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# Photoredox-Catalyzed Three-Component Tandem Process: An Assembly of Complex Trifluoromethylated Phthalans and Isoindolines

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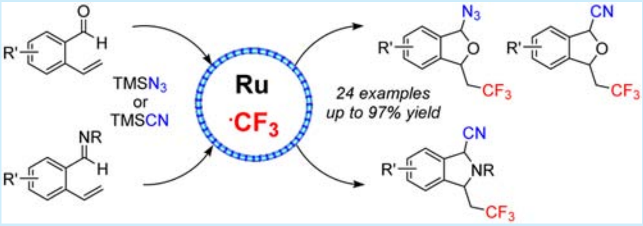
Supporting Information

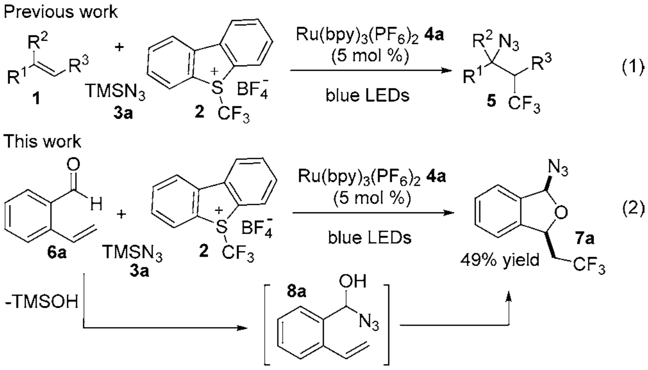
**ABSTRACT:** A novel photoredox-mediated tandem three-component process afforded a wide variety of $CF_3$-containing phthalans and isoindolines in respectable yields and with moderate to excellent diastereoselectivity.



Trifluoromethylated heterocycles have found extensive use in medicinal and agricultural chemistry.[1,2] Indeed, the incorporation of a $CF_3$ group into heterocyclic compounds often exhibits remarkably different chemical, physical, and biological properties in comparison with their fluorine-free analogues.[1,2] As a result, much effort has been devoted toward the development of efficient methods for the synthesis of $CF_3$-containing heterocyclic compounds. However, although phthalans (1,3-dihydroisobenzofurans) and 1,3-disubstituted isoindolines are ubiquitous in various pharmaceutical agents,[3,4] very few synthetic methods have been developed for the preparation of trifluoromethylated analogues.[5] This highlights the need for further synthetic developments in this area.

During our study of photocatalyzed three-component azidotrifluoromethylation of olefins (Scheme 1, eq 1),[6a,b] we had opportunities to attempt the trifluoromethylation of 2-vinylbenzaldehyde (**6a**) with Umemoto's reagent (**2**) in the presence of azidotrimethylsilane ($TMSN_3$, **3a**) and $Ru(bpy)_3(PF_6)_2$ photocatalyst **4a** under visible light irradiation (blue LEDs).[6−9] The only product formed was not the expected $\beta$-trifluoromethylated azide **5** but, to our surprise, the 1-azido-3-trifluoroethyl-1,3-phthalan **7a** in 49% yield with excellent diastereoselectivity in favor of the *cis*-diastereomer (Scheme 1, eq 2).[10] This exciting finding was attributed to the fact that the $\alpha$-azido alcohol intermediate **8a**, *in situ* generated by azide addition, could further undergo a photoredox-mediated intramolecular oxytrifluoromethylation via a tandem process.[9l,n−p] To the best of our knowledge, such a three-component tandem reaction has never been reported.[6−11] This, in conjunction with the general lack of synthetic methods of $CF_3$-containing phthalans and isoindolines, prompted us to examine in detail this novel tandem transformation and to report herein our preliminary results.

