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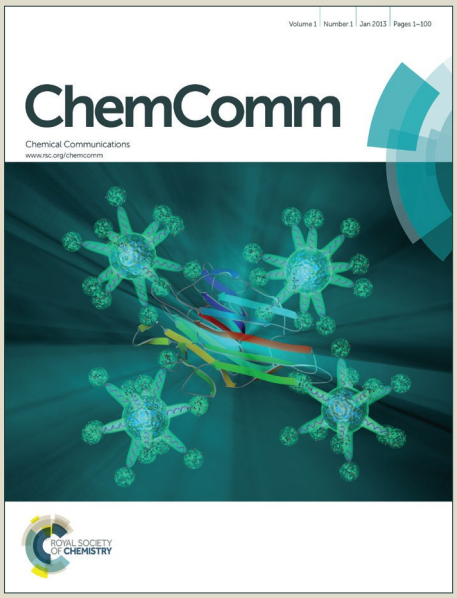

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COMMUNICATION

Operationally Simple Hydrotrifluoromethylation of Alkene with Sodium Triflinate Enabled by Ir-Photoredox Catalysis

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We reported herein a single component of Ir-photoredox catalyst is capable to catalyze hydrotrifluoromethylation of terminal alkenes and Michael acceptors with sodium triflinate (Langlois reagent) in methanol under an irradiation condition at room temperature. Various synthetically useful functional groups including ester, amide, ether, aldehyde, sulfone, ketone and aryl boronate can be well tolerated in this reaction.

Due to the significantly improving effect of trifluoromethyl substituent on biological properties of small molecules by increasing its lipophilicity and metabolic stability,[1] new methodologies to introduce trifluoromethyl onto small molecules has attracted intensive attention from synthetic chemists.[2] After extensive exploration to introduce trifluoromethyl substituent onto unsaturated[3] and allylic carbon[4] atoms, efforts to construct C(sp_3)-CF_3 bond appears its emergency[5]. The methods to install trifluoromethyl group onto terminal C(sp_3) atom in a aliphatic chain include reactions of trifluoromethyl reagents[6] with alkyl halides,[7] alkyl boronic acids[8] and terminal alkene[9], among which hydrofunctionalization of terminal olefin is most appealing due to its atom economy and generation of less waste comparing with substitution reactions.[10] Photoredox catalysis has been demonstrated as a powerful method to generate radical species without the necessity of using stoichiometric redox agents, and to tame the reactivity of active radical in a controllable manner, which was recently applied for trifluorometlation.[11,12] Meanwhile, hydrotrifluoromethylation of alkenes was first achieved by using a ruthenium photoredox catalyst and expensive Umemoto reagent by Gouverneur et al.[9b] Hydrotrifluoromethyaltion of alkenes using low-cost Langlois reagent[6d] is more appealing. Nicewice et al. reported acridinium photoredox catalyst combining with a thiophenol additive is capable to catalyze alkene hydrotrifluoromethylation with Langlois reagent for an ample scope of olefins.[9c] Although reported, the development of new operationally simple catalytic system for hydrotrifluoromethylation with low cost reagent is still desirable. In this work we discovered that a simple component of Ir-catalyst in methanol under irradiation is capable to catalyze hydrotrifluoromethylation of alkenes using Langlois reagent. This reaction exhibits excellent anti-Markovnikov selecticvity, and can also be extended to electron deficient Michael acceptors including α,β-unsaturated sulfone, ester, amide and ketone. The advantages of this method include operational simplicity and good functional group compatibility.

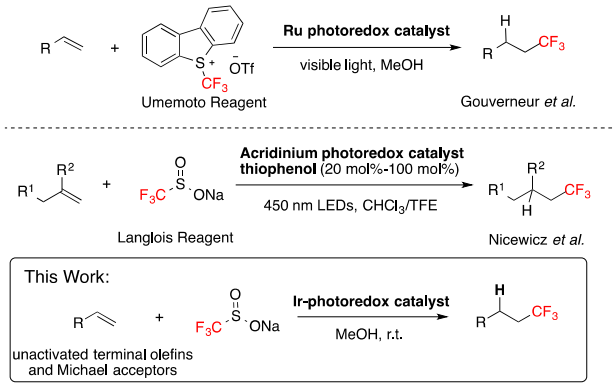

Figure 1. Photoredox-catalyzed hydrotrifluoromethylation of alkene.

