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Blue Light Induced Difluoroalkylation of Alkynes and Alkenes

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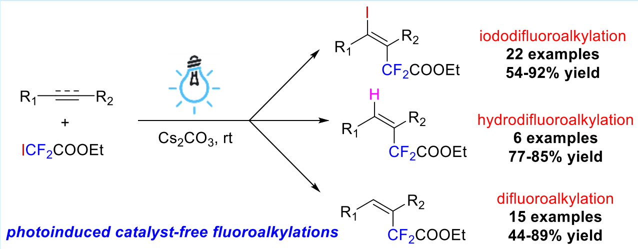
Supporting Information

ABSTRACT: The difluoroalkylation of alkynes and alkenes by direct photoexcitation of ethyl difluoroiodoacetate is described. Under catalyst- and oxidant-free conditions, iododifluoroalkylation and hydrodifluoroalkylation products were generated from alkynes, and difluoroalkylation products were prepared from alkenes. This methodology provides a streamlined access to difluoroalkylated organic compounds starting from simple alkynes or alkenes.



The introduction of fluorine atoms into organic molecules may lead to dramatic changes in their properties such as lipophilicity, metabolic stability, and bioavailability.[1] Fluorine-containing structural motifs play important roles in pharmaceuticals and agrochemicals; more than 20% of the pharmaceuticals and agrochemicals on the market are organofluorines. Thus, the selective introduction of fluorine or fluorinated groups into the drug candidates has been regarded as a powerful strategy in drug design and screening.[2] Direct fluoroalkylation has received much attention, as it serves as a straightforward method for the synthesis of organofluorines. Over the past decade, remarkable progress has been made in the transition-metal catalyzed fluoroalkylation of arenes.[3] Although the traditional fluoroalkylation reactions by using transition metal catalysts are powerful,[4] the addition reaction of halo-fluoroalkanes to alkenes or alkynes via the atom transfer radical addition (ATRA) strategy has emerged as an attractive methodology, which was facilitated by transition metal,[5] light,[6] or radical initiators.[7] The advantages of this method include the easy availability of the reagents and the great synthetic versatility of the halofluoroalkene products (for cross-coupling[5b,c,7a] or functional group transformations[8]). However, the use of transition metal, photocatalysts, or radical initiators may undermine its industrial applications due to some drawbacks, as it is expensive and oxygen sensitive and may leave toxic trace metal contaminants. Because of the broad applications of halofluoroalkenes, the development of eco-friendly, synthetically efficient methodologies from easily accessible raw materials under simple and mild reaction conditions is still highly desirable.

In this decade, a surge of interest has led the photocatalyzed reactions to the forefront of synthetic methodology, and the processes serve as environmentally friendly methods for promoting selective radical reactions.[9] Our group has previously investigated the photocatalyzed oxidative dehydrogenation of hydrazobenzenes[10] and transfer hydrogenation of cyclic N-sulfonylimines.[11] We then questioned whether the direct photoexcitation of specific functional groups by taking advantage of the visible light absorptivity to provide an efficient method for the synthesis of useful synthons. Herein, we describe three photocatalyst- and oxidant free-difluoroalkylation reactions with ethyl difluoroiodoacetate: (i) iododifluoroalkylation of alkynes; (ii) hydrodifluoroalkylation of alkynes; (iii) the difluoroalkylation of alkenes.

We initially began our studies by evaluating the effect of a suitable base, which was reported to promote the generation of free radicals.[12] Reaction optimization was conducted with 1-phenyl-1-propyne **1a** and ethyl difluoroiodoacetate (2 equiv) under irradiation with a blue light-emitted diode (LED) at room temperature in the presence of a base (Table 1). To our delight, the generation of the desired iododifluoroalkylation product **2a** was observed by using some organic bases such as TEA, TMEDA, DIPEA, and DBU (Table 1, entries 1−4). The inorganic bases were also effective, and the use of Cs_2CO_3 has given a good yield of 88% (Table 1, entries 5−8). Next, some other solvents besides acetonitrile were screened. DMF and DMSO proved to be effective (Table 1, entries 9−10). Interestingly, no iododifluoroalkylation product **2a** was detected by using THF as a reaction solvent, but gave the hydrodifluoroalkylation product **3a** in 68% yield (Table 1, entry 11). It could be explained by the transfer hydrogenation of the vinyl radical intermediate with THF as a hydrogen donor.[12] However, no **3a** was detected by using 1,4-dioxane instead of THF (Table 1, entry 12). By reacting at a high concentration, **2a** and **3a** were obtained with 89% and 81% yield, respectively (Table 1, entries 13−14). The following control experiments established the requirement of light. No