**Scheme 1. Use of 2-Vinylbenzaldehyde 6a in the Photoredox-Catalyzed Azidotrifluoromethylation of Styrenes**



We then optimized the reaction conditions of this one-pot photoredox-catalyzed transformation, and the results are summarized in Table 1. First, the amount of $TMSN_3$ **3a** was examined (entries 1−4). The desired product **7a** was reached in 67% yield when 5.0 equiv of **3a** were used in $CH_2Cl_2$ at rt, and no improvement was observed with 10 equiv (entry 3). Subsequently, various solvents were screened, revealing that freshly distilled $CH_2Cl_2$ was the best choice for the reaction (entry 4). The addition of molecular sieves or $MgSO_4$ to remove the water had adverse effects, possibly due to a poor transmission of light in this photoredox reaction (entries 5−7). No beneficial effect was then observed when a Lewis base was used to activate $TMSN_3$ (entries 8−10).[12] No product was form with $NaN_3$. Attempts with other photoredox catalysts, such as $Ru(bpy)_3Cl_2$, [Ir-

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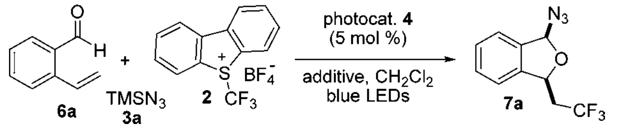
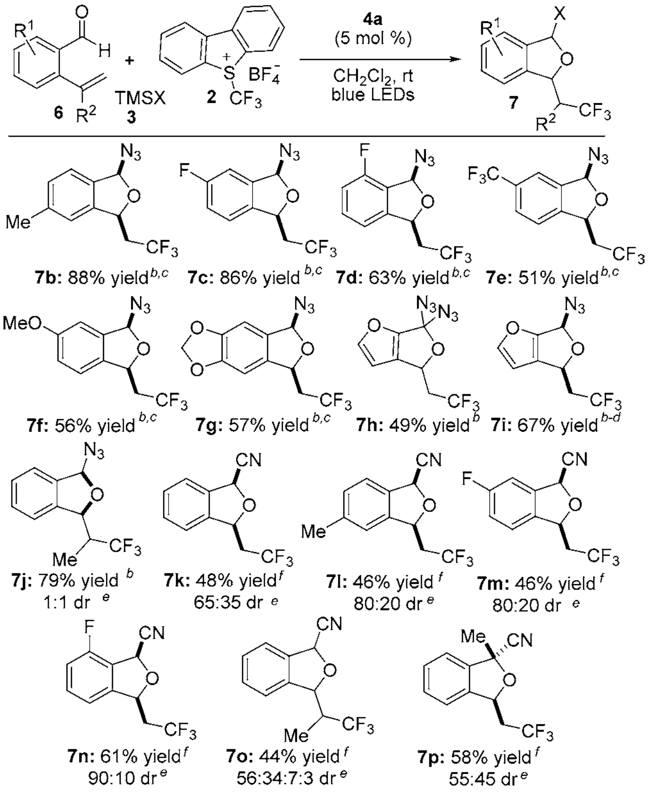
**Table 1. Survey of Reaction Conditions**[a]



| entry | photocat. | equiv of **3a** | additive | yield (%)[b] |
|---|---|---|---|---|
| 1 | $Ru(bpy)_3(PF_6)_2$ (**4a**) | 3 | | 49 |
| 2 | **4a** | 5 | | 67 |
| 3 | **4a** | 10 | | 66 |
| 4 | **4a** | 5 | | 79[c,d] |
| 5 | **4a** | 5 | 4 Å MS | 31[c] |
| 6 | **4a** | 5 | 3 Å MS | <10[c] |
| 7 | **4a** | 5 | $MgSO_4$ | <10[c] |
| 8 | **4a** | 5 | MgO[e] | 69[c] |
| 9 | **4a** | 5 | $P(OEt)_3$[e] | 49[c] |
| 10 | **4a** | 5 | $Ph_3PO$[e] | 30[c] |
| 11 | $Rubpy_3Cl_2$ (**4b**) | 5 | | 45[c] |
| 12 | $[Ir(ppy)_2(dtbbpy)]PF_6$ (**4c**) | 5 | | 50[c] |
| 13 | $[Ru(bpz)_3(PF_6)_2]$ (**4d**) | 5 | | <5[c] |
| 14 | **4a** | 5 | | 0[f] |

[a] General conditions: **6a** (0.10 mmol), **2** (0.15 mmol), **4** (0.05 equiv), and $TMSN_3$ in $CH_2Cl_2$ (2 mL) irradiated at rt for 2 h. [b] Yields referred to chromatographically pure product. [c] Reaction performed in dry $CH_2Cl_2$. [d] Maintained at constant room temperature of 20 °C. [e] With 25 mol %. [f] With $NaN_3$.

