Biosensing and Chemometrics
College of Chemistry and Chemical Engineering, Hunan University
Changsha 410082 (P. R. China).
E-mail: ztanze@gmail.com

[b] J. Wu, Prof. G. Wang
Department of Chemistry
Collaborative Innovation Center of Chemical Science and Engineering
Tianjin University, Tianjin 300072 (P. R. China)
E-mail: wanggw@tju.edu.cn

Supporting information and the ORCID identification number(s) for the author(s) of this article can be found under http://dx.doi.org/10.1002/chem.201600229.

Table 1. Optimization of the reaction conditions[a]



1a + nC_4F_9I (2a) → 3a

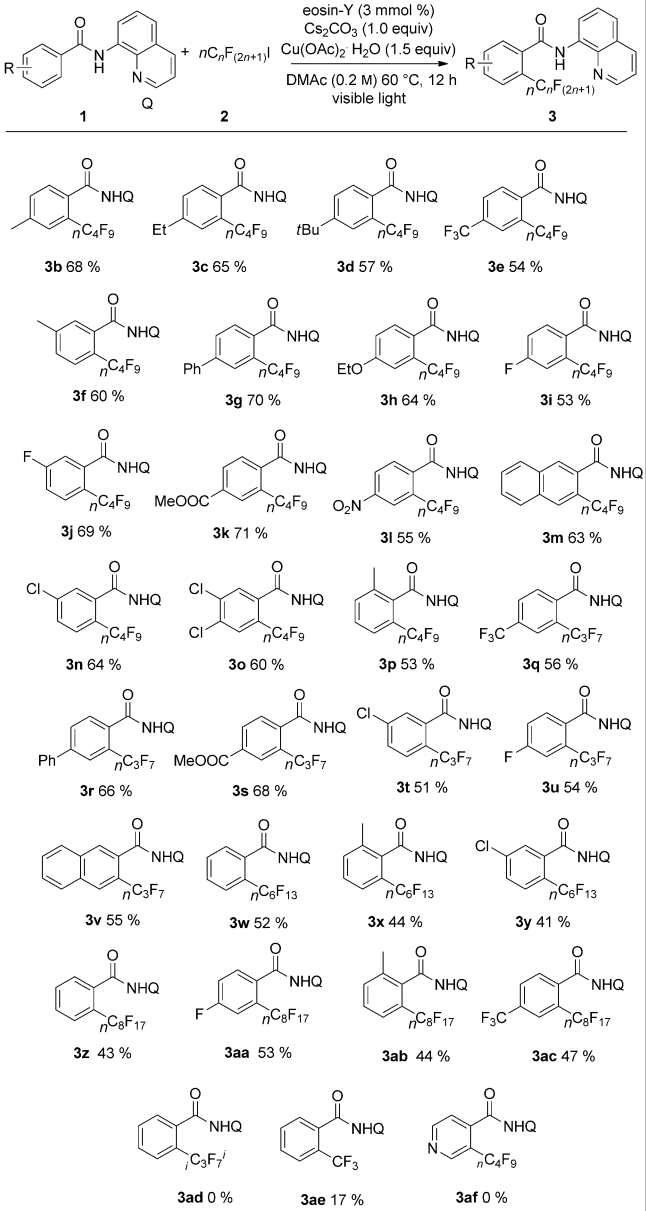
Entry	Cu salts	Photocatal.	Base	Solvent	Yield [%][b]
1	$Cu(OAc)_2$	[Ru][c]	K_2CO_3	DMF	21
2	$Cu(OAc)_2$	eosin-Y	K_2CO_3	DMF	55
3	$Cu(OAc)_2{\cdot}H_2O$	eosin-Y	Cs_2CO_3	DMF	63
4	$Cu(OAc)_2{\cdot}H_2O$	eosin-Y	Cs_2CO_3	DMAc	71
5[d]	$Cu(OAc)_2{\cdot}H_2O$	eosin-Y	Cs_2CO_3	DMAc	<5
6	$Cu(OAc)_2{\cdot}H_2O$	eosin-Y	–	DMAc	trace
7[e]	$Cu(OAc)_2{\cdot}H_2O$	eosin-Y	Cs_2CO_3	DMAc	trace
8	–	eosin-Y	Cs_2CO_3	DMAc	trace
9	$Cu(OAc)_2{\cdot}H_2O$	–	Cs_2CO_3	DMAc	<5
10[d]	$Cu(OAc)_2{\cdot}H_2O$	–	Cs_2CO_3	DMAc	<5