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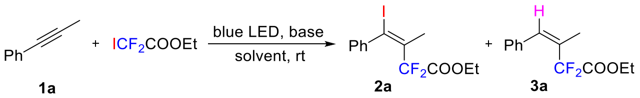
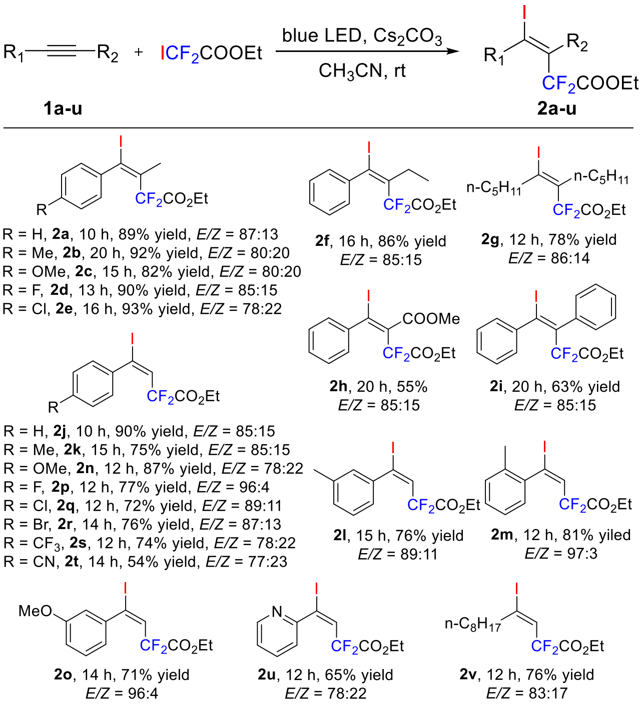
Table 1. Reaction Conditions Optimization[a]



Entry	Base	Solvent	Time (h)	Yield (%)[b]	
				2a	3a
1	TEA	CH_3CN	24	63	trace
2	TMEDA	CH_3CN	24	72	trace
3	DIPEA	CH_3CN	24	40	nd
4	DBU	CH_3CN	24	32	nd
5	Na_2CO_3	CH_3CN	24	25	nd
6	K_2CO_3	CH_3CN	24	50	nd
7	Cs_2CO_3	CH_3CN	12	88	nd
8	KO^tBu	CH_3CN	24	7	nd
9	Cs_2CO_3	DMF	16	73	nd
10	Cs_2CO_3	DMSO	16	82	nd
11	Cs_2CO_3	THF	60	trace	68
12	Cs_2CO_3	1,4-dioxane	60	69	nd
13[c]	Cs_2CO_3	CH_3CN	10	89	nd
14[c]	Cs_2CO_3	THF	60	trace	81
15[c,d]	$C_{s2}CO_3$	CH_3CN	12	nd	nd
16[c,e]	Cs_2CO_3	CH_3CN	24	11	nd
17[f]	Cs_2CO_3	CH_3CN	24	nd	nd