**Scheme 2. Scope of the Photoredox-Catalyzed Reaction with Representative Vinylbenzaldehydes 6**[a]



[a] Yields referred to chromatographically pure product. [b] General conditions: **6** (0.10 mmol), **2** (0.15 mmol), $TMSN_3$ **3a** (0.50 mmol), and **4a** (0.05 equiv), in $CH_2Cl_2$ (2 mL) irradiated at rt for 2 h. [c] >95:5 dr determined by $^1H$ NMR. [d] For 1 h. [e] Determined by $^1H$ NMR. [f] General conditions: **6** (0.10 mmol), **2** (0.15 mmol), TMSCN **3b** (0.20 mmol), and **4a** (0.05 equiv), in $CH_2Cl_2$ (2 mL) irradiated at rt for 2 h.

$(ppy)_2(dtbbpy)]PF_6$, and $[Ru(bpz)_3(PF_6)_2]$, were not as successful as $Ru(bpy)_3(PF_6)_2$ (5 mol %).

The scope of this novel synthesis of 1-azido-3-trifluoroethyl-1,3-phthalans was next assessed by varying the structures of vinylbenzaldehyde. As shown in Scheme 2, the *ortho*-, *meta*-, and *para*-substituted aryl groups were all compatible, leading to the respective phthalans (**7b**−**7d**) in good to excellent yields with high diatereoselectivities. It was also found that the substrates bearing a strong electron-withdrawing group such as $CF_3$ (**6e**) as well as a strong electon-donating group such as OMe (**6f**) gave diminished yields (**7e** and **7f**, respectively). On the other hand, 6-vinylbenzo[*d*][1,3]dioxole-5-carbaldehyde (**6g**) was largely converted to the azidotrifluoromethylated phthalan **7g** (57%) along with a small amount of two other nontrifluoromethylated products. The first one was identified as *cis*-5,7-diazido-6,7-dihydro-5*H*-indeno[5,6-*d*][1,3]dioxole **7g′**, and its structure was confirmed by X-ray diffraction (see Supporting Information (SI) for details).[13] The second product was the corresponding 2,3-dihydro-1,3-epoxyindene **7g″** in which $N_3$ and $CF_3$ groups were not incorporated (see the SI for details). Surprisingly, with 3-vinylfuran-2-carbaldehyde (**6h**) as the substrate in the photocatalyzed tandem reaction, the unexpected diazido-trifluoromethylated adduct **7h** was the only isolated product (49%). This probably resulted from an overoxidation of **6h** followed by *in situ* addition of azide.[14] Fortunately, reducing the reaction time from 2 to 1 h resulted in exclusive formation of desired *cis*-**7i**, without detection of diazide product **7h**. However, further attempts to perform the reaction with ketones failed in this tandem reaction, and only a complex mixture was obtained. Additionally, the substrate with an internal alkene **6j** was also suitable to deliver **7j** in 79% yield as a mixture of two diastereomers (1:1 dr). Then, we tried to extend this three-component tandem reaction to trimethylsilyl cyanide (TMSCN).[6b] Unfortunately, under the same reaction conditions, the expected 3-trifluoroethyl-1,3-phthalan 1-carbonitrile (**7k**) was not observed. Only degraded products together with some unreacted starting materials were recovered. However, when 2 equiv of TMSCN were used instead of 5, we were pleased to see the formation of **7k** in 48% yield. Using these optimal conditions, electron-rich as well as electron-poor aromatic rings were suitable substrates, affording the corresponding phthalans **7l** and **7m** in respectable yields and with an 80:20 mixture of diastereomers in favor of *cis* (determined by X-ray).[13] A slightly better yield and excellent diastereoselectivity were achieved with the *ortho*-substituted fluorobenzyl aldehyde **6d**. Furthermore, internal alkene **6j** was successfully used in the present system, leading to the corresponding cyano-trifluoromethylated phthalan **7o** as a mixture of four diastereomers in a ratio of 56:34:7:3. Finally, we tested the reaction with a ketone-substituted product **6p** and were pleased to isolate the expected 1-cyano-3-trifluoroethylphtalan **7p** as the major product (58% yield), together with the cyanotrifluoromethylated adduct (36% yield).