[a] Reaction conditions: *N*-(quinolin-8-yl)benzamide (0.5 mmol), n-C_4F_9I (2.5 mmol), $Cu(OAc)_2{\cdot}H_2O$ (0.8 mmol), eosin-Y (3 mol%), Cs_2CO_3 (0.5 mmol), DMAc (0.2 M), N_2, 60 °C, under visible light,12 h. [b] Isolated yield. [c] [Ru] = $[Ru(bpy)Cl_2]{\cdot}6H_2O$. [d] Without fluorescent light. [e] *T* at RT.

K_2CO_3 in DMF at 60 °C under the irradiation of a 26 W fluorescent LED light bulb for 12 h, the desired product perfluoro-*n*-butylated benzamide **3a** was isolated in 21% yield (Table 1, entry 1). Since we found a large amount of **1a** remained intact, optimization of the reaction conditions is conducted to obtain a better yield. When the photoredox catalyst $[Ru(bpy)_3Cl_2]{\cdot}6H_2O$ was switched to an organic dye eosin-Y,[15c,i,18] much to our delight, we found that higher conversion was reached in a much shorter time and the desired product **3a** was obtained in 55% yield (Table 1, entry 2). The catalyst loading can be as low as 3 mol%. After a series of tests on the source of copper salts, we found that $Cu(OAc)_2{\cdot}H_2O$ performed the best as compared to other catalysts including $CuCl_2$, CuCl, CuI, CuO, $CuBr_2$, and $Cu_2(OH)_2CO_3$ (please see the Supporting Information). Optimization studies also showed that a further increase in yield could be obtained when K_2CO_3 was replaced with Cs_2CO_3 (Table 1, entry 3). However, other bases such as 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), NaOAc, $KHCO_3$ etc. all proved to be less efficient (please see the Supporting Information). Finally the yield could be elevated to 71% when we ran the experiment in *N*,*N*-dimethylacetamide (DMAc), whereas the use of DMSO, 1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone (DMPU), and *N*-methylpyrrolidone (NMP) gave either comparable or slightly lower yields (Table 1, entry 4 and the Supporting Information). If the light was turned off, very little reaction took place, which suggests that light was essential for the reaction to proceed (Table 1, entry 5). It also should be noted that no product was formed in the absence of base (Table 1, entry 6). Running the reaction at 60–70 °C led to much fewer side products while lower temperature resulted in a much slower reaction. No desired product was isolated when either the reaction was run at room temperature or in the absence of $Cu(OAc)_2{\cdot}H_2O$ (Table 1, entries 7 and 8). On the other hand, the desired product was formed in less than 5% yield when eosin-Y was omitted in the presence (or absence) of visible light, indicating the reaction is truly a photocatalytic reaction (Table 1, entries 9 and 10). Based on these results, we decided to set reacting the *N*-(quinolin-8-yl) benzamide with five equivalents of n-C_4F_9I and one equivalent of Cs_2CO_3 in the presence of 3 mol% eosin-Y and 1.6 eqiuvalents of $Cu(OAc)_2{\cdot}H_2O$ in DMAc under the irradiation of a 26 W fluorescent bulb at 60 °C for 12 h as our optimized standard conditions.

With the optimized conditions in hand, the scope and limitation of the reaction were examined and the results were summarized in Table 2. From the table we can see that benzamides with a wide variety of different substituents can be efficiently

Table 2. Photocatalytic and copper-promoted perfluoroalkylation of benzamides[a,b]



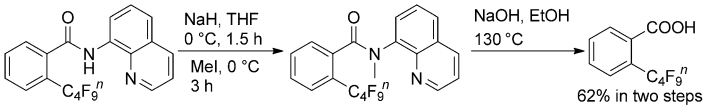
[a] Reaction run under standard conditions. [b] Isolated yields.

perfluoro-*n*-butylated in yields between 53–71% (Table 2, **3b**–**3p**). Not only electron-withdrawing groups but also -donating groups are well tolerated on the phenyl ring of the benzamides. Substrates bearing groups such as methyl, ethyl, *tert*-butyl, phenyl, fluoro, chloro, ethoxy, trifluoromethyl, and nitro as well as ester groups all underwent the desired perfluoroalkylation in good yields. We do see that substrates bearing an *ortho*-substituent did give the desired products in slightly lower yields, indicating the reaction was slightly sensitive to steric hindrance (Table 2, **3p**, **3x**, and **3ab**). As for the perfluoroalkylation reagent, we were able to successfully carry out the corresponding perfluoro-*n*-hexylation, perfluoro-*n*-octylation, as well as perfluoro-*n*-propylation and all the desired perfluoralkylated products were isolated in yields ranging between 41–68% (Table 2, **3q**–**3ac**).