Our study started by choosing (hex-5-en-1-yloxy)benzene (**1a**) as model substrate. It was found after exposing a reaction mixture composed of **1a** (0.25 mmol), Langlois reagent (0.75 mmol) and Ir-photoredox catalyst in a mixture of DMF and water for 24 h, anti-Markovnikov type hydrotrifluoro-methylation product was detected in 19% yield by GC-MS (entry 1). Screening the solvent (entry 2-9) revealed that methanol is the best solvent, while using other solvents mixed with water or using other alcohols as solvent all gave inferior results.

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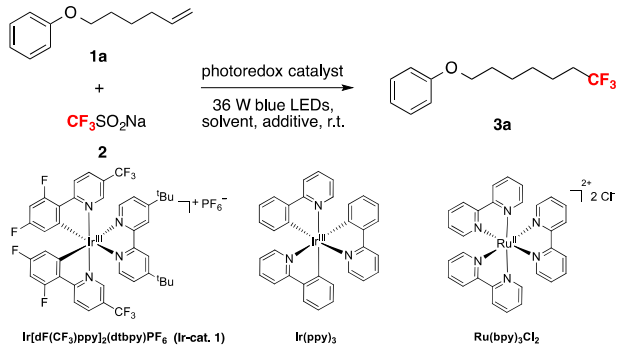
Table 1. Optimization of reaction conditions[a]

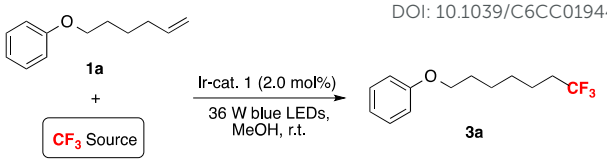


Entry	Catalyst	Additive (2 eq.)	Solvent	Yield[b]
1	Ir-cat.1	/	DMF/H_2O=1:1	19%
2	Ir-cat.1	/	DMSO/H_2O=1:1	14%
3	Ir-cat.1	/	MeOH/H_2O=1:1	41%
4	Ir-cat.1	/	CH_3CN/H_2O=1:1	23%
5	Ir-cat.1	/	CH_2Cl_2/H_2O=1:1	28%
6	Ir-cat.1	/	MeOH	61%
7	Ir-cat.1	/	EtOH	49%
8	Ir-cat.1	/	^{i}PrOH	38%
9	Ir-cat.1	/	^{t}BuOH	11%
11	Ir-cat.1	K_2HPO_4	MeOH	28%
12	Ir-cat.1	formic acid	MeOH	42%
13	Ir-cat.1	benzoic acid	MeOH	trace
14	Ir-cat.1	phenol	MeOH	58%
15	Ir-cat.1	TsOH	MeOH	46%
16	Ir-cat.1	H_2O	MeOH	51%
17[c]	Ir-cat.1	/	MeOH	52%
18[d]	Ir-cat.1	/	MeOH	64%
19[d,e]	**Ir-cat.1**	/	**MeOH**	**81%**
20[d,e]	$Ru(bpy)_3Cl_2$	/	MeOH	N.R
21[d,e]	*fac*-Ir(ppy)$_3$	/	MeOH	N.R
22[d,e,f]	Ir-cat.1	/	MeOH	N.R
23[d,e]	/	/	MeOH	N.R

[a] Reaction condition: **1a** (0.25 mmol), **2a** (0.75 mmol), photoredox catalyst (2.0 mol %), solvent (2.0 mL), irradiation with 36 W blue LEDs at room temperature for 24 h under argon. [b] GC yields using benzophenone as an internal standard. [c] Using 1.0 mol % of Ir-cat.1. [d] **2** (0.5 mmol). [e] Solvent (3.0 mL). [f] without irridiation.

Adding proton source to enhance the acidity of the reaction mixture failed to further increase the yield of hydrotrifluoromethylation product (entry 11-16). Reducing the loading of the photoredox catalyst to 1 mol% caused a slight decrease in yield. The best yield was achieve by reducing the amount of Langlois reagent to 2.0 equivalent and further diluting the reaction mixture (0.083M) (Entry 19). The reaction did not proceed either without irradiation (entry 22) or in the absence of the photoredox catalyst (entry 23). $Ru(bpy)_3Cl_2$ [$E_{1/2}^{red}$ ($*Ru^{II}/Ru^{I}$) = +0.77 V, $E_{1/2}^{red}$ (Ru^{II}/Ru^{I}) = -1.33 V vs. SCE][11e] and $Ir(ppy)_3$ [$E_{1/2}^{red}$ ($*Ir^{III}/Ir^{II}$) = +0.31 V, $E_{1/2}^{red}$ (Ir^{III}/Ir^{II}) = -2.19 V vs. SCE][11e] are totally ineffective for this reaction (entry 20, 21).