Next, using the same strategy as for phthalans, the reaction of 4-methoxy-*N*-(2-vinylbenzylidene)-benzene-sulfonamide (**9a**) and $TMSN_3$ (**3a**) led to the formation of a complex mixture of products. However, to our delight, this novel tandem reaction was successful when TMSCN was used, providing the desired product **10a** in excellent. This new multicomponent process provides a rapid access to isoindoline-1-carboxylic acid, an important scaffold in the preparation of biologically active compounds, especially against cancer and for treatment of

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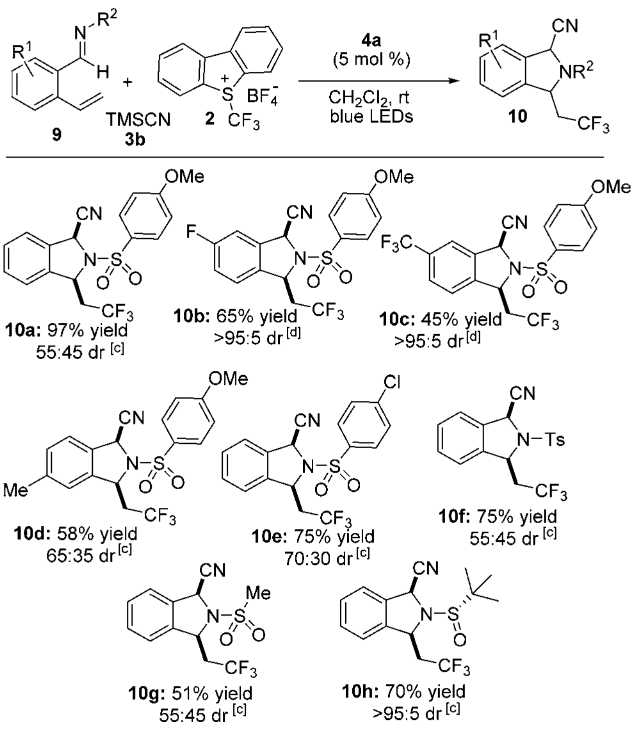
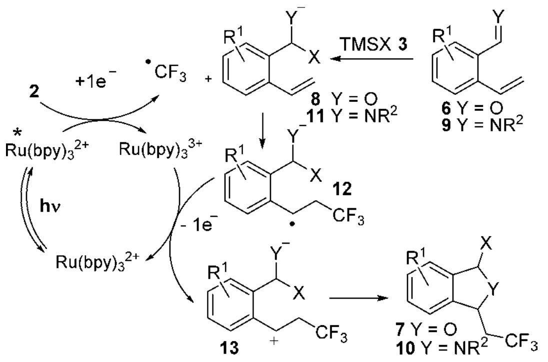
### Scheme 3. Scope of the Photoredox-Catalyzed Reaction with Representative Vinylimines[a,b]



[a]Yields referred to chromatographically pure product. [b]General conditions: **6** (0.10 mmol), **2** (0.15 mmol), TMSN$_3$ **3a** (0.50 mmol), and **4a** (0.05 equiv), in CH$_2$Cl$_2$ (2 mL) irradiated at rt for 2 h. [c]>95:5 dr determined by $^1$H NMR. [d]For 1 h. [e]Determined by $^1$H NMR. [f]General conditions: **6** (0.10 mmol), **2** (0.15 mmol), TMSCN **3b** (0.20 mmol), and **4a** (0.05 equiv), in CH$_2$Cl$_2$ (2 mL) irradiated at rt for 2 h.