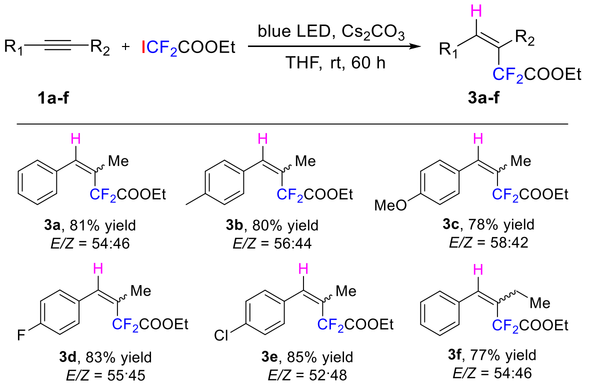
[a]Reaction conditions: **1a** (0.2 mmol), ICF_2COOEt (0.4 mmol), and base (0.4 mmol) in solvent (2 mL) were irradiated by 30 W blue LED at room temperature. [b]The total isolated yield of *E*- and *Z*-products (unreacted **1a** was responsible for the cases with low yield). [c]1 mL of solvent was used. [d]Reacted in dark. [e]Reacted in natural light. [f]The $BrCF_2COOEt$ (0.4 mmol) was used instead of ICF_2COOEt. Nd - not determined.

Scheme 1. Substrate Scope of Iododifluoroalkylation[a]



[a]Reaction conditions: **1** (0.2 mmol), ICF_2COOEt (0.4 mmol), and Cs_2CO_3 (0.4 mmol) in CH_3CN (1 mL) was irradiated by 30 W blue LED at room temperature. Notes: Yields were calculated by the total isolated yields of *E*- and *Z*-products; the *E*/*Z* ratios were determined by ^{19}F NMR and ^1H NMR spectroscopy.

Scheme 2. Substrate Scope of Hydrodifluoroalkylation[a]



[a]Reaction conditions: **1** (0.2 mmol), ICF_2COOEt (0.4 mmol), and Cs_2CO_3 (0.4 mmol) in THF (1 mL) was irradiated by 30 W blue LED at room temperature. Notes: Yields were calculated by the total isolated yields of *E*- and *Z*-products; the *E*/*Z* ratios were determined by ^{19}F NMR and ^1H NMR spectroscopy.

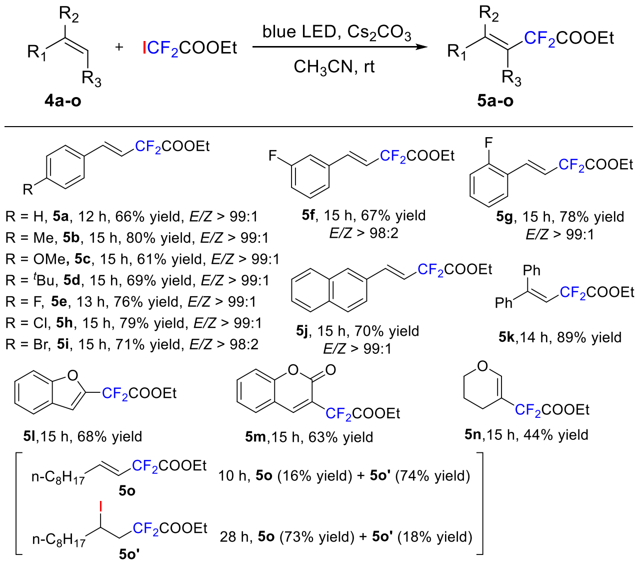
reaction proceeded in the dark (Table 1, entry 15), and the reaction exposed to natural light reacted slowly to give **2a** in 11% yield over 24 h (Table 1, entry 16). By using the difluorobromoacetate instead of difluoroiodoacetate, no reaction took place (Table 1, entry 17).

With the optimized conditions in hand, we then investigated the scope of the iododifluoroalkylation reaction with various alkynes (Scheme 1). In general, a wide range of alkynes could be transformed into the corresponding iododifluoroalkylation products, and the (*E*) stereoisomers were obtained as the major isomers. With electron-withdrawing or electron-donating groups on the para-positions, the internal alkynes reacted smoothly to give the fluorine tagged benzyl iodides (**2b**−**e**). 1-Phenyl-1-butyne and the internal alkyne with alkyl substituents also reacted well (**2f**−**g**). Slightly reduced yields were obtained by using alkynes with electron-withdrawing substituents (**2h**−**i**). Next, a range of terminal alkynes was investigated. In general, terminal alkynes bearing aryl groups of different electronic properties with substituents at various positions were all suitable for the present transformation, and preferable *E*/*Z* stereoselectivities were obtained by the increase of steric hindrance (**2j**−**t**). Terminal alkynes with pyridyl or alkyl substitutions also participated readily in the present protocol (**2u**−**v**).

