

Direct C–H trifluoromethylation of di- and trisubstituted alkenes by photoredox catalysis

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Full Research Paper

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Abstract

Background: Trifluoromethylated alkene scaffolds are known as useful structural motifs in pharmaceuticals and agrochemicals as well as functional organic materials. But reported synthetic methods usually require multiple synthetic steps and/or exhibit limitation with respect to access to tri- and tetrasubstituted CF₃-alkenes. Thus development of new methodologies for facile construction of C_{alkenyl}–CF₃ bonds is highly demanded.

Results: The photoredox reaction of alkenes with 5-(trifluoromethyl)dibenzo[*b,d*]thiophenium tetrafluoroborate, Umemoto's reagent, as a CF₃ source in the presence of [Ru(bpy)₃]²⁺ catalyst (bpy = 2,2'-bipyridine) under visible light irradiation without any additive afforded CF₃-substituted alkenes via direct C_{alkenyl}–H trifluoromethylation. 1,1-Di- and trisubstituted alkenes were applicable to this photocatalytic system, providing the corresponding multisubstituted CF₃-alkenes. In addition, use of an excess amount of the CF₃ source induced double C–H trifluoromethylation to afford geminal bis(trifluoromethyl)alkenes.

Conclusion: A range of multisubstituted CF₃-alkenes are easily accessible by photoredox-catalyzed direct C–H trifluoromethylation of alkenes under mild reaction conditions. In particular, trifluoromethylation of triphenylethene derivatives, from which synthetically valuable tetrasubstituted CF₃-alkenes are obtained, have never been reported so far. Remarkably, the present facile and straightforward protocol is extended to double trifluoromethylation of alkenes.

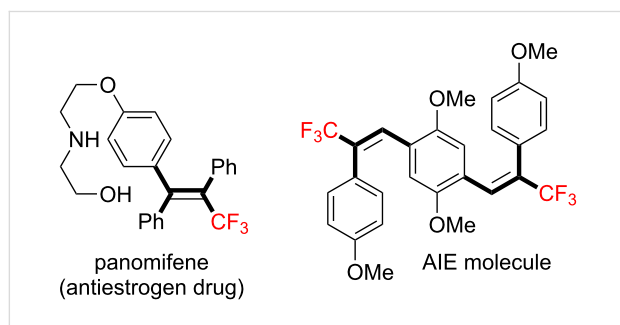
Introduction

The trifluoromethyl (CF₃) group is a useful structural motif in many bioactive molecules as well as functional organic materials [1-6]. Thus, the development of new methodologies for

highly efficient and selective incorporation of a CF₃ group into diverse skeletons has become a hot research topic in the field of organic synthetic chemistry [7-12]. Recently, radical trifluoro-

methylation by photoredox catalysis [13–23] with ruthenium(II) polypyridine complexes (e.g., $[\text{Ru}(\text{bpy})_3]^{2+}$ (bpy: 2,2'-bipyridine)), the relevant Ir cyclometalated complexes (e.g., *fac*- $\text{Ir}(\text{ppy})_3$ (ppy: 2-phenylpyridine)) and organic dyes has been developed; the trifluoromethyl radical ($\cdot\text{CF}_3$) can be easily generated from conventional CF_3 radical precursors such as CF_3I , $\text{CF}_3\text{SO}_2\text{Cl}$ and $\text{CF}_3\text{SO}_2\text{Na}$ through visible-light-induced single-electron transfer (SET) processes [24–32]. On the other hand, we have intensively developed trifluoromethylations of olefins by the Ru and Ir photoredox catalysis using easy-handling and shelf-stable electrophilic trifluoromethylating reagents [33–36] ($^+\text{CF}_3$) such as Umemoto's reagent (**1a**, 5-(trifluoromethyl)dibenzo[*b,d*]thiophenium tetrafluoroborate) and Togni's reagents **1b** (1-(trifluoromethyl)-1 λ^3 ,2-benziodoxol-3(*H*)-one) and **1c** (3,3-dimethyl-1,3-dihydro-1 λ^3 ,2-benziodoxole) [37–41]. It was found that electrophilic trifluoromethylating reagents ($^+\text{CF}_3$) can serve as more efficient CF_3 radical sources under mild photocatalytic reaction conditions. In addition, the putative $\beta\text{-CF}_3$ carbocation intermediate formed through SET photoredox processes is playing a key role in our reaction systems (*vide infra*).

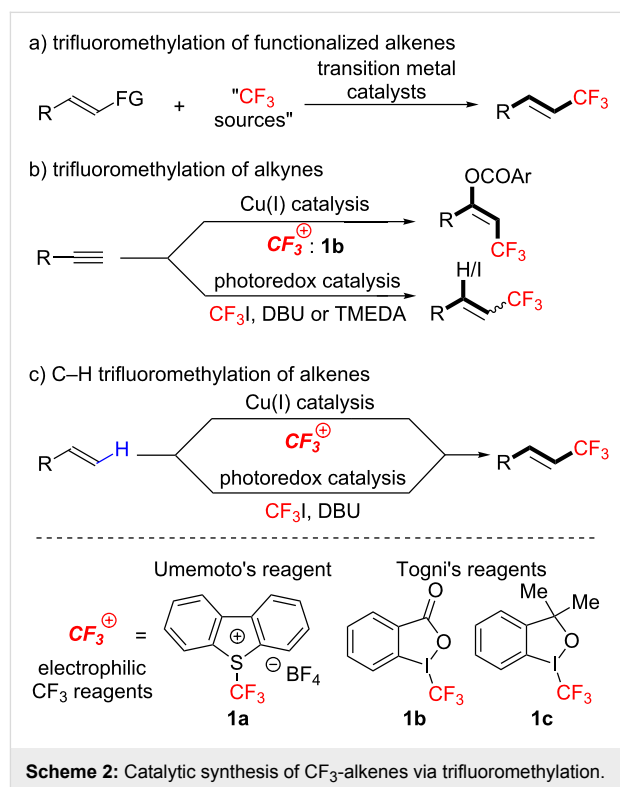
Trifluoromethylated alkenes, especially multi-substituted CF_3 -alkenes (3,3,3-trifluoropropene derivatives), have attracted our attention as fascinating scaffolds for agrochemicals, pharmaceuticals, and fluorescent molecules (Scheme 1) [3,42–45].