diabetes, dyslipidemia, atherosclerosis, and obesity.[15] As shown in Scheme 3, a range of vinylbenzaldehydes reacted smoothly with TMSCN, affording **10b–d** with moderate to excellent yields. Surprisingly, in the case of **10b** and **10c**, we observed complete isomerization of the *cis–trans* mixture into the *cis*-isomer after purification on silica gel. Various sulfonyl groups were tolerated giving the corresponding cyanotrifluoromethylated products **10e–g** in good yields.[13] It is interesting to note that, in most cases, the mixtures of diastereomers were found to be separable by column chromatography. Finally, the Ellman chiral *N-tert*-butanesulfinyl imine **9h** was successfully engaged in this tandem multicomponent reaction yielding **10h** in 70% yield as a single *cis*-diastereomer (determined by X-ray).[13] To gain more insights into the reaction mechanism, a series of control experiments was performed. Initially, the photocatalyzed process of **6h** was monitored by $^1$H NMR spectroscopy (see SI for details). The formation of $\alpha$-siloxy-azide **8h** was clearly observed after 20 min. The starting material was completely consumed 10 min later, and we observed 40% conversion of final product **7i**. This conversion continued for about 1 h until the starting material **6h** was consumed. Moreover, when the azido alcohol **8h** was isolated and subsequently submitted to photocatalytic trifluoromethylation, only **7i** was formed. It is interesting to note that no azidotrifluoromethylated adduct **5** was isolated, indicating that **5** is not an intermediate in this reaction. Additionally, to validate the present photoredox-catalyzed tandem radical reaction, experiments in the absence of irradiation and/or [Ru(bpy)$_3$(PF$_6$)$_2$] **4a** were also conducted. The $\alpha$-azido alcohol derivative **8h** was the sole product formed. Finally, the reaction was significantly inhibited by radical scavengers such as TEMPO, benzoquinone (BQ), and 1,4-dinitrobenzene. On the basis of the above-mentioned results as well as other reports,[6−9] a plausible reaction mechanism is shown in Scheme 4. First, the nucleophilic addition of azide or cyanide to aldehyde or imine results in the formation of $\alpha$-hydroxy or $\alpha$-amino-azide **8** and **11**, respectively. At the same time, $\cdot CF_3$ is generated from Umemoto's reagent **2** through single electron transfer reduction by excited-state *Ru(bpy)$_3^{2+}$.[8] Afterward, regioselective radical addition to aldehyde **6** or imine **9** would generate a benzyl radical **12** which would then be oxidized by Ru(bpy)$_3^{3+}$ to afford **13**. Finally, product **7** or **10** is formed by intramolecular trapping of **13** with a hydroxy or amino group, respectively. Based on these first results, we assume that the kinetically favored oxy- or aminocyclization and the slow concentration of **13** guarantee the success of the overall tandem process.

### Scheme 4. Plausible Reaction Mechanism



In summary, we have described a novel visible-light photoredox promoted three-component tandem process for the synthesis of CF$_3$-containing phthalans and isoindolines from readily accessible starting materials. This original tandem-type process is applicable to a wide range of aldehydes and imines, including chiral ones. The broad substrate scope makes the method highly efficient and widely applicable, providing an easy and entirely novel route toward variously functionalized trifluoromethylated phthalans and isoindolines. Further exploration of the reaction scope and other types of multicomponent tandem reactions is currently under investigation.

## ■ ASSOCIATED CONTENT

### Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b01257.

Detailed experimental procedures and spectral data for all new compounds (PDF)

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### Notes

The authors declare no competing financial interest.

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## ■ REFERENCES

(1) (a) Gakh, A. A.; Shermolovich, Y. *Curr. Top. Med. Chem.* **2014**, *14*, 952. (b) Sodeoka, M.; Egami, H. *Pure Appl. Chem.* **2014**, *86*, 1247. (c) Meyer, F. *Chem. Commun.* **2016**, *52*, 3077.

(2) For reviews, see: (a) Kirsch, P. *Modern Fluoroorganic Chemistry: Synthesis, Reactivity, Applications*, 2nd, Completely Revised and Enlarged Edition; Wiley: New York, 2013. (b) Bégué, J. P.; Bonnet-Delpon, D. *Bioorganic and Medical Chemistry of Fluorine*; Wiley-VCH: Weinheim, 2008. (c) *Fluorine in Medicinal Chemistry and Chemical Biology*; Ojima, I., Ed.; Wiley-Blackwell: Chichester, 2009. (d) Muller, K.; Faeh, C.; Diederich, F. *Science* **2007**, *317*, 1881. (e) O'Hagan, D. *Chem. Soc. Rev.* **2008**, *37*, 308. (f) Hagmann, W. K. *J. Med. Chem.* **2008**, *51*, 4359. (g) Purser, S.; Moore, P. R.; Swallow, S.; Gouverneur, V. *Chem. Soc. Rev.* **2008**, *37*, 320. (h) Furuya, T.; Kamlet, A. S.; Ritter, T. *Nature* **2011**, *473*, 470. (i) Tomashenko, O. A.; Grushin, V. V. *Chem. Rev.* **2011**, *111*, 4475. (j) Wang, J.; Sánchez-Roselló, M.; Aceña, J. L.; del Pozo, C.; Sorochinsky, A. E.; Fustero, S.; Soloshonok, V. A.; Liu, H. *Chem. Rev.* **2014**, *114*, 2432.