Subsequently, by using THF as reaction solvent, some representative alkyl-substituted alkynes were subjected to the optimized reaction conditions (Scheme 2). All of the tested alkynes were successfully transformed to the hydrodifluoroalkylation products as diastereoisomers in about 1:1 *E*/*Z* ratios in good yields. However, by using ethynylbenzene **1j**, only the iododifluoroalkylation product **2j** (76% yield) was obtained.

Furthermore, the current reaction condition was successfully applied to the alkenes. Interestingly, the reactions have afforded the difluoroalkylation products rather than the iododifluoroalkylation products (Scheme 3). A broad range of alkenes with various functional groups, such as alkyls, alkoxy, and halogens, in different positions reacted well with excellent *E*/*Z* stereoselectivity, with no obvious steric effect observed (**5a**−**j**). A 1,1-disubstituted alkene also gave the desired

Scheme 3. Substrate Scope of Difluoroalkylation[a]

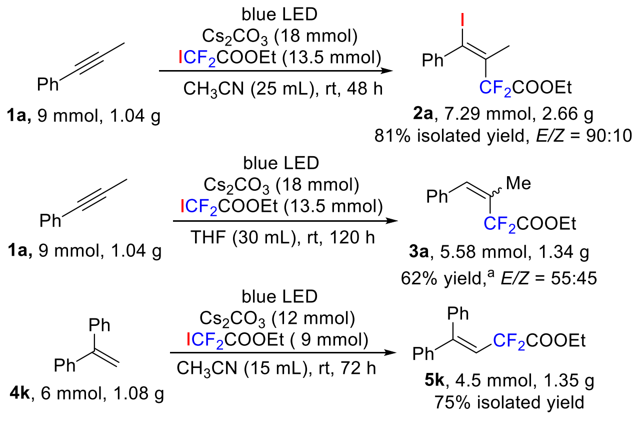


[a]Reaction conditions: **4** (0.2 mmol), ICF$_2$COOEt (0.4 mmol), and Cs$_2$CO$_3$ (0.4 mmol) in CH$_3$CN (1 mL) was irradiated by 30 W blue LED at room temperature. Notes: Yields were calculated by the total isolated yields of *E*- and *Z*-products; the *E*/*Z* ratios were determined by ^{19}F NMR and ^{1}H NMR spectroscopy.

product in good yield (**5k**). Benzofuran and coumarin were selectively difluoroalkylated at specific positions, respectively (**5l**−**m**). When the 3,4-dihydro-2*H*-pyran, which is an aliphatic internal alkene bearing a nonconjugated double bond, was employed, the target difluoroalkylation product was obtained in reduced yield (**5n**). By using a long-chain aliphatic alkene, the iododifluoroalkylation product **5o**′ was obtained as the major product (74% yield). It is interesting to note that the iododifluoroalkylation product **5o**′ could transfer to the difluoroalkylation product **5o** in the reaction mixture, finally giving **5o** in 73% yield over 28 h.

Importantly, three gram-scale experiments have been demonstrated, and all of the reactions proceeded smoothly with satisfactory results (Scheme 4). Thus, the present synthetic methodology may offer a cost-effective practical access to highly functionalized difluoroalkylated molecules.