Scheme 1: Representative examples of multisubstituted CF_3 -alkenes.

Conventional approaches to CF_3 -alkenes require multiple synthetic steps [46–54]. In contrast, “trifluoromethylation” is a promising protocol to obtain diverse CF_3 -alkenes easily. Several catalytic synthetic methods via trifluoromethylation have been developed so far [38,55–62]. Most of these reactions require prefunctionalized alkenes as a substrate (Scheme 2a). Additionally, only a limited number of examples for synthesis of tri/tetra-substituted CF_3 -alkenes have been reported so far. Recently, the groups of Szabó and Cho described trifluoromethylation of alkynes, leading to trifluoromethylated alkenes but the application to the synthesis of tetrasubstituted CF_3 -alkenes is not well documented (Scheme 2b) [63,64]. Another

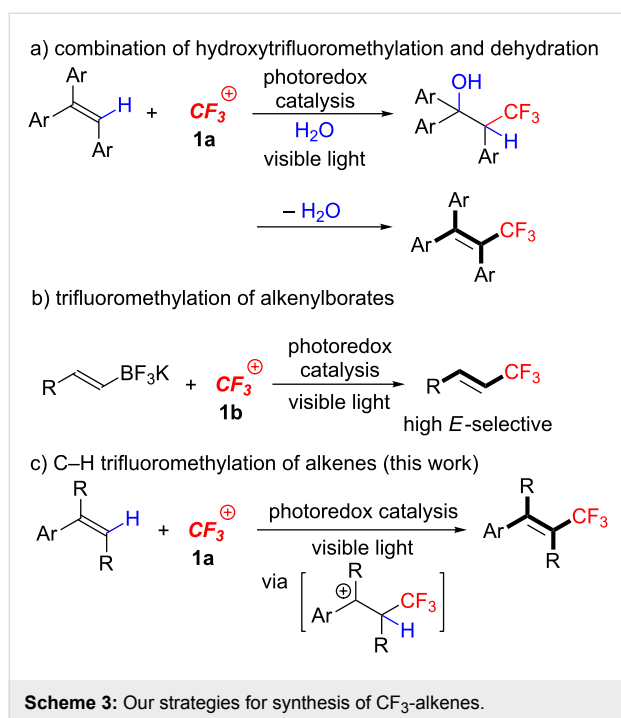
straightforward approach is direct C–H trifluoromethylation of alkenes (Scheme 2c). The groups of Loh, Besset, Cahard, Sodeoka and Xiao showed that copper catalysts can induce a C–H trifluoromethylation of alkenes by electrophilic CF_3 reagents ($^+\text{CF}_3$) [65–69]. In addition, Cho et al. reported that the reaction of unactivated alkenes with gaseous CF_3I in the presence of a Ru photocatalyst, $[\text{Ru}(\text{bpy})_3]^{2+}$, and a base, DBU (diazabicyclo[5,4,0]undec-7-ene) produced CF_3 -alkenes through iodotrifluoromethylation of alkenes followed by base-induced E2 elimination [70]. To the best of our knowledge, however, the development of synthetic methods for tri- and tetrasubstituted CF_3 alkenes through $\text{C}_{\text{alkenyl}}\text{-H}$ trifluoromethylation of simple alkenes have been left much to be desired.



Scheme 2: Catalytic synthesis of CF_3 -alkenes via trifluoromethylation.

Previously, we reported on the synthesis of CF_3 -alkenes via sequential photoredox-catalyzed hydroxytrifluoromethylation and dehydration (Scheme 3a) [37] and photoredox-catalyzed trifluoromethylation of alkenylborates (Scheme 3b) [38]. These results prompted us to explore photoredox-catalyzed C–H trifluoromethylation of di- and trisubstituted alkenes (Scheme 3c). Herein we disclose a highly efficient direct C–H trifluoromethylation of di- and trisubstituted alkenes with easy-handling and shelf-stable Umemoto's reagent **1a** by visible-light-driven photoredox catalysis under mild conditions. This photocatalytic protocol allows us easy access to a range of multi-substituted trifluoromethylated alkenes. In addition, our methodology can

be extended to a double trifluoromethylation of 1,1-disubstituted alkenes.