Table 2. Investigation of different trifluoromethyl sources[a]



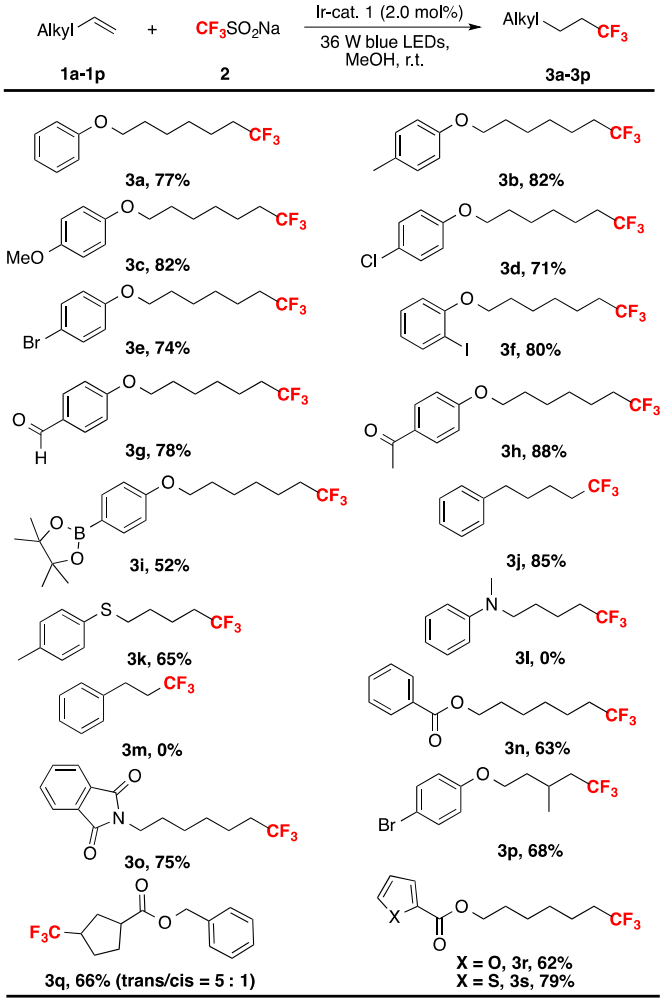
CF_3COOH	CF_3COONa	$F_3C-\bar{B}(OMe)_3\ K^+$	$TMSCF_3$/KF	CF_3SO_2Na
0%	0%	< 5%	0%	81%

[a] Reaction condition: **1a** (0.25 mmol), **2** (0.5 mmol), photoredox catalyst (2.0 mol %), MeOH (3.0 mL), irradiation with 36 W blue LEDs at room temperature for 24 h under argon.

The effectiveness of $Ir[dF(CF_3)ppy]_2(dtbpy)PF_6$ [$E_{1/2}^{red}$ ($*Ir^{III}/Ir^{II}$) = +1.21 V, $E_{1/2}^{red}$ (Ir^{III}/Ir^{II}) = -1.37 V vs. SCE][11e] compared with other photoredox catalyst can be rationalized from its redox potentials. The redox potential of Langlois reagent is 1.05 V (vs. SCE).[13] From these redox potentials, it is reasonable that $Ir[dF(CF_3)ppy]_2(dtbpy)PF_6$ is capable to oxidize triflinate anion, while $Ru(bpy)_3Cl_2$ and $Ir(ppy)_3$ are unable to oxidize triflinate anion to generate trifluoromethyl radical. Compared with the reaction system reported by Nicewicz et al., it is noteworthy that our reaction only needs a single component of Ir-catalyst, while in Nicewice's system, a thiophenol additive is necessary.[9c] This observation may also be rationalized by comparing the redox potential of the two catalyst. The acridinium catalyst [$E_{1/2}^{red}$ ($*A/A^-$) = +2.06 V, E_{ox} (A/A^-) = -0.57 V vs. SCE][14] used in Nicewicz's reaction is strong enough to oxidize triflinate, but compared with $Ir[dF(CF_3)ppy]_2(dtbpy)PF_6$, the reduction power of its reduced form is much weaker. From these potential values, it is reasonable that alkyl 2-trifluoromethyl methylene radical is able to oxidatively regenerate $Ir[dF(CF_3)ppy]_2(dtbpy)$ PF_6, but unable to regenerate acridinium catalyst. We also screened other possible trifluoromethyl sources (Table 2), such as trifluoroacetate, $CF_3^-B(OMe)_3K^+$ and $TMSCF_3$/KF. However, only CF_3SO_2Na is effective.