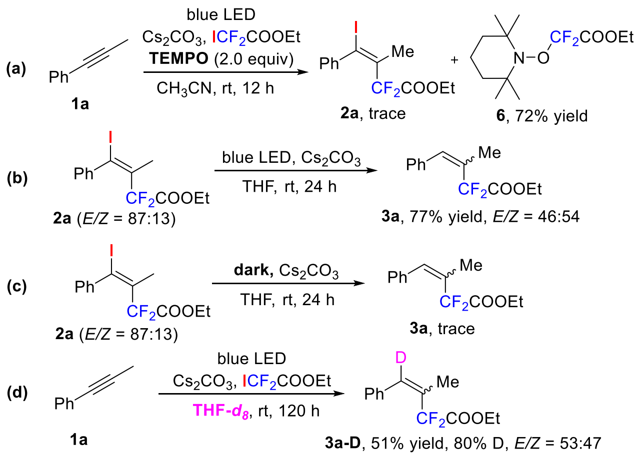
Scheme 4. Gram-Scale Experiments



[a]Yield was calculated from NMR spectrum.

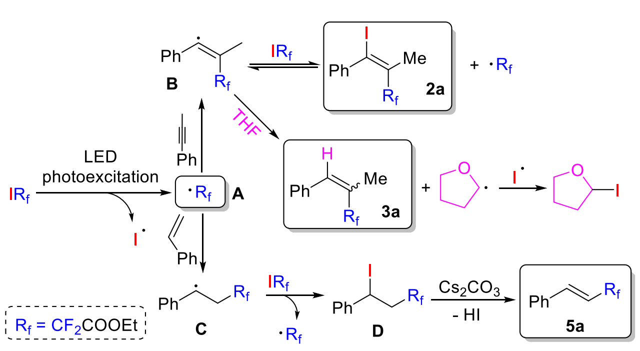
Finally, to rationalize the reaction pathway, several control experiments were performed (Scheme 5). The reaction was completely quenched in the presence of 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO), and the trapped product **6** was obtained as expected (Scheme 5a). This result indicated that a difluoroalkyl radical might be involved in this process. By irradiation of **2a** with THF as solvent, the corresponding hydrodifluoroalkylation product **3a** was obtained in 77% yield (Scheme 5b), but the reaction did not take place in the dark (Scheme 5c). These results indicated the iododifluoroalkylation product **2a** could serve as the intermediate in the hydrodifluoroalkylation reaction, which was promoted by the LED irradiation. The deuterium-difluoroalkylation reaction by using THF-d_8 as solvent has successfully afforded product **3a-D** with 80% deuterium incorporation (Scheme 5d). Therefore, the THF played a role as the hydrogen donor in the hydrodifluoroalkylation reactions. Ultraviolet−visible spectroscopy of ICF$_2$COOEt showed a strong absorption signal at 360 nm, while none was observed for **1a**. This showed that it is ICF$_2$COOEt that absorbs light in the present reaction (please see Supporting Information for details).

Scheme 5. Control Experiments



On the basis of the results of control experiments and related references,[5−7,13] the proposed mechanism of the difluoroalkylation reactions is outlined in Scheme 6. The reactions are initiated with the difluoroalkyl radical **A**, which is generated directly by photoexcitation of ethyl difluoroiodoacetate. In the case of an alkyne, radical **A** adds to the prop-1-yn-1-ylbenzene forming a vinyl radical **B**. The latter could abstract an iodine atom to result in formation of the

Scheme 6. Proposed Reaction Mechanism



iododifluoroalkylation product **2a**. Alternatively, the photoexcitation of **2a** could also generate vinylic radical **B**, to undergo hydrogen abstraction from THF to provide the hydrodifluoroalkylation product **3a**. In the case of an alkene, the benzylic radical **C** is formed by the addition of the difluoroalkyl radical **A** to styrene. Subsequently, benzyl radical **C** abstract an iodine atom from ethyl difluoroiodoacetate to give the iododifluoroalkylation intermediate **D**, which finally transforms into the difluoroalkylation product **5a** by HI elimination.