Results and Discussion

The results of investigations on the reaction conditions are summarized in Table 1. We commenced examination of photo-

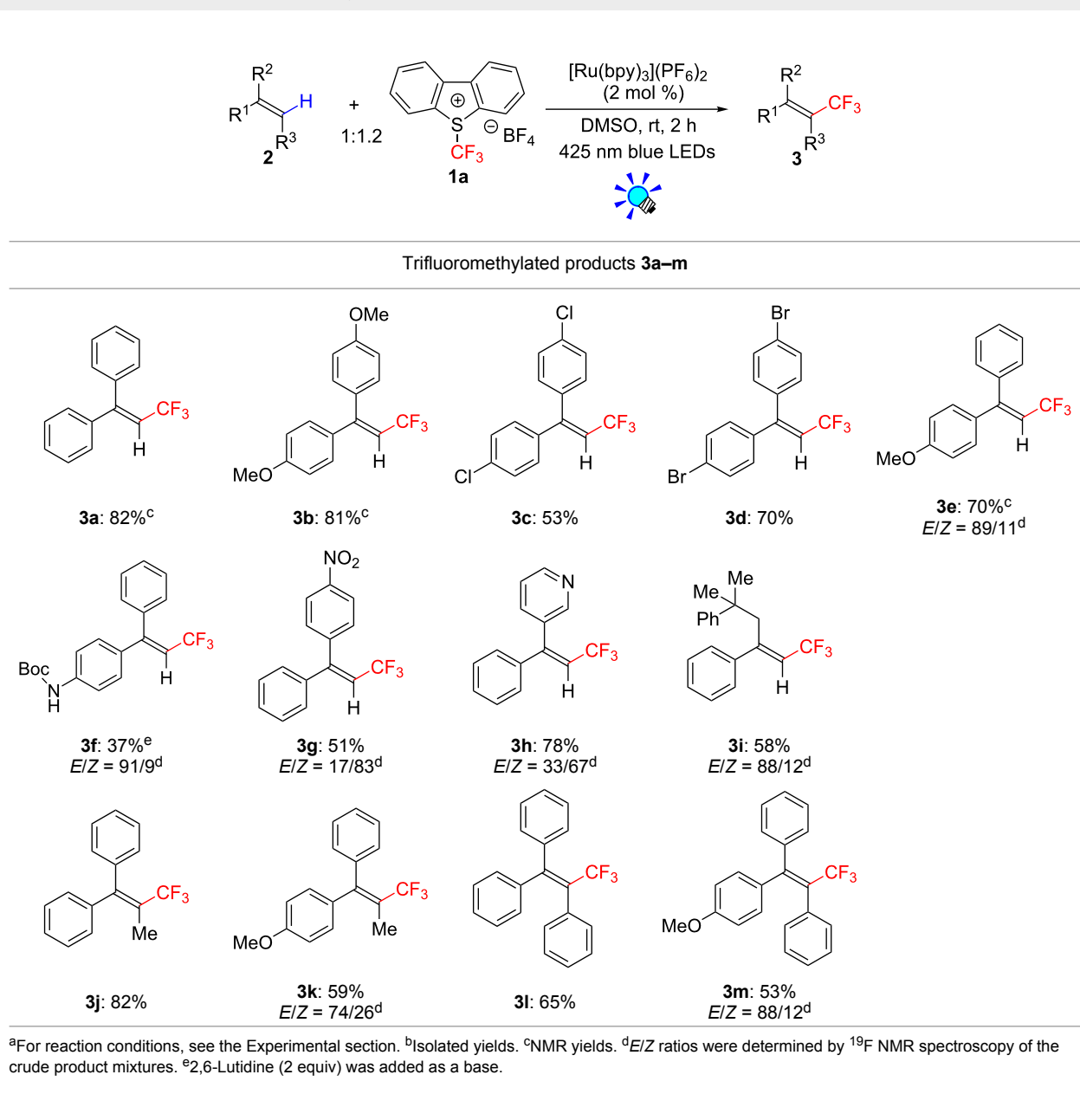
catalytic trifluoromethylation of 1,1-diphenylethene **2a** with 1 equivalent of Umemoto's reagent **1a** in the presence of 5 mol % *fac*-Ir(ppy)₃, a photoredox catalyst, and 2 equivalents of K₂HPO₄, a base, in [D₆]-DMSO under visible light irradiation (blue LEDs: λ_{max} = 425 nm) for 2 h. As a result, 3,3,3-trifluoro-1,1-diphenylpropene (**3a**) was obtained in an 82% NMR yield (Table 1, entry 1). The choice of ⁺CF₃ reagents turned out to be crucial for the yield of **3a**. Togni's reagents **1b** and **1c** gave **3a** in lower yields (Table 1, entries 2 and 3). We also found that DMSO is suitable for the present reaction (Table 1, entries 4–6). Other solvent systems gave substantial amounts of the hydroxytrifluoromethylated byproduct, which we reported previously [37]. In addition, the present C–H trifluoromethylation proceeds even in the absence of a base (Table 1, entry 7). Another photocatalyst, [Ru(bpy)₃](PF₆)₂, also promoted the present reaction, providing the product **3a** in an 85% NMR yield (Table 1, entry 8). The Ru catalyst is less expensive than the Ir catalyst; thus, we chose the Ru photocatalyst for the experiments onward. Notably, product **3a** was obtained neither in the dark nor in the absence of photocatalyst (Table 1, entries 9 and 10), strongly supporting that the photoexcited species of the photoredox catalyst play key roles in the reaction.