Unfortunately, attempts to carry out the perfluoroalkylation with perfluoro-2-iodopropane failed (Table 2, **3ad**). It should be mentioned that in a related study reported by Chatani,[19] when **1a** was treated with perfluoro-2-iodopropane in toluene in the presence of nickel salt, what was actually formed was the benzylated product instead of the perfluoro-isopropylated product, even though a perfluoroisopropyl radical was proposed as the intermediate. Even more disappointingly, trifluoromethylation with CF_3I, the most important transformation in terms of synthetic value, only provided the desired product **3ae** in 17% yield (Table 2, **3ae**). Since it has been reported that the generation of trifluoromethyl radicals from CF_3I was not efficient with eosin-Y, we next examined the reaction using $[Ru(bpy)_3Cl_2]\cdot 6H_2O$ as the catalyst.[15h,i] However, much to our disappointment, the reaction did not improve either. We surmise that the problem of trifluoromethylation may have something to do with the low boiling point of CF_3I. This problem, in theory, can be resolved by running the reaction in a continuous flow reactor.[15h,i,20] In addition, we also found pyridine-derived amide was not applicable for the perfluoro-*n*-butylation either (Table 2, **3af**).

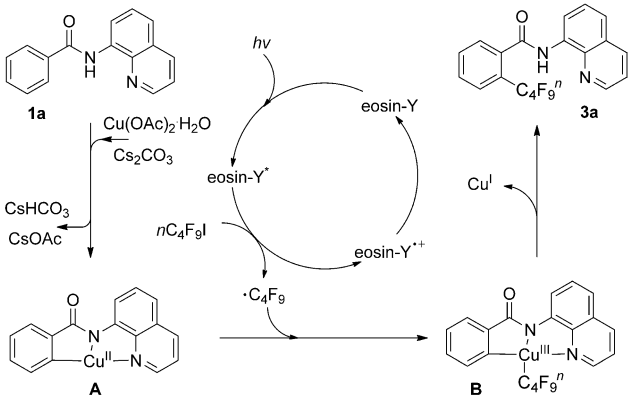
To prove the mechanism of this transformation, a control experiment was conducted under the optimized conditions. When a stoichiometric amount of radical scavenger 2,2,6,6-tetramethylpiperidine *N*-oxide (TEMPO) was added to the perfluoro-*n*-butylation reaction, no desired product was detected. This result suggested that our reaction is likely to involve a radical process. Additionally, the kinetic isotopic effect (KIE) was examined by studying the intermolecular competition reaction between **1a** and its deuterated analogue $[D_5]$**1a**, and K_H/K_D was determined to be around 3.0. This large KIE observed suggested that the cleavage of the *ortho* C–H bond may be involved in the rate-determining step (Scheme 2). Additionally, we have carried out reactions to see whether the reaction is a chain process or not. We have turned off the lamp after running the reaction of **1a** with **2a** under the standard conditions for 4 h and an hour later, the lamp was switched on again.[21] What we have found is that the yield of **3a** did not increase after the light was turned off and it started to go up again when the lamp was switched back on. This means that the reaction is a photoinduced process in which no chain propagation is involved.

Next the removal of the 8-aminoquinoline auxiliary was demonstrated (Scheme 3). Though direct hydrolysis of the isolated product **3a** was not successful, the hydrolysis was smoothly effected after N-methylation with methyl iodide followed by regular alcohol hydrolysis; and 2-(perfluoro-*n*-butyl)benzoic acid was isolated in 62% overall yield.

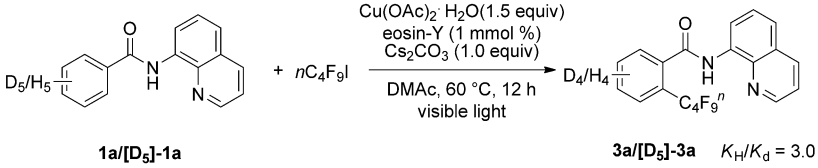


Scheme 3. Removal of the 8-aminoquinoline auxiliary.