In summary, a method of the generation of difluoroalkyl radical was established by direct photoexcitation of ethyl difluoroiodoacetate. The catalyst- and oxidant-free conditions were successfully applied to alkynes and alkenes to afford the iododifluoroalkylation products and the difluoroalkylation products, respectively. By fine turning the reaction solvent, the hydrodifluoroalkylation of alkynes was also developed. The control experiments have revealed that the iododifluoroalkylation product could serve as the intermediate in the hydrodifluoroalkylation reaction with THF as the hydrogen donor.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.9b03855.

Experimental procedures and characterization data (PDF)

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) O'Hagan, D. *Chem. Soc. Rev.* **2008**, *37*, 308−319. (b) Furuya, T.; Kamlet, A. S.; Ritter, T. *Nature* **2011**, *473*, 470−477. (c) Tomashenko, O. A.; Grushin, V. V. *Chem. Rev.* **2011**, *111*, 4475−4521.

(2) (a) Purser, S. P.; Moore, R.; Swallow, S.; Gouverneur, V. *Chem. Soc. Rev.* **2008**, *37*, 320−330. (b) Müller, K.; Faeh, C.; Diederich, F. *Science* **2007**, *317*, 1881−1886. (c) Hagmann, W. K. *J. Med. Chem.* **2008**, *51*, 4359−4369. (d) Wang, J.; Sanchez-Rosello, M.; Acena, J. L.; del Pozo, C.; Sorochinsky, A. E.; Fustero, S.; Soloshonok, V. A.; Liu, H. *Chem. Rev.* **2014**, *114*, 2432−2506. (e) Romanenko, V.; Kukhar, P. *Chem. Rev.* **2006**, *106*, 3868−3935.

(3) (a) Koike, T.; Akita, M. *Acc. Chem. Res.* **2016**, *49*, 1937−1945. (b) Besset, T.; Schneider, C.; Cahard, D. *Angew. Chem., Int. Ed.* **2012**, *51*, 5048−5050; *Angew. Chem.* **2012**, *124*, 5134−5136. (c) Wang, W.-Q.; Yu, Q.-W.; Zhang, Q.; Li, J.-W.; Hui, F.; Yang, J.-M.; Lü, J. *Youji Huaxue* **2018**, *38*, 1569−1585. (d) Zhang, Y.; Ye, S.-Y.; Ji, M.-M.; Li, L.-S.; Guo, D.-M.; Zhu, G.-G. *J. Org. Chem.* **2017**, *82*, 6811−6818.

(4) (a) Feng, Z.; Xiao, Y.-L.; Zhang, X.-G. *Acc. Chem. Res.* **2018**, *51*, 2264−2278. (b) Song, H.-X.; Han, Q.-Y.; Zhao, C.-L.; Zhang, C.-P. *Green Chem.* **2018**, *20*, 1662−1731.