The scope and limitations of the present photocatalytic trifluoromethylation of alkenes are summarized in Table 2. 1,1-Diphenylethenes with electron-donating substituents, MeO (**2b**), and halogens, Cl (**2c**) and Br (**2d**), smoothly produced the corresponding trisubstituted CF₃-alkenes (**3b–d**) in good yields.

Table 1: Optimization of photocatalytic trifluoromethylation of 1,1-diphenylethene **2a**.^a

Entry	Photocatalyst	CF ₃ reagent	Solvent	Base	NMR yield (%)
1	<i>fac</i> -Ir(ppy) ₃	1a	[D ₆]-DMSO	K ₂ HPO ₄	82
2	<i>fac</i> -Ir(ppy) ₃	1b	[D ₆]-DMSO	K ₂ HPO ₄	17
3	<i>fac</i> -Ir(ppy) ₃	1c	[D ₆]-DMSO	K ₂ HPO ₄	47
4	<i>fac</i> -Ir(ppy) ₃	1a	CD ₃ CN	K ₂ HPO ₄	57
5	<i>fac</i> -Ir(ppy) ₃	1a	CD ₂ Cl ₂	K ₂ HPO ₄	22
6	<i>fac</i> -Ir(ppy) ₃	1a	[D ₆]-acetone	K ₂ HPO ₄	29
7	<i>fac</i> -Ir(ppy) ₃	1a	[D ₆]-DMSO	none	81
8	[Ru(bpy) ₃](PF ₆) ₂	1a	[D ₆]-DMSO	none	85
9	none	1a	[D ₆]-DMSO	none	0
10 ^b	[Ru(bpy) ₃](PF ₆) ₂	1a	[D ₆]-DMSO	none	0

^aFor reaction conditions, see the Experimental section. ^bIn the dark.

Table 2: The scope of the present trifluoromethylation of alkenes.^{a, b}

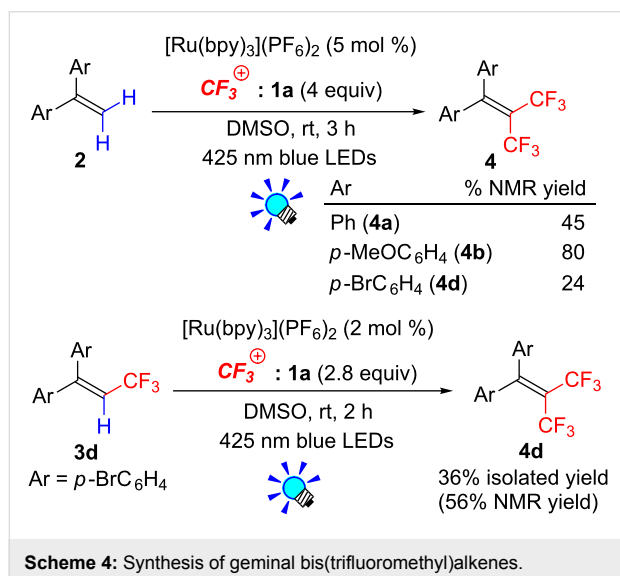
In the reactions of unsymmetrically substituted substrates (**2e–h**), products were obtained in good to moderate yields but consisted of mixtures of *E* and *Z*-isomers. Based on the experimental results, the *E/Z* ratios are susceptible to the electronic structure of the aryl substituent. Reactions afforded the major isomers, in which the CF₃ group and the electron-rich aryl substituent are arranged in *E*-fashion. In addition, the present photocatalytic reaction can be tolerant of the Boc-protected amino group (**2f**) or pyridine (**2h**). Moreover, a substrate with an alkyl substituent, 2,4-diphenyl-4-methyl-1-pentene (**2i**), was also applicable to this transformation, whereas the reaction of

1,2-disubstituted alkenes such as *trans*-stilbene provided complicated mixtures of products.

Next, we extended the present C–H trifluoromethylation to trisubstituted alkenes. The reactions of 1,1-diphenylpropene derivatives **2j** and **2k** (*E/Z* = 1/1) afforded the corresponding tetrasubstituted CF₃-alkenes **3j** and **3k** in 82% and 59% (*E/Z* = 74/26) yields, respectively. Triphenylethenes **2l** and **2m** (only *E*-isomer) are also applicable to this photocatalytic C–H trifluoromethylation. Remarkably, the *E*-isomer of **3m** is a key intermediate for the synthesis of panomifene, which is known as

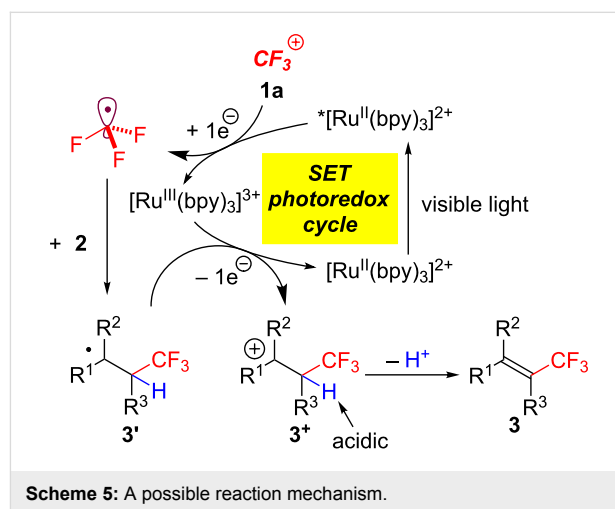
an antiestrogen drug [71,72]. These results show that the present protocol enables the efficient construction of a $C_{\text{alkenyl}}\text{-CF}_3$ bond through direct C–H trifluoromethylation of 1,1-disubstituted and trisubstituted aryl alkenes.