Based on the reported literature[22] and the evidence above, a plausible mechanism for the photocatalysis-assisted and copper-promoted perfluoroalkylation of the C–H bond of *N*-(quinolin-8-yl)benzamides is shown in Scheme 4. Firstly, A cyclometalated complex **A** is generated from C–H activation of **1a** with copper salt. Meanwhile, perfluoroalkyl radicals are formed by the reaction of perfluoroalkyl iodides with excited



Scheme 4. Proposed reaction mechanism.



Scheme 2. Deuterium-labeling experiment.

photoredox catalyst eosin-Y. Next the generated perfluoroalkyl radicals react with Cu^{II}-complex **A** to form a Cu^{III}-complex **B**. Finally reductive elimination of Cu^{III}-complex **B** affords the desired product **3 a**.

In summary, we have developed a novel and highly selective method for the synthesis of *ortho*-perfluoroalkylated benzamides starting from *N*-8-quinolinyl benzamides and perfluoroalkyl iodides by copper-promoted C–H activation of aryl sp^2 C–H bonds. Notably the reaction employs an organic dye as the photoredox catalyst and visible light as the reaction initiator. The catalyst is cheap and the reaction is very simple to run. Our protocol represents one of the few examples of merging photoredox chemistry with transition-metal-catalyzed or -promoted C–H activation together.[16a,23] Further studies on the clarification of the reaction mechanism and application to other substrates are underway and the results will be reported in due course.

Experimental Section

General reaction

Benzamide **1 a** (0.5 mmol), $Cu(OAc)_2{\cdot}H_2O$ (150 mg, 0.75 mmol), eosin-Y (11 mg, 3 mmol%), Cs_2CO_3 (163 mg, 0.5 mmol), perfluorobutyl iodide **2 a** (2.5 mmol), and anhydrous DMAc (1 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 60 °C under the irradiation of CFL for 12 h. After the completion of the reaction, the mixture was extracted with ethyl acetate 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 (8:1 to 10:1) gave the desired product **3 a** in 71% yield.

Acknowledgements

G. Wang would like to thank the National Basic Research Program of China (2015CB856500) for financial support.

Keywords: C–H activation · chelation-assisted · Cu-promoted · perfluoroalkylation · photocatalysis

[1] For selected recent reviews on the functionalization of C–H bonds: a) D. A. Colby, R. G. Bergman, J. A. Ellman, *Chem. Rev.* **2010**, *110*, 624–655; b) P. Sehnal, R. J. K. Taylor, I. J. S. Fairlamb, *Chem. Rev.* **2010**, *110*, 824–889; c) T. W. Lyons, M. S. Sanford, *Chem. Rev.* **2010**, *110*, 1147–1169; d) L.-M. Xu, B.-J. Li, Z. Yang, Z.-J. Shi, *Chem. Soc. Rev.* **2010**, *39*, 712–733.

[2] a) J. Roane, O. Daugulis, *Org. Lett.* **2013**, *15*, 5842–5845; b) T. Truong, K. Klimovica, O. Daugulis, *J. Am. Chem. Soc.* **2013**, *135*, 9342–9345; c) L. D. Tran, J. Roane, O. Daugulis, *Angew. Chem. Int. Ed.* **2013**, *52*, 6043–6046; *Angew. Chem.* **2013**, *125*, 6159–6162; d) L. D. Tran, I. Popov, O. Daugulis, *J. Am. Chem. Soc.* **2012**, *134*, 18237–18240; e) L. Grigorjeva, O. Daugulis, *Org. Lett.* **2014**, *16*, 4688–4690; f) L. Grigorjeva, O. Daugulis, *Org. Lett.* **2014**, *16*, 4684–4687; g) L. Grigorjeva, O. Daugulis, *Org. Lett.* **2015**, *17*, 1204–1207; h) L. Grigorjeva, O. Daugulis, *Angew. Chem. Int. Ed.* **2014**, *53*, 10209–10212; *Angew. Chem.* **2014**, *126*, 10373–10376; i) O. Daugulis, J. Roane, L. D. Tran, *Acc. Chem. Res.* **2015**, *48*, 1053–1064; j) D. Shabashov, O. Daugulis, *J. Am. Chem. Soc.* **2010**, *132*, 3965–3972.