(3) Recent review on phthalan syntheses: (a) Karmakar, R.; Pahari, P.; Mal, D. *Chem. Rev.* **2014**, *114*, 6213. For selected examples of bioactive phthalans, see: (b) DeBernardis, J. F.; Arendsen, D. L.; Kyncl, J. J.; Kerkman, D. J. *J. Med. Chem.* **1987**, *30*, 178. (c) Lovey, R. G.; Elliott, A. J.; Kaminski, J. J.; Loebenberg, D.; Parmegiani, R. M.; Rane, D. F.; Girijavallabham, V. M.; Pike, R. E.; Guzik, H. *J. Med. Chem.* **1992**, *35*, 4221. (d) Namikoshi, M.; Kobayashi, H.; Yoshimoto, T.; Meguro, S. *Chem. Lett.* **2000**, 308. (e) Strobel, G.; Ford, E.; Worapang, J.; Harper, J. K.; Arif, A. M.; Grant, D. M.; Fung, P. C. W.; Chau, R. M. W. *Phytochemistry* **2002**, *60*, 179. (f) Harper, J. K.; Arif, A. M.; Ford, E. J.; Strobel, G. A.; Porco, J. A., Jr.; Tomer, D. P.; Oneill, K. L.; Heider, E. M.; Grant, D. M. *Tetrahedron* **2003**, *59*, 2471. (g) Pahari, P.; Senapati, B.; Mal, D. *Tetrahedron Lett.* **2004**, *45*, 5109. (h) García, D.; Foubelo, F.; Yus, M. *Tetrahedron* **2008**, *64*, 4275.

(4) Selected examples of bioactive isoindolines: (a) Portevin, B.; Tordjman, C.; Pastoureau, P.; Bonnet, J.; De Nanteuil, G. *J. Med. Chem.* **2000**, *43*, 4582. (b) Ewing, D. F.; Len, C.; Mackenzie, G.; Petit, J. P.; Ronco, G.; Villa, P. *J. Pharm. Pharmacol.* **2001**, *53*, 945. (c) Stuk, T. L.; Assink, B. K.; Bates, R. C.; Erdman, D. T.; Fedij, V.; Jennings, S. M.; Lassig, J. A.; Smith, R. J.; Smith, T. L. *Org. Process Res. Dev.* **2003**, *7*, 851. (d) Estiarte, M. A.; Johnson, R. J.; Kaub, C. J.; Gowlugari, S.; O'Mahony, D. J. R.; Nguyen, M. T.; Emerling, D. E.; Kelly, M. G.; Kincaid, J.; Vincent, F.; Duncton, M. A. J. *MedChemComm* **2012**, *3*, 611.

(5) Examples of syntheses of $CF_3$-containing phthalans: (a) Konno, T.; Moriyasu, K.; Kinugawa, K.; Ishihara, T. *Org. Biomol. Chem.* **2010**, *8*, 1718. (b) Hu, B.-L.; Li, C.-L.; Liao, Z.-Y.; Zhang, X.-G. *Synlett* **2013**, *24*, 2748. (c) Yuan, H.; Gong, Y. *J. Fluorine Chem.* **2013**, *149*, 125. Only example of synthesis of $CF_3$-containing isoindolines: (d) Fustero, S.; Ibáñez, I.; Barrio, P.; Maestro, M. A.; Catalán, S. *Org. Lett.* **2013**, *15*, 832.

(6) (a) Dagousset, G.; Carboni, A.; Magnier, E.; Masson, G. *Org. Lett.* **2014**, *16*, 4340. (b) Carboni, A.; Dagousset, G.; Magnier, E.; Masson, G. *Org. Lett.* **2014**, *16*, 1240. (c) Carboni, A.; Dagousset, G.; Magnier, E.; Masson, G. *Chem. Commun.* **2014**, *50*, 14197. (d) Carboni, A.; Dagousset, G.; Magnier, E.; Masson, G. *Synthesis* **2015**, *47*, 2439. (e) Courant, T.; Masson, G. *Chem. - Eur. J.* **2012**, *18*, 423.