With the optimal reaction condition in hand, we tested the olefin scope. The hydrotrifluoromethylation exhibits excellent regioselectivity. Anti-Markovnikov selectivity was exclusively obtained for terminal olefins. This reaction also possesses good functional-group-compatibility, as demonstrated in Table 3, ether (**3c**), aldehyde (**3g**), methyl ketone (**3h**), sulfide (**3k**), ester (**3n**) and amide (**3o**) are all well tolerated. Aryl chloride (**3d**), aryl bromide (**3e**), aryl pinacol boronate **(3i)** and especially aryl iodide (**3f**) are all compatible, which are useful for further modification through cross-coupling reactions. Photoredox catalyzed deiodination[15] was not observed. Tertiary aniline structure was not compatible **(3l)**, probably due to the strong reductive quenching ability of aniline.[16] Although styrene type substrate is unreactive **(3m)**, 1,1-disubstituted olefin is also amenable substrate, as demonstrated by **3p**. Although internal olefins were not suitable substrate and delivered a complicated mixture, a symmetric cyclic alkene, cyclopent-3-ene-1-carboxylate gave hydrotrifluoro-methylation product in 66% yield with a diastereoselectivity of 5:1, in which trans-isomer was the major isomer **(3q)**. Remarkably, heterocycles such as furan and thiophene are well tolerated **(3r, 3s)**.

Table 3. Reaction scope of unactivated alkenes[a,b]

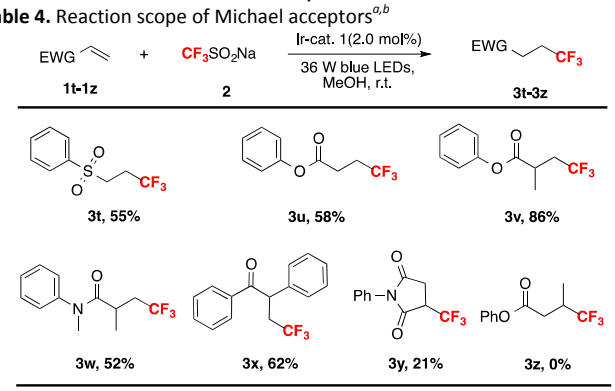


[a] Reaction condition: **1a** (0.25 mmol), **2a** (0.50 mmol), **Ir-cat.1** (2.0 mol %), MeOH (3.0 mL), irradiation with 36 W blue LEDs at room temperature for 24 h under argon. [b] Yields based on isolated products.

We were delighted to find this reaction is not only suitable for electronically unbiased terminal alkene, but also can be applied to Michael acceptors.[17] It should be noted that alkene of Michael acceptor type was not demonstrated in the report by Gouverneou et al.,[9b] and was demonstrated as a relatively low yield example in Nicewicz's report.[9c] Table 4 demonstrates the scope for Michael acceptors. α,β-Unsaturated sulfone (**3t**), ester (**3u**, **3v**), amide (**3w**), ketone (**3x**) are all amenable substrates. Substituent at the α-position of the Michael acceptor are tolerable (**3v**, **3w**, **3x**), but a methyl substituent at the β-position (internal olefin) shuts down the reaction (**3z**). Cyclic Michael acceptor, 1-phenyl-1H-pyrrole-2,5-dione, a substrate demonstrated by Rueping et al. recently,[9d] also worked under our reaction condition, but delivered the product in only 21% yield (**3y**).