[3] For recent reviews on the functionalization of C–H bonds utilizing bidentate chelation assistance: a) M. Corbet, F. De Campo, *Angew. Chem. Int. Ed.* **2013**, *52*, 9896–9898; *Angew. Chem.* **2013**, *125*, 10080–10082; b) G. Rouquet, N. Chatani, *Angew. Chem. Int. Ed.* **2013**, *52*, 11726–11743; *Angew. Chem.* **2013**, *125*, 11942–11959; c) K. Hirano, M. Miura, *Chem. Lett.* **2015**, *44*, 868–873; d) L. C. M. Castro, N. Chatani, *Chem. Lett.* **2015**, *44*, 410–421.

[4] a) M. Nishino, K. Hirano, T. Satoh, M. Miura, *Angew. Chem. Int. Ed.* **2013**, *52*, 4457–4461; *Angew. Chem.* **2013**, *125*, 4553–4557; b) R. Odani, K. Hirano, T. Satoh, M. Miura, *J. Org. Chem.* **2013**, *78*, 11045–11052; c) K. Takamatsu, K. Hirano, M. Miura, *Org. Lett.* **2015**, *17*, 4066–4069; d) W. Miura, K. Hirano, M. Miura, *Org. Lett.* **2015**, *17*, 4034–4037; e) R. Odani, M. Nishino, K. Hirano, T. Satoh, M. Miura, *Heterocycles* **2014**, *88*, 595–602; f) A. M. Suess, M. Z. Ertem, C. J. Cramer, S. S. Stahl, *J. Am. Chem. Soc.* **2013**, *135*, 9797–9804; g) X. Wu, Y. Zhao, G. Zhang, H. Ge, *Angew. Chem. Int. Ed.* **2014**, *53*, 3706–3710; *Angew. Chem.* **2014**, *126*, 3780–3784; h) X. Wu, Y. Zhao, H. Ge, *Chem. Sci.* **2015**, *6*, 5978–5983; i) Z. Wang, Y. Kuninobu, M. Kanai, *Org. Lett.* **2014**, *16*, 4790–4793; j) Z. Wang, J. Ni, Y. Kuninobu, M. Kanai, *Angew. Chem. Int. Ed.* **2014**, *53*, 3496–3499; *Angew. Chem.* **2014**, *126*, 3564–3567.

[5] a) H.-W. Liang, W. Ding, K. Jiang, L. Shuai, Y. Yuan, Y. Wei, Y.-C. Chen, *Org. Lett.* **2015**, *17*, 2764–2767; b) F.-R. Gou, X.-C. Wang, P.-F. Huo, H.-P. Bi, Z.-H. Guan, Y.-M. Liang, *Org. Lett.* **2009**, *11*, 5726–5729; c) M. Iwasaki, Y. Tsuchiva, K. Nakajima, Y. Nishihara, *Org. Lett.* **2014**, *16*, 4920–4923; d) S.-Y. Zhang, Q. Li, G. He, W. A. Nack, G. Chen, *J. Am. Chem. Soc.* **2013**, *135*, 12135–12141; e) K. Chen, F. Hu, S.-Q. Zhang, B.-F. Shi, *Chem. Sci.* **2013**, *4*, 3906–3911; f) K. S. Kanyiva, Y. Kuninobu, M. Kanai, *Org. Lett.* **2014**, *16*, 1968–1971.

[6] a) A. Yokota, Y. Aihara, N. Chatani, *J. Org. Chem.* **2014**, *79*, 11922–11932; b) Y. Aihara, N. Chatani, *Chem. Sci.* **2013**, *4*, 664–670; c) Y. Aihara, N. Chatani, *J. Am. Chem. Soc.* **2013**, *135*, 5308–5311; d) K. Shibata, N. Chatani, *Org. Lett.* **2014**, *16*, 5148–5151; e) J. Yi, L. Yang, C. Xia, F. Li, *J. Org. Chem.* **2015**, *80*, 6213–6221; f) X. Cong, Y. Li, X. Zeng, *Org. Lett.* **2014**, *16*, 3926–3929; g) Q. Yan, Z. Chen, W. Yu, H. Yin, Z. Liu, Y. Zhang, *Org. Lett.* **2015**, *17*, 2482–2485; h) C. Lin, D. Li, B. Wang, J. Yao, Y. Zhang, *Org. Lett.* **2015**, *17*, 1328–1331; i) X. Wang, R. Qiu, C. Yan, V. P. Reddy, L. Zhu, X. Xu, S.-F. Yin, *Org. Lett.* **2015**, *17*, 1970–1973; j) X. Wu, Y. Zhao, H. Ge, *J. Am. Chem. Soc.* **2015**, *137*, 4924–4927.