During the course of our study on the C–H trifluoromethylation of 1,1-diarylethenes **2**, we found that a detectable amount of bis(trifluoromethyl)alkenes **4** was formed through double C–H trifluoromethylation. In fact, the photocatalytic trifluoromethylation of **2a,b** and **d** with 4 equivalents of Umemoto's reagent **1a** in the presence of 5 mol % of $[\text{Ru}(\text{bpy})_3](\text{PF}_6)_2$ with irradiation from blue LEDs for 3 h gave geminal bis(trifluoromethyl)ethene (**4a,b** and **d**) in 45, 80 and 24% NMR yields, respectively (Scheme 4). Substituents on the benzene ring significantly affect the present double trifluoromethylation. Reaction of the electron-rich alkene **2b** afforded 1,1-anisyl-2,2-bis(trifluoromethyl)ethene (**4b**) in a better yield than other alkenes **2a** and **2d**. Additionally, we found that photocatalytic trifluoromethylation of CF_3 -alkene **3d** in the presence of an excess amount of Umemoto's reagent **1a** produced bis(trifluoromethyl)alkenes **4d** in a better yield (56% yield) compared to the above-mentioned one-pot double trifluoromethylation of **2d**.

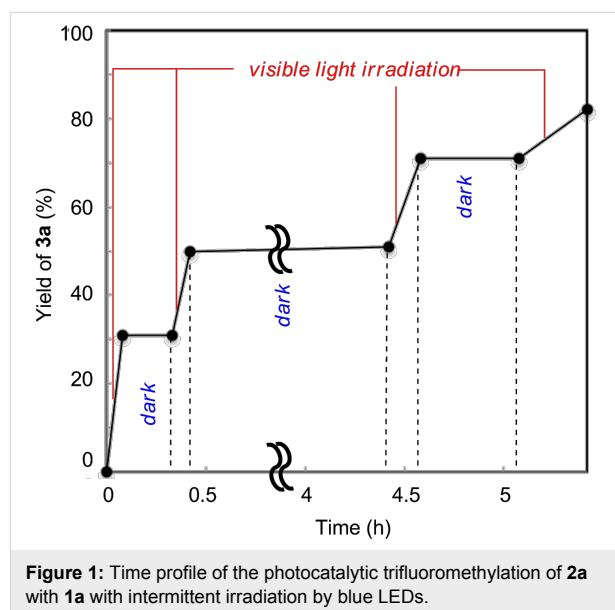


A possible reaction mechanism based on SET photoredox processes is illustrated in Scheme 5. According to our previous photocatalytic trifluoromethylation [37–41], the trifluoromethyl radical ($\cdot\text{CF}_3$) is generated from an one-electron-reduction of electrophilic Umemoto's reagent **1a** by the photoactivated Ru catalyst, $^*[\text{Ru}(\text{bpy})_3]^{2+}$. $\cdot\text{CF}_3$ reacts with alkene **2** to give the benzyl radical-type intermediate **3'** in a regioselective manner. Subsequent one-electron-oxidation by highly oxidizing Ru species, $[\text{Ru}^{\text{III}}(\text{bpy})_3]^{3+}$, produces $\beta\text{-CF}_3$ carbocation intermediate **3⁺**. Finally, smooth elimination of the olefinic proton, which

is made acidic by the strongly electron-withdrawing CF_3 substituent, provides trifluoromethylated alkene **3**. Preferential formation of one isomer in the reaction of unsymmetrical substrates is attributed to the population of the rotational conformers of the $\beta\text{-CF}_3$ carbocation intermediate **3⁺**. Our experimental result is consistent with the previous report [71], which described *E*-selective formation of the tetrasubstituted CF_3 -alkene **3m** via a $\beta\text{-CF}_3$ carbocation intermediate. In the presence of an excess amount of CF_3 reagent **1a**, further C–H trifluoromethylation of CF_3 -alkene **3** proceeds to give bis(trifluoromethyl)alkene **4**.



We cannot rule out a radical chain propagation mechanism, but the present transformation requires continuous irradiation of visible light (Figure 1), thus suggesting that chain propagation is not a main mechanistic component.



Conclusion

We have developed highly efficient C–H trifluoromethylation of alkenes using Umemoto's reagent as a CF₃ source by visible-light-driven photoredox catalysis. This reaction can be applied to multi-substituted alkenes, especially, 1,1-disubstituted and trisubstituted aryl alkenes, leading to tri- and tetrasubstituted CF₃-alkenes. The present straightforward method for the synthesis of multisubstituted CF₃-alkenes from simple aryl alkenes is the first report. In addition, we can extend the present photocatalytic system to double trifluoromethylation. Further development of this protocol in the synthesis of bioactive organofluorine molecules and fluorescent molecules is a continuing effort in our laboratory.

Experimental

Typical NMR experimental procedure (reaction conditions in Table 1)

Under N₂, [Ru(bpy)₃](PF₆)₂ (1.1 mg, 1.3 μmol), Umemoto's reagent **1a** (8.5 mg, 25 μmol), 1,1-diphenylethylene (**2a**, 4.3 μL, 25 μmol), SiEt₄ (~1 μL) as an internal standard, and [D₆]-DMSO (0.5 mL) were added to an NMR tube. The reaction was carried out at room temperature (water bath) under irradiation of visible light (placed at a distance of 2–3 cm from 3 W blue LED lamps: $h\nu = 425 \pm 15$ nm).