The synthetic utility of this reaction is further demonstrated by applying it to modify an estrone derivative. The trifluomethylated estrone derivative was obtained in good yield (Figure 2). Simple radical-trapping experiments were conducted. The addition of 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO) or styrene kills this reaction,[4c,18] supporting an outer-sphere radical mechanism involved (Figure 3). When deuterated methanol was applied as solvent, it was found that deuterium atom was incorporated into the internal position of olefin (Figure 4). Since hydrotrifluoromethylation can also be detected when using ^{t}BuOH as solvent (table 1, entry 9), it is possible that MeOH just works as a protonation reagent, but does not involve in the redox cycle.[19]

Table 4. Reaction scope of Michael acceptors[a,b]



[a] Reaction condition: **1a** (0.50 mmol), **2a** (1.0 mmol), Ir-cat.1 (2.0 mol %), MeOH (3.0 mL), irradiation with 36 W blue LEDs at room temperature for 24 h under argon. [b] Yields based on isolated products.

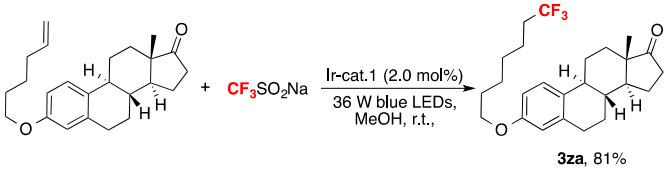


Figure 2. Modification of an estrone derivative.

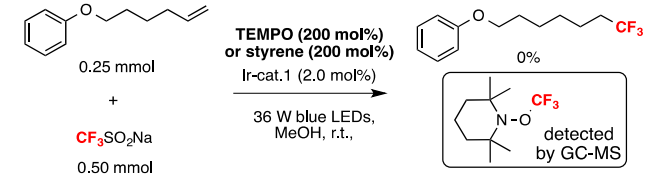


Figure 3. Radical-trapping experiment.

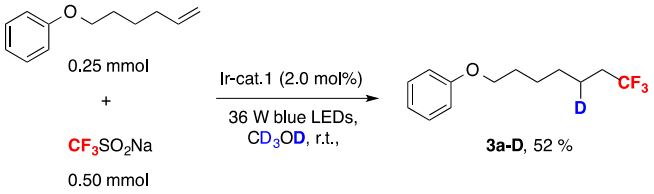


Figure 4. Isotope-labelling experiment.

Figure 5 demonstrates the possible mechanism. The sulfinate anion reductively quenches excited *Ir(III) catalyst to generate trifluoromethyl radical. The trifluoromethyl radical reacts with olefin to generate a relatively stable methylene radical. The methylene radical possessing a strong electron-withdrawing CF_3 group adjacent to the radical center may have higher oxidative potential compared with normal secondary carbon radical,[20] and can oxidize Ir(II) to regenerate Ir(III) ($E_{1/2}^{red}$ (Ir^{III}/Ir^{II}) = -1.37 V vs. SCE) to complete the catalytic cycle.[21]

In summary, we discovered that a single component of Ir-photoredox catalyst is capable to catalyze hydrotrifluoromethylation of simple alkene and Michael acceptors with Langlois reagent in methanol under an irradiation condition. Various synthetically useful functional groups including ester, amide, ether, aldehyde, sulfone,

ketone and aryl boronate can be well tolerated. This report offers a simple and convenient method to access various trifluoromethylated aliphatic compounds using easily accessible and relatively low-cost starting materials.

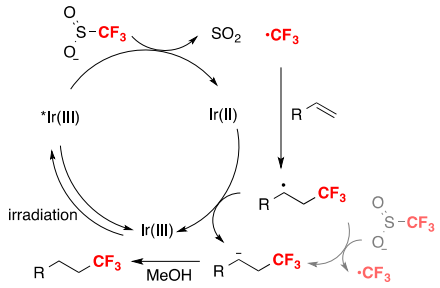


Figure 5. Proposed mechanism.