(7) For recent reviews on photoredox catalysis, see: (a) Ravelli, D.; Dondi, D.; Fagnoni, M.; Albini, A. *Chem. Soc. Rev.* **2009**, *38*, 1999. (b) Zeitler, K. *Angew. Chem., Int. Ed.* **2009**, *48*, 9785. (c) Yoon, T. P.; Ischay, M. A.; Du, J. *Nat. Chem.* **2010**, *2*, 527. (d) Inagaki, A.; Akita, M. *Coord. Chem. Rev.* **2010**, *254*, 1220. (e) Narayanam, J. M. R.; Stephenson, C. R. J. *Chem. Soc. Rev.* **2011**, *40*, 102. (f) Teplý, F. *Collect. Czech. Chem. Commun.* **2011**, *76*, 859. (g) Maity, S.; Zheng, N. *Synlett* **2012**, *23*, 1851. (h) Xuan, J.; Xiao, W.-J. *Angew. Chem., Int. Ed.* **2012**, *51*, 6828. (i) Tucker, J. W.; Stephenson, C. R. J. *J. Org. Chem.* **2012**, *77*, 1617. (j) Shi, L.; Xia, W. *Chem. Soc. Rev.* **2012**, *41*, 7687. (k) Xi, H. Y. Y.; Lei, A. *Org. Biomol. Chem.* **2013**, *11*, 2387. (l) Yoon, T. P. *ACS Catal.* **2013**, *3*, 895. (m) Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C. *Chem. Rev.* **2013**, *113*, 5322. (n) Koike, T.; Akita, M. *Synlett* **2013**, *24*, 2492. (o) Schultz, D. M.; Yoon, T. P. *Science* **2014**, *343*, 1239176. (p) Koike, T.; Akita, M. *Inorg. Chem. Front.* **2014**, *1*, 562. (q) Hopkinson, M. N.; Sahoo, B.; Li, J.-L.; Glorius, F. *Chem. - Eur. J.* **2014**, *20*, 3874. (r) Meggers, E. *Chem. Commun.* **2015**, *51*, 3290. (s) Kärkäs, M. D.; Matsuura, B. S.; Stephenson, C. R. J. *Science* **2015**, *349*, 1285.

(8) For recent reviews on photoredox-catalyzed perfluoroalkylation, see: (a) Koike, T.; Akita, M. *Top. Catal.* **2014**, *57*, 967. (b) Egami, H.; Sodeoka, M. *Angew. Chem., Int. Ed.* **2014**, *53*, 8294. (c) Cao, M.-Y.; Ren, X.; Lu, Z. *Tetrahedron Lett.* **2015**, *56*, 3732. (d) Alonso, C.; Martínez de Marigorta, E.; Rubiales, G.; Palacios, F. *Chem. Rev.* **2015**, *115*, 1847. (e) Barata-Vallejo, S.; Bonesi, S. M.; Postigo, A. *Org. Biomol. Chem.* **2015**, *13*, 11153.