General procedure for the photocatalytic C–H trifluoromethylation of alkenes (reaction conditions in Table 2)

A 20 mL Schlenk tube was charged with Umemoto's reagent **1a** (102 mg, 0.3 mmol, 1.2 equiv), [Ru(bpy)₃](PF₆)₂ (4.3 mg, 2 mol %), alkene **2** (0.25 mmol), and DMSO (2.5 mL) under N₂. The tube was irradiated for 2 h at room temperature (water bath) with stirring by 3 W blue LED lamps ($h\nu = 425 \pm 15$ nm) placed at a distance of 2–3 cm. After the reaction, H₂O was added. The resulting mixture was extracted with Et₂O, washed with H₂O, dried (Na₂SO₄), and filtered. The filtrate was concentrated in vacuo. The product was purified by the two methods described below.

For products **3b**, **3e**, **3f**, **3g**, **3h**, **3k** and **3m**, the residue was purified by column chromatography on silica gel (eluent: hexane and diethyl ether) to afford the corresponding product **3**. Further purification of **3f** by GPC provided pure **3f**. For products **3a**, **3c**, **3d**, **3i**, **3j**, and **3l**, the residue was treated by mCPBA (74 mg, ca. 0.3 mmol) in CH₂Cl₂ to convert the dibenzothiophene to sulfoxide, which was more easily separated from the products. After the solution was stirred at room temperature for 2 h, an aqueous solution of Na₂S₂O₃·5H₂O was added to the solution, which was extracted with CH₂Cl₂. The organic layer was washed with H₂O, dried (Na₂SO₄), and filtered. The filtrate was concentrated in vacuo and the residue was purified by flash

column chromatography on silica gel (eluent: hexane) to afford the corresponding product **3**. Further purification of **3c** and **3d** by GPC provided pure **3c** and **3d**.

Procedures for the photocatalytic double C–H trifluoromethylation of 1,1-bis(4-methoxyphenyl)ethylene (**2b**)

A 20 mL Schlenk tube was charged with Umemoto's reagent **1a** (340 mg, 1.0 mmol, 4 equiv), [Ru(bpy)₃](PF₆)₂ (10.7 mg, 5 mol %), **2b** (60 mg, 0.25 mmol), and DMSO (5 mL) under N₂. The tube was irradiated for 3 h at room temperature (water bath) with stirring by 3 W blue LED lamps ($h\nu = 425 \pm 15$ nm) placed at a distance of 2–3 cm. After reaction, H₂O was added. The resulting mixture was extracted with Et₂O, washed with H₂O, dried (Na₂SO₄), and filtered. The filtrate was concentrated in vacuo and the residue was purified by flash column chromatography on silica gel (hexane→hexane/Et₂O = 29:1) to afford **4b** as a product mixture with **3b**. Further purification by GPC provided pure **4b** in 44% isolated yield (42 mg, 0.11 mmol). Isolated yield was much lower than the NMR yield because of the difficulty of separation of **3b** and **4b**.

Supporting Information

Supporting information features experimental procedures and full spectroscopic data for all new compounds (**3c**, **3d**, **3f**, **3g**, **3h**, **3i**, **3k**, **4a**, and **4d**).

Supporting Information File 1

Experimental procedures and NMR spectra.
[<http://www.beilstein-journals.org/bjoc/content/supplementary/1860-5397-10-108-S1.pdf>]

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References

- Hiyama, T. In *Organofluorine Compounds: Chemistry and Applications*; Yamamoto, H., Ed.; Springer: Berlin, 2000.
doi:10.1007/978-3-662-04164-2
- Ojima, I. *Fluorine in Medicinal Chemistry and Chemical Biology*; Wiley-Blackwell: Chichester, 2009.
- Shimizu, M.; Hiyama, T. *Angew. Chem., Int. Ed.* **2005**, *44*, 214–231.
doi:10.1002/anie.200460441
- Ma, J.-A.; Cahard, D. *J. Fluorine Chem.* **2007**, *128*, 975–996.
doi:10.1016/j.jfluchem.2007.04.026