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Notes and references

1. (a) M. Schlosser, *Angew. Chem., Int. Ed.*, 2006, **45**, 5432; (b) K. Muller, C. Faeh and F. Diederich, *Science*, 2007, **317**, 1881.
2. For selected reviews: (a) J. Nie, H.-C. Guo, D. Cahard and J.-A. Ma, *Chem. Rev.*, 2011, **111**, 455; (b) X.-F. Wu, H. Neumann and M. Beller, *Chem. Asian J.*, 2012, **7**, 1744; (c) A. Studer, *Angew. Chem., Int. Ed.*, 2012, **51**, 8950; (d) L. Chu and F.-L. Qing, *Acc. Chem. Res.*, 2014, **47**, 1513; (e) E. Merino and C. Nevado, *Chem. Soc. Rev.*, 2014, **43**, 6598; (f) H. Egami and M. Sodeoka, *Angew. Chem., Int. Ed.*, 2014, **53**, 8294.
3. (a) E. J. Cho, T. D. Senecal, T. Kinzel, Y. Zhang, D. A. Watson and S. L. Buchwald, *Science*, 2010, **328**, 1679; (b) C.-P. Zhang, J. Cai, C.-B. Zhou, X.-P. Wang, X. Zheng, Y.-C. Gu and J.-C. Xiao, *Chem. Commun.*, 2011, **47**, 9516; (c) H. Morimoto, T. Tsubogo, N. D. Litvinas and J. F. Hartwig, *Angew. Chem., Int. Ed.*, 2011, **50**, 3793; (d) Y. Fujiwara, J. A. Dixon, F. O'Hara, E. D. Dunder, D. D. Dixon, R. A. Rodriguez, R. D. Baxter, B. Herlé, N. Sach, M. R. Collins, Y. Ishihara and P. S. Baran, *Nature*, 2012, **492**, 95.
4. (a) A. T. Parsons and S. L. Buchwald, *Angew. Chem., Int. Ed.*, 2011, **50**, 9120; (b) X. Wang, Y. Ye, S. Zhang, J. Feng, Y. Xu, Y. Zhang and J. Wang, *J. Am. Chem. Soc.*, 2011, **133**, 16410; (c) L. Chu and F.-L. Qing, *Org. Lett.*, 2012, **14**, 2106; (d) R. Shimizu, H. Egami, Y. Hamashima and M. Sodeoka, *Angew. Chem., Int. Ed.*, 2012, **51**, 4577; (e) S. Mizuta, O. Galicia-López, K. M. Engle, S. Verhoog, K. Wheelhouse, G. Rassias and V. Gouverneur, *Chem. Eur. J.*, 2012, **18**, 8583.
5. T. Furuya, A. S. Kamlet and T. Ritter, *Nature*, 2011, **473**, 470.
6. (a) T. Umemoto and S. Ishihara, *Tetrahedron Lett.*, 1990, **31**, 3579; (b) T. Umemoto, *Chem. Rev.*, 1996, **96**, 1757; (c) I. Kieltsch, P. Eisenberger and A. Togni, *Angew. Chem., Int. Ed.*, 2007, **46**, 754; (d) B. R. Langlois, E. Laurent and N. Roidot, *Tetrahedron Lett.*, 1991, **32**, 7525; (e) I. Ruppert, K. Schlich and W. Volbach, *Tetrahedron Lett.*, 1984, **25**, 2195; (f) S. K. S. Prakash, R. Krishnamurti and G. A. Olah, *J. Am. Chem. Soc.*, 1989, **111**, 393.
7. (a) D.-B. Su, J.-X. Duan and Q.-Y. Chen, *Tetrahedron Lett.*, 1991, **32**, 7689; (b) Q.Y.-Chen and J.-X. Duan, *J. Chem. Soc., Chem. Commun.*, 1993, 1389; (c) J. Kim and J. M. Shreeve, *Org. Biomol. Chem.*, 2004, **2**, 2728.
8. J. Xu, B. Xiao, C.-Q. Xie, D.-F. Luo, L. Liu, and Y. Fu, *Angew. Chem., Int. Ed.*, 2012, **51**, 12551.
9. (a) X. Wu, L. Chu and F.-L. Qing, *Angew. Chem., Int. Ed.*, 2013, **52**, 2198; (b) S. Mizuta, S. Verhoog, K. M. Engle, T. Khotavivattana, M. O'Duill, K. Wheelhouse, G. Rassias, M. Médebielle and V. Gouverneur, *J. Am. Chem. Soc.*, 2013, **135**, 2505. (c) D. J. Wilger, N. J. Gesmundo and D. A. Nicewicz, *Chem. Sci.*, 2013, **4**, 3160; (d) Q. Lefebvre, N. Hoffmann and M. Rueping, *Chem. Commun.*, 2016, **52**, 2493.