[7] W. Ma, L. Ackermann, *ACS Catal.* **2015**, *5*, 2822–2825.

[8] a) E. R. Fruchey, B. M. Monks, S. P. Cook, *J. Am. Chem. Soc.* **2014**, *136*, 13130–13133; b) B. M. Monks, E. R. Fruchey, S. P. Cook, *Angew. Chem. Int. Ed.* **2014**, *53*, 11065–11069; *Angew. Chem.* **2014**, *126*, 11245–11249; c) T. Matsubara, S. Asako, L. Ilies, E. Nakamura, *J. Am. Chem. Soc.* **2014**, *136*, 646–649; d) S. Asako, L. Ilies, E. Nakamura, *J. Am. Chem. Soc.* **2013**, *135*, 17755–17757; e) R. Shang, L. Ilies, S. Asako, E. Nakamura, *J. Am. Chem. Soc.* **2014**, *136*, 14349–14352.

[9] a) J. Liu, S. Zhuang, Q. Gui, X. Chen, Z. Yang, Z. Tan, *Adv. Synth. Catal. Adv. Syn. Catal.* **2015**, *357*, 732–738; b) J. Liu, L. Yu, S. Zhuang, Q. Gui, X. Chen, Z. Tan, *Chem. Commun.* **2015**, *51*, 6418–6421; c) W.-H. Rao, B.-F. Shi, *Org. Lett.* **2015**, *17*, 2784–2787; d) D. Katayev, K. F. Pfister, T. Wendling, L. J. Gooβen, *Chem. Eur. J.* **2014**, *20*, 9902–9905.

[10] For some recent examples, see: a) M. Shang, H.-L. Wang, S.-Z. Sun, H.-X. Dai, J.-Q. Yu, *J. Am. Chem. Soc.* **2014**, *136*, 11590–11593; b) M. Shang, S.-Z. Sun, H.-L. Wang, B. N. Laforteza, H.-X. Dai, J.-Q. Yu, *Angew. Chem. Int. Ed.* **2014**, *53*, 10439–10442; *Angew. Chem.* **2014**, *126*, 10607–10610; c) S. Zhao, Y.-J. Liu, S.-Y. Yan, F.-J. Chen, Z.-Z. Zhang, B.-F. Shi, *Org. Lett.* **2015**, *17*, 3338–3341; d) F.-J. Chen, G. Liao, X. Li, J. Wu, B.-F. Shi, *Org. lett.* **2014**, *16*, 5644–5647.

[11] a) J.-A. Ma, D. Cahard, *Chem. Rev.* **2004**, *104*, 6119–6146; b) X. Liu, C. Xu, M. Wang, Q. Liu, *Chem. Rev.* **2015**, *115*, 683–730; c) J.-A. Ma, D. Cahard, *Chem. Rev.* **2008**, *108*, 1–43; d) P. Kirsch, *Modern Fluoroorganic Chemistry*, Wiley-VCH, Weinheim, **2004**.

[12] For some recent examples, see: a) L. He, K. Natte, J. Rabeah, C. Taeschler, H. Neumann, A. Brickner, M. Beller, *Angew. Chem. Int. Ed.* **2015**, *54*, 4320–4324; *Angew. Chem.* **2015**, *127*, 4394–4398; b) B. Yang, X.-H. Xu, F.-L. Qing, *Org. Lett.* **2015**, *17*, 1906–1909; c) A. Bravo, H. R. Bjørsvik, F. Fontana, L. Liguori, A. Mele, F. Minisci, *J. Org. Chem.* **1997**, *62*, 7128–7136; d) J. Xie, X. Yuan, A. Abdukader, C. Zhu, J. Ma, *Org. Lett.* **2014**, *16*, 1768–1771; e) B. Zhang, A. Studer, *Org. Lett.* **2014**, *16*, 3990–3993; f) T. Xu, C. W. Cheung, X. Hu, *Angew. Chem. Int. Ed.* **2014**, *53*, 4910–4914; *Angew. Chem.* **2014**, *126*, 5010–5014.