5. Shibata, N.; Mizuta, S.; Toru, T. *J. Synth. Org. Chem., Jpn.* **2008**, *66*, 215–228.
6. Ma, J.-A.; Cahard, D. *Chem. Rev.* **2008**, *108*, PR1–PR43. doi:10.1021/cr800221v
7. Tomashenko, O. A.; Grushin, V. V. *Chem. Rev.* **2011**, *111*, 4475–4521. doi:10.1021/cr1004293
8. Furuya, T.; Kamlet, A. S.; Ritter, T. *Nature* **2011**, *473*, 470–477. doi:10.1038/nature10108
9. Amii, H. *J. Synth. Org. Chem., Jpn.* **2011**, *69*, 752–762.
10. Studer, A. *Angew. Chem., Int. Ed.* **2012**, *51*, 8950–8958. doi:10.1002/anie.201202624
11. Macé, Y.; Magnier, E. *Eur. J. Org. Chem.* **2012**, 2479–2494. doi:10.1002/ejoc.201101535
12. Liang, T.; Neumann, C. N.; Ritter, T. *Angew. Chem., Int. Ed.* **2013**, *52*, 8214–8264. doi:10.1002/anie.201206566
13. Yoon, T. P.; Ischay, M. A.; Du, J. *Nat. Chem.* **2010**, *2*, 527–532. doi:10.1038/nchem.687
14. Narayanam, J. M. R.; Stephenson, C. R. J. *Chem. Soc. Rev.* **2011**, *40*, 102–113. doi:10.1039/b913880n
15. Teplý, F. *Collect. Czech. Chem. Commun.* **2011**, *76*, 859–917. doi:10.1135/cccc2011078
16. Tucker, J. W.; Stephenson, C. R. J. *J. Org. Chem.* **2012**, *77*, 1617–1622. doi:10.1021/jo202538x
17. Xuan, J.; Xiao, W.-J. *Angew. Chem., Int. Ed.* **2012**, *51*, 6828–6838. doi:10.1002/anie.201200223
18. Maity, S.; Zheng, N. *Synlett* **2012**, *23*, 1851–1856. doi:10.1055/s-0032-1316592
19. Shi, L.; Xia, W. *Chem. Soc. Rev.* **2012**, *41*, 7687–7697. doi:10.1039/c2cs35203f
20. Xi, Y.; Yi, H.; Lei, A. *Org. Biomol. Chem.* **2013**, *11*, 2387–2403. doi:10.1039/c3ob40137e
21. Hari, D. P.; König, B. *Angew. Chem., Int. Ed.* **2013**, *52*, 4734–4743. doi:10.1002/anie.201210276
22. Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C. *Chem. Rev.* **2013**, *113*, 5322–5363. doi:10.1021/cr300503r
23. Reckenthäler, M.; Griesbeck, A. G. *Adv. Synth. Catal.* **2013**, *355*, 2727–2744. doi:10.1002/adsc.201300751
24. Nagib, D. A.; MacMillan, D. W. C. *Nature* **2011**, *480*, 224–228. doi:10.1038/nature10647
25. Nguyen, J. D.; Tucker, J. W.; Konieczynska, M. D.; Stephenson, C. R. J. *J. Am. Chem. Soc.* **2011**, *133*, 4160–4163. doi:10.1021/ja108560e
26. Ye, Y.; Sanford, M. S. *J. Am. Chem. Soc.* **2012**, *134*, 9034–9037. doi:10.1021/ja301553c
27. 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. doi:10.1021/ja401022x
28. Kim, E.; Choi, S.; Kim, H.; Cho, E. *J. Chem.–Eur. J.* **2013**, *19*, 6209–6212. doi:10.1002/chem.201300564
29. Wilger, D. J.; Gesmundo, N. J.; Nicewicz, D. A. *Chem. Sci.* **2013**, *4*, 3160–3165. doi:10.1039/c3sc51209f
30. Jiang, H.; Cheng, Y.; Zhang, Y.; Yu, S. *Eur. J. Org. Chem.* **2013**, 5485–5492. doi:10.1002/ejoc.201300693
31. Xu, P.; Xie, J.; Xue, Q.; Pan, C.; Cheng, Y.; Zhu, C. *Chem.–Eur. J.* **2013**, *19*, 14039–14042. doi:10.1002/chem.201302407
32. Koike, T.; Akita, M. *Top. Catal.* **2014**. doi:10.1007/s11244-014-0259-7
33. Umemoto, T. *Chem. Rev.* **1996**, *96*, 1757–1778. doi:10.1021/cr941149u
And see references therein.
34. Eisenberger, P.; Gischig, S.; Togni, A. *Chem.–Eur. J.* **2006**, *12*, 2579–2586. doi:10.1002/chem.200501052
35. Kieltch, I.; Eisenberger, P.; Togni, A. *Angew. Chem., Int. Ed.* **2007**, *46*, 754–757. doi:10.1002/anie.200603497
36. Shibata, N.; Matsnev, A.; Cahard, D. *Beilstein J. Org. Chem.* **2010**, *6*, No. 65. doi:10.3762/bjoc.6.65
37. Yasu, Y.; Koike, T.; Akita, M. *Angew. Chem., Int. Ed.* **2012**, *51*, 9567–9571. doi:10.1002/anie.201205071
38. Yasu, Y.; Koike, T.; Akita, M. *Chem. Commun.* **2013**, *49*, 2037–2039. doi:10.1039/c3cc39235j
39. Yasu, Y.; Koike, T.; Akita, M. *Org. Lett.* **2013**, *15*, 2136–2139. doi:10.1021/ol4006272
40. Koike, T.; Akita, M. *Synlett* **2013**, *24*, 2492–2505. doi:10.1055/s-0033-1339874
41. Yasu, Y.; Arai, Y.; Tomita, R.; Koike, T.; Akita, M. *Org. Lett.* **2014**, *16*, 780–783. doi:10.1021/ol403500y
42. Rivkin, A.; Chou, T.-C.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **2005**, *44*, 2838–2850. doi:10.1002/anie.200461751
43. Shimizu, M.; Takeda, Y.; Higashi, M.; Hiyama, T. *Angew. Chem., Int. Ed.* **2009**, *48*, 3653–3656. doi:10.1002/anie.200900963
44. Shimizu, M.; Takeda, Y.; Higashi, M.; Hiyama, T. *Chem.–Asian J.* **2011**, *6*, 2536–2544. doi:10.1002/asia.201100176
45. Shi, Z.; Davies, J.; Jang, S.-H.; Kaminsky, W.; Jen, A. K.-Y. *Chem. Commun.* **2012**, *48*, 7880–7882. doi:10.1039/c2cc32380j
46. Kimura, M.; Yamazaki, T.; Kitazume, T.; Kubota, T. *Org. Lett.* **2004**, *6*, 4651–4654. doi:10.1021/ol0481941
47. Konno, T.; Takehana, T.; Mishima, M.; Ishihara, T. *J. Org. Chem.* **2006**, *71*, 3545–3550. doi:10.1021/jo0602120
48. Takeda, Y.; Shimizu, M.; Hiyama, T. *Angew. Chem., Int. Ed.* **2007**, *46*, 8659–8661. doi:10.1002/anie.200703759
49. Shimizu, M.; Takeda, Y.; Hiyama, T. *Bull. Chem. Soc. Jpn.* **2011**, *84*, 1339–1341. doi:10.1246/bcsj.20110240
50. Prakash, G. K. S.; Krishnan, H. S.; Jog, P. V.; Iyer, A. P.; Olah, G. A. *Org. Lett.* **2012**, *14*, 1146–1149. doi:10.1021/ol300076y
51. Omote, M.; Tanaka, M.; Ikeda, A.; Nomura, S.; Tarui, A.; Sato, K.; Ando, A. *Org. Lett.* **2012**, *14*, 2286–2289. doi:10.1021/ol300670n
52. Debien, L.; Quiclet-Sire, B.; Zard, S. S. *Org. Lett.* **2012**, *14*, 5118–5121. doi:10.1021/ol3023903
53. Zine, K.; Petriguet, J.; Thibonnet, J.; Abarbri, M. *Synlett* **2012**, 755–759. doi:10.1055/s-0031-1290596
54. Aikawa, K.; Shimizu, N.; Honda, K.; Hioki, Y.; Mikami, K. *Chem. Sci.* **2014**, *5*, 410–415. doi:10.1039/c3sc52548a
55. Duan, J.; Dolbier, W. R., Jr.; Chen, Q.-Y. *J. Org. Chem.* **1998**, *63*, 9486–9489. doi:10.1021/jo9816663
56. Hafner, A.; Bräse, S. *Adv. Synth. Catal.* **2011**, *353*, 3044–3048. doi:10.1002/adsc.201100528
57. Cho, E. J.; Buchwald, S. L. *Org. Lett.* **2011**, *13*, 6552–6555. doi:10.1021/ol202885w
58. Parsons, A. T.; Senecal, T. D.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2012**, *51*, 2947–2950. doi:10.1002/anie.201108267
59. He, Z.; Luo, T.; Hu, M.; Cao, Y.; Hu, J. *Angew. Chem., Int. Ed.* **2012**, *51*, 3944–3947. doi:10.1002/anie.201200140
60. Li, Y.; Wu, L.; Neumann, H.; Beller, M. *Chem. Commun.* **2013**, *49*, 2628–2630. doi:10.1039/c2cc36554e
61. Li, Z.; Cui, Z.; Liu, Z.-Q. *Org. Lett.* **2013**, *15*, 406–409. doi:10.1021/ol3034059
62. Patra, T.; Deb, A.; Manna, S.; Sharma, U.; Maiti, D. *Eur. J. Org. Chem.* **2013**, 5247–5250. doi:10.1002/ejoc.201300473