10. (a) D. A. Nicewicz and D. S. Hamilton, *Synlett*, 2014, **25**, 1191; (b) Y. Yang, S.-L. Shi, D. Niu, P. Liu and S. L. Buchwald, *Science*, 2015, **349**, 62; (c) J. C. Lo, J. Gui, Y. Yabe, C. M. Pan and P. S. Barn, *Nature*, 2014, **516**, 343.
11. For selected reviews, see: (a) M. A. Miranda and H. Garcia, *Chem. Rev.*, 1994, **94**, 1063; (b) J. M. R. Narayanam and C. R. J. Stephenson, *Chem. Soc. Rev.*, 2011, **40**, 102; (c) J. Xuan and W.-J. Xiao, *Angew. Chem. Int. Ed.*, 2012, **51**, 6828; (d) L. Shi and W. Xia, *Chem. Soc. Rev.*, 2012, **41**, 7687; (e) C. K. Prier, D. A. Rankic and D. W. C. MacMillan, *Chem. Rev.*, 2013, **113**, 5322; (f) M. Reckenthäler and A. G. Griesbeck, *Adv. Synth. Catal.*, 2013, **355**, 2727; (g) J. Xie, H. Jin, P. Xu and C. Zhu, *Tetrahedron Lett.*, 2014, **55**, 36; (h) D. M. Schultz and T. P. Yoon, *Science* 2014, **343**, 1239176; (i) T. Koike and M. Akita, *Top. Catal.*, 2014, **57**, 967; (j) S. Barata-Vallejo, S. M. Bonesi and A. Postigo, *Org. Biomol. Chem.*, 2015, **13**, 11153; (k) E. J. Cho, *Chem. Rec.*, 2016, **16**, 47.
12. For selected examples, see: (a) N. Iqbal, S. Choi, E. Kim and E. J. Cho, *J. Org. Chem.*, 2012, **77**, 11383; (b) N. Iqbal, S. Choi, E. Ko and E. J. Cho, *Tetrahedron Lett.*, 2012, **53**, 2005; (c) N. Iqbal, J. Jung, S. Park and E. J. Cho, *Angew. Chem. Int. Chem.*, 2014, **53**, 539; (d) J. Xie, X. Yuan, A. Abdukader, C. Zhu and J. Ma, *Org. Lett.*, 2014, **16**, 1768; (e) B. Sahoo, J.-L. Li and F. Glorius, *Angew. Chem. Int. Ed.*, 2015, **54**, 11577. (f) W.-M. Cheng, R. Shang, H.-Z. Yu and Y. Fu, *Chem. Eur. J.*, 2015, **21**, 13191. (e) S. Park, J. M. Joo and E. J. Cho, *Eur. J. Org. Chem.*, 2015, 4093.
13. J.-B. Tommasino, A. Brondex, M. Médebielle, M. Thomalla, B. R. Langlois and T. Billard, 2002, 1697.
14. (a) D. S. Hamilton and D. A. Nicewicz, *J. Am. Chem. Soc.*, 2012, **134**, 18577; (b) J.-M. Grandjean and D. A. Nicewicz, *Angew. Chem., Int. Ed.*, 2013, **52**, 3967.
15. J. D. Nguyen, E. M. D'Amato, J. M. R. Narayanam and C. R. J. Stephenson, *Nature Chem.*, 2012, **4**, 854.
16. C. K. Prier and D. W. C. MacMillan, *Chem. Sci.*, 2014, **5**, 4173.
17. (a) Y. Miyake, K. Nakajima and Y. Nishibayashi *Chem. Commun.*, 2013, **49**, 7854; (b) L.-L. Chu, C. Ohta, Z.-W. Zuo and D. W. C. MacMillan, *J. Am. Chem. Soc.*, 2014, **136**, 10886; (c) G.-Z. Wang, R. Shang, W.-M. Cheng and Y. Fu, *Org. Lett.*, 2015, **17**, 4830.
18. Y. Li and A. Studer, *Angew. Chem., Int. Ed.*, 2012, **51**, 8221.
19. When CD_3OH was used as solvent, **3a-D** was not obtained.
20. (a) W. R. Dolbier Jr, *Chem. Rev.*, 1996, **96**, 1557; (b) Y. Fu, L. Liu, H.-Z. Yu, Y.-M. Wang and Q.-X. Guo, *J. Am. Chem. Soc.*, 2005, **127**, 7227; (c) S. Barata-Vallejo and A. Postigo, *Eur. J. Org. Chem.*, 2012, 1889.
21. The quantum yield of the reaction was measured to be 3.1 by using a reported method (see the SI), which suggests that a short chain radical mechanism is also probably concomitant. According to suggestion of one referee, a pathway involving hydrogen abstraction from methanol to alkyl radical generating methoxy radical followed by oxidation of Ir(II) by methoxy radical to finish the photoredox cycle can not be ruled out.