(5) (a) Wu, G.-J.; von Wangelin, A. *J. Chem. Sci.* **2018**, *9*, 1795−1802. (b) Xu, T.; Cheung, C. W.; Hu, X.-L. *Angew. Chem., Int. Ed.* **2014**, *53*, 4910−4914; *Angew. Chem.* **2014**, *126*, 5010−5014. (c) Li, G.; Cao, Y.-X.; Luo, C.-G.; Su, Y.-M.; Li, Y.; Lan, Q.; Wang, X.-S. *Org. Lett.* **2016**, *18*, 4806−4809. (d) Li, G.; Wang, T.; Fei, F.; Su, Y.-M.; Li, Y.; Lan, Q.; Wang, X.-S. *Angew. Chem., Int. Ed.* **2016**, *55*, 3491−3495; *Angew. Chem.* **2016**, *128*, 3552−3556. (e) Wang, X.-Y.; Zhao, S.; Liu, J.; Zhu, D.-S.; Guo, M.-J.; Tang, X.-Y.; Wang, G.-W. *Org. Lett.* **2017**, *19*, 4187−4190. (f) Feng, Z.; Min, Q.-Q.; Zhao, H.-Y.; Gu, J.-W.; Zhang, X.-G. *Angew. Chem., Int. Ed.* **2015**, *54*, 1270−1274; *Angew. Chem.* **2015**, *127*, 1286−1290. (g) Wang, Q.; Zheng, L.; He, Y.-T.; Liang, Y.-M. *Chem. Commun.* **2017**, *53*, 2814−2817. (h) He, Y.-T.; Li, L.-H.; Wang, Q.; Wu, W.-S.; Liang, Y.-M. *Org. Lett.* **2016**, *18*, 5158−5161. (i) Xiong, H.-G.; Li, Y.-J.; Qian, B.; Wei, R.-B.; Van der Eycken, E. V.; Bao, H.-L. *Org. Lett.* **2019**, *21*, 776−779. (j) Zhang, P.-B.; Ying, J.-X.; Tang, G.; Zhao, Y.-F. *Org. Chem. Front.* **2017**, *4*, 2054−2057. (k) Ma, J.-J.; Yi, W.-B. *Org. Biomol. Chem.* **2017**, *15*, 4295−4299. (l) Li, D.-K.; Mao, T.-T.; Huang, J.-B.; Zhu, Q. *J. Org. Chem.* **2018**, *83*, 10445−10452. (m) Feng, X.-R.; Wang, X.-Y.; Chen, H.-T.; Tang, X.-Y.; Guo, M.-J.; Zhao, W.-T.; Wang, G.-W. *Org. Biomol. Chem.* **2018**, *16*, 2841−2845. (n) Deng, W.-L.; Li, Y.-J.; Li, Y.-G.; Bao, H.-L. *Synthesis* **2018**, *50*, 2974−2980.

(6) (a) Wallentin, C.-J.; Nguyen, J. D.; Finkbeiner, P.; Stephenson, C. R. J. *J. Am. Chem. Soc.* **2012**, *134*, 8875−8884. (b) Zhong, J.-J.; Yang, C.; Chang, X.-Y.; Zou, C.; Lu, W.; Che, C.-M. *Chem. Commun.* **2017**, *53*, 8948−8951. (c) Mizuta, S.; Verhoog, S.; Engle, K. M.; Khotavivattana, T.; O'Duill, M.; Wheelhouse, K.; Rassias, G.; Médebielle, M.; Gouverneur, V. *J. Am. Chem. Soc.* **2013**, *135*, 2505−2508. (d) Iqbal, N.; Jung, J.; Park, S.; Cho, E. *Angew. Chem., Int. Ed.* **2014**, *53*, 539−542. (e) Rawner, T.; Lutsker, E.; Kaiser, C. A.; Reiser, O. *ACS Catal.* **2018**, *8*, 3950−3956. (f) Yu, C.; Iqbal, N.; Park, S.; Cho, E. *Chem. Commun.* **2014**, *50*, 12884−12887. (g) Yajima, T.; Ikegami, M. *Eur. J. Org. Chem.* **2017**, *2017*, 2126−2129. (h) Li, L.-X.; Ma, Y.-N.; Tang, M.; Guo, J.; Yang, Z.; Yan, Y.-Z.; Ma, X.-T.; Tang, L. *Adv. Synth. Catal.* **2019**, *361*, 3723−3728. (i) Liu, Y.; Chen, X.-L.; Sun, K.; Li, X.-Y.; Zeng, F.-L.; Liu, X.-C.; Qu, L.-B.; Zhao, Y.-F.; Yu, B. *Org. Lett.* **2019**, *21*, 4019−4024. (j) Zeng, F.-L.; Sun, K.; Chen, X.-L.; Yuan, X.-Y.; He, S.-Q.; Liu, Y.; Peng, Y.-Y.; Qu, L.-B.; Lv, Q.-Y.; Yu, B. *Adv. Synth. Catal.* **2019**, *361*, 5176−5181.