[13] J. Q. Huang, W. D. Meng, F.-L. Qing, *J. Fluorine Chem.* **2007**, *128*, 1469–1477.

[14] For some recent examples, see: a) Z. Zhu, K. Chen, L. Yu, X. Tang, M. Shi, *Org. Lett.* **2015**, *17*, 5994 – 5997; b) G. Han, Y. Liu, Q. Wang, *Org. Lett.* **2014**, *16*, 3188 – 3191.

[15] a) D. A. Nagib, M. E. Scott, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2009**, *131*, 10875 – 10877; b) Y. Ye, M. S. Sanford, *J. Am. Chem. Soc.* **2012**, *134*, 9034 – 9037; c) M. Neumann, S. Füldner, B. König, K. Zeitler, *Angew. Chem. Int. Ed.* **2011**, *50*, 951 – 954; *Angew. Chem.* **2011**, *123*, 981 – 985; d) Ł. Woźniak, J. J. Murphy, P. Melchiorre, *J. Am. Chem. Soc.* **2015**, *137*, 5678 – 5681; e) N. Iqbal, S. Choi, E. Kim, E. J. Cho, *J. Org. Chem.* **2012**, *77*, 11383 – 11387; f) P. V. Pham, D. A. Nagib, D. W. C. MacMillan, *Angew. Chem. Int. Ed.* **2011**, *50*, 6119 – 6122; *Angew. Chem.* **2011**, *123*, 6243 – 6246; g) N. J. W. Straathof, B. J. P. Tegelbeckers, V. Hessel, X. Wang, T. Noël, *Chem. Sci.* **2014**, *5*, 4768 – 4773; h) N. J. W. Straathof, H. P. L. Gemoets, X. Wang, J. C. Schouten, V. Hessel, T. Noël, *ChemSusChem* **2014**, *7*, 1612 – 1617; i) N. J. W. Straathof, D. Osch, A. Schouten, X. Wang, J. Schouten, V. Hessel, T. Noël, *J. Flow Chem.* **2014**, *4*, 12 – 17.

[16] a) H. Liu, Z. Gu, X. Jiang, *Adv. Synth. Catal.* **2013**, *355*, 617 – 626; b) N. Iqbal, S. Choi, E. Ko, E. J. Cho, *Tetrahedron Lett.* **2012**, *53*, 2005 – 2008.

[17] J. Xuan, W.-J. Xiao, *Angew. Chem. Int. Ed.* **2012**, *51*, 6828 – 6838; *Angew. Chem.* **2012**, *124*, 6934 – 6944.

[18] D. P. Hari, B. König, *Org. Lett.* **2011**, *13*, 3852 – 3855.

[19] Y. Aihara, M. Tobisu, Y. Fukumoto, N. Chatani, *J. Am. Chem. Soc.* **2014**, *136*, 15509 – 15512.

[20] N. J. W. Straathof, Y. Su, V. Hessel, T. Noël, *Nat. Protoc.* **2016**, *11*, 10 – 21.

[21] For a related example on determining whether a photocatalytic process is a chain process or not, see: S. Barata-Vallejo, D. E. Yerien, A. Postigo, *Eur. J. Org. Chem.* **2015**, 7869 – 7875.

[22] a) B. Yao, D.-X. Wang, Z.-T. Huang, M.-X. Wang, *Chem. Commun.* **2009**, 2899 – 2901; b) A. Casitas, A. E. King, T. Parella, M. Costas, S. S. Stahl, X. Ribas, *Chem. Sci.* **2010**, *1*, 326 – 330; c) X. Ribas, D. A. Jackson, B. Donnadieu, J. Mahia, T. Parella, R. Xifra, B. Hedman, K. O. Hodgson, A. Llobet, T. D. P. Stack, *Angew. Chem. Int. Ed.* **2002**, *41*, 2991 – 2994; *Angew. Chem.* **2002**, *114*, 3117 – 3120.

[23] D. Kalyani, K. B. McMurtrey, S. R. Neueldt, M. S. Sanford, *J. Am. Chem. Soc.* **2011**, *133*, 18566 – 18569.

Received: January 18, 2016
Published online on March 16, 2016