(9) Photocatalyzed trifluoromethylation of heterocycles: (a) Nagib, D. A.; MacMillan, D. W. C. *Nature* **2011**, *480*, 224. (b) Iqbal, N.; Choi, S.; Ko, E.; Cho, E. J. *Tetrahedron Lett.* **2012**, *53*, 2005. (c) Ye, Y.; Sanford, M. S. *J. Am. Chem. Soc.* **2012**, *134*, 9034. (d) Cui, L.; Matusaki, Y.; Tada, N.; Miura, T.; Uno, B.; Itoh, A. *Adv. Synth. Catal.* **2013**, *355*, 2203. (e) Xie, J.; Yuan, X.; Abdukader, A.; Zhu, C.; Ma, J. *Org. Lett.* **2014**, *16*, 1768. (f) Pitre, S. P.; McTiernan, C. D.; Ismaili, H.; Scaiano, J. C. *ACS Catal.* **2014**, *4*, 2530. (g) Straathof, N. J. W.; Gemoets, H. P. L.; Wang, X.; Schouten, J. C.; Hessel, V.; Noël, T. *ChemSusChem* **2014**, *7*, 1612. (h) Beatty, J. W.; Douglas, J. J.; Cole, K. P.; Stephenson, C. R. J. *Nat. Commun.* **2015**, *6*, 7919. (i) Baar, M.; Blechert, S. *Chem. - Eur. J.* **2015**, *21*, 526. (j) Choi, W. J.; Choi, S.; Ohkubo, K.; Fukuzumi, S.; Cho, E. J.; You, Y. *Chem. Sci.* **2015**, *6*, 1454. Photocatalyzed oxytrifluoromethylation of alkenes: (k) Yasu, Y.; Koike, T.; Akita, M. *Angew. Chem., Int. Ed.* **2012**, *51*, 9567. (l) Kim, E.; Choi, S.; Kim, H.; Cho, E. J. *Chem. - Eur. J.* **2013**, *19*, 6209. (m) Tomita, R.; Yasu, Y.; Koike, T.; Akita, M. *Angew. Chem., Int. Ed.* **2014**, *53*, 7144. (n) Yasu, Y.; Arai, Y.; Tomita, R.; Koike, T.; Akita, M. *Org. Lett.* **2014**, *16*, 780. (o) Thomoson, C. S.; Dolbier, W. R., Jr. *J. Fluorine Chem.* **2015**, *178*, 327. (p) Noto, N.; Miyazawa, K.; Koike, T.; Akita, M. *Org. Lett.* **2015**, *17*, 3710. (q) Tang, X. J.; Thomoson, C. S.; Dolbier, W. R., Jr. *Org. Lett.* **2014**, *16*, 4594. Photocatalyzed azido or aminotrifluoromethylation of alkenes: (r) Yasu, Y.; Koike, T.; Akita, M. *Org. Lett.* **2013**, *15*, 2136. (s) Xu, P.; Hu, K.; Gu, Z.; Cheng, Y.; Zhu, C. *Chem. Commun.* **2015**, *51*, 7222. Photocatalyzed carbotrifluoromethylation: (t) Xu, P.; Xie, J.; Xue, Q.; Pan, C.; Cheng, Y.; Zhu, C. *Chem. - Eur. J.* **2013**, *19*, 14039. Photocatalyzed trifluoromethylation of acids: (u) Xu, P.; Abdukader, A.; Hu, K.; Cheng, Y.; Zhu, C. *Chem. Commun.* **2014**, *50*, 2308.

(10) Established by NOESY NMR analysis (see the Supporting Information for details).

(11) For recent reviews on tandem reactions involving a trifluoromethylation step, see: (a) Merino, E.; Nevado, C. *Chem. Soc. Rev.* **2014**, *43*, 6598. (b) Wang, S.-M.; Han, J.-B.; Zhang, C.-P.; Qin, H.-L.; Xiao, J.-C. *Tetrahedron* **2015**, *71*, 7949.

(12) (a) Rendler, S.; Oestreich, M. *Synthesis* **2005**, *2005*, 1727. (b) Gawronski, J.; Wascinska, N.; Gajewy, J. *Chem. Rev.* **2008**, *108*, 5227. (c) Denmark, S. E.; Beutner, G. L. *Angew. Chem., Int. Ed.* **2008**, *47*, 1560.

(13) Crystallographic data for **7g′**, **7m**, **7p**, **10d**, **10d**, and **10h** (see the Supporting Information for details).

(14) Selected examples of photocatalyzed oxidation of benzylic or vinylic position: (a) Rueping, M.; Vila, C.; Szadkowska, A.; Koenigs, R. M.; Fronert, J. *ACS Catal.* **2012**, *2*, 2810. (b) Pirnot, M. T.; Rankic, D. A.; Martin, D. B. C.; MacMillan, D. W. C. *Science* **2013**, *339*, 1593. (c) Petronijevic, F. R.; Nappi, M.; MacMillan, D.W. C. *J. Am. Chem. Soc.* **2013**, *135*, 18323. (d) Rackl, D.; Kais, V.; Kreitmeier, P.; Reiser, O. *Beilstein J. Org. Chem.* **2014**, *10*, 2157. (e) Liu, Z.; Zhang, Y.; Cai, Z.; Sun, H.; Cheng, X. *Adv. Synth. Catal.* **2015**, *357*, 589.

(15) Morán-Ramallal, R.; Gotor-Fernández, V.; Laborda, P.; Sayago, F. J.; Cativiela, C.; Gotor, V. *Org. Lett.* **2012**, *14*, 1696 and references cited herein.