(7) (a) Fang, X.; Yang, X.-Y.; Yang, X.-J.; Mao, S.-J.; Wang, Z.-H.; Chen, G.-R.; Wu, F.-H. *Tetrahedron* **2007**, *63*, 10684−10692. (b) Motoda, D.; Kinoshita, H.; Shinokubo, H.; Oshima, K. *Adv. Synth. Catal.* **2002**, *344*, 261−265. (c) Jennings, M. P.; Cork, E. A.; Ramachandran, P. V. *J. Org. Chem.* **2000**, *65*, 8763−8766. (d) Li, Y.; Li, H.; Hu, J. *Tetrahedron* **2009**, *65*, 478−483. (e) Wang, D.-F.; Wu, J.-J.; Huang, J.-W.; Liang, J.-Q.; Peng, P.; Chen, H.; Wu, F.-H. *Tetrahedron* **2017**, *73*, 3478−3484.

(8) (a) Belhomme, M.-C.; Poisson, T.; Pannecoucke, X. *J. Org. Chem.* **2014**, *79*, 7205−7211. (b) Fujikawa, K.; Fujioka, Y.; Kobayashi, A.; Amii, H. *Org. Lett.* **2011**, *13*, 5560−5563. (c) Sun, X.-Y.; Yu, S.-Y. *Org. Lett.* **2014**, *16*, 2938−2941. (d) Liang, J.-Q.; Huang, G.-Z.; Peng, P.; Zhang, T.-Y.; Wu, J.-J.; Wu, F.-H. *Adv. Synth. Catal.* **2018**, *360*, 2221−2227.

(9) Selected reviews: (a) Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C. *Chem. Rev.* **2013**, *113*, 5322−5363. (b) Tucker, J. W.; Stephenson, C. R. J. *J. Org. Chem.* **2012**, *77*, 1617−1622. (c) Shi, L.; Xia, W.-J. *Chem. Soc. Rev.* **2012**, *41*, 7687−7697. (d) Bach, T.; Hehn, J. P. *Angew. Chem., Int. Ed.* **2011**, *50*, 1000−1045. (e) Yoon, T. P.; Ischay, M. A.; Du, J. *Nat. Chem.* **2010**, *2*, 527−532.

(10) Lv, H.-P.; Laishram, R. D.; Li, J.-Y.; Zhou, Y.-Y.; Xu, D.-D.; More, S.; Dai, Y.-Z.; Fan, B.-M. *Green Chem.* **2019**, *21*, 4055−4061.

(11) Zhang, X.-X.; Chen, J.-C.; Gao, Y.; Li, K.-K.; Zhou, Y.-Y.; Sun, W.-Q.; Fan, B.-M. *Org. Chem. Front.* **2019**, *6*, 2410−2414.

(12) Selected examples of the base promoted free radical reactions: (a) Yanagisawa, S.; Ueda, K.; Taniguchi, T.; Itami, K. *Org. Lett.* **2008**, *10*, 4673−4676. (b) Liu, W.; Cao, H.; Zhang, H.; Zhang, H.; Chung, K. H.; He, C.; Wang, H.-B.; Kwong, F. Y.; Lei, A.-W. *J. Am. Chem. Soc.* **2010**, *132*, 16737−16740. (c) Shirakawa, E.; Zhang, X.-J.; Hayashi, T. *Angew. Chem., Int. Ed.* **2011**, *50*, 4671−4674. (d) Wei, W.-T.; Dong, X.-J.; Nie, S.-Z.; Chen, Y.-Y.; Zhang, X.-J.; Yan, M. *Org. Lett.* **2013**, *15*, 6018−6021. (e) Evoniuk, C. J.; Gomes, G. P.; Hill, S. P.; Fujita, S.; Hanson, K.; Alabugin, I. V. *J. Am. Chem. Soc.* **2017**, *139*, 16210−16221.

(13) (a) Ren, Y.-Y.; Zheng, X.; Zhang, X.-G. *Synlett* **2018**, *29*, 1028−1032. (b) Meyer, C. F.; Hell, S. M.; Misale, A.; Trabanco, A. A.; Gouverneur, V. *Angew. Chem., Int. Ed.* **2019**, *58*, 8829−8833. (c) Lin, Q.-Y.; Xu, X.-H.; Zhang, K.; Qing, F.-L. *Angew. Chem.* **2016**, *128*, 1501−1505.

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