63. Janson, P. G.; Ghoneim, I.; Ilchenko, N. O.; Szabó, K. J. *Org. Lett.* **2012**, *14*, 2882–2885. doi:10.1021/ol3011419
64. Iqbal, N.; Jung, J.; Park, S.; Cho, E. J. *Angew. Chem., Int. Ed.* **2014**, *53*, 539–542. doi:10.1002/anie.201308735
65. Feng, C.; Loh, T.-P. *Chem. Sci.* **2012**, *3*, 3458–3462. doi:10.1039/c2sc21164e
66. Egami, H.; Shimizu, R.; Sodeoka, M. *Tetrahedron Lett.* **2012**, *53*, 5503–5506. doi:10.1016/j.tetlet.2012.07.134
67. Feng, C.; Loh, T.-P. *Angew. Chem., Int. Ed.* **2013**, *52*, 12414–12417. doi:10.1002/anie.201307245
68. Wang, X.-P.; Lin, J.-H.; Zhang, C.-P.; Xiao, J.-C.; Zheng, X. *Beilstein J. Org. Chem.* **2013**, *9*, 2635–2640. doi:10.3762/bjoc.9.299
69. Besset, T.; Cahard, D.; Pannecoucke, X. *J. Org. Chem.* **2014**, *79*, 413–418. doi:10.1021/jo402385g
70. Iqbal, N.; Choi, S.; Kim, E.; Cho, E. J. *J. Org. Chem.* **2012**, *77*, 11383–11387. doi:10.1021/jo3022346
71. Németh, G.; Kapiller-Dezsofi, R.; Lax, G.; Simig, G. *Tetrahedron* **1996**, *52*, 12821–12830. doi:10.1016/0040-4020(96)00763-6
72. Liu, X.; Shimizu, M.; Hiyama, T. *Angew. Chem., Int. Ed.* **2004**, *43*, 879–882. doi:10.1002/anie.200353032
- And see references for the bioactivity therein.

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