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Trifluoromethylation of aromatic alkenes by visible-light-driven photoredox catalysis: Direct conversion of alkenes to 3-trifluoromethyl-1-propenyl and 1,3-bis(trifluoromethyl)-1-propenyl derivatives

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ABSTRACT

Photoredox-catalyzed trifluoromethylation of alkenes using Umemoto's reagent as a CF_3 source under visible light irradiation has been developed. A Ru photocatalyst, $[Ru(bpy)_3](PF_6)_2$ (bpy = 2,2′-bipyridine), is useful for the present trifluoromethylation and preferable formation of 3-trifluoromethyl-1-propenyl derivatives is observed. Use of an excess amount of Umemoto's reagent readily induces double trifluoromethylation of electron-rich alkenes, resulting in 1,3-bis(trifluoromethyl)-1-propenyl skeleton.

1. Introduction

For the past few years, catalytic trifluoromethylation of alkenes has been recognized as one of the useful strategies for access to a variety of organofluorine compounds bearing $C(sp^3)$–CF_3 bonds [1,2]. In 2011, trifluoromethylation of simple *unactivated aliphatic* alkenes *via* allylic C–H bond cleavage using electrophilic CF_3 reagents such as Umemoto's reagent **1a** [3] and Togni's regent **1b** [4] was reported by the groups of Buchwald, Fu, Liu and Wang (Scheme 1(a)). These reactions are useful methods for synthesis of *linear* allyl compounds bearing a CF_3 group, but outcomes of the reactions with respect to *branched* alkenes and *aromatic* alkenes were not well-documented [5,6]. In 2012, the groups of Sodeoka and Gouverneur developed the Cu-catalyzed desilylative trifluoromethylation of allylsilanes using Togni's reagent **1b** as a CF_3 source, leading to *branched* alkenes and *aromatic* alkenes bearing a CF_3 group at the allylic position (Scheme 1(b)) [7]. Furthermore, Gouverneur and co-workers showed that photoredox-catalyzed trifluoromethylation of allylsilanes using electrophilic CF_3 reagents yielded internal alkenes with a CF_3 group at the allylic position [8]. The CF_3-allyl compounds are known as important synthetic intermediates for further functionalization and biologically active molecules [9]. Thus, development of a simple method for synthesis of CF_3-allyl compounds is still of great value.

Recently, photoredox catalysis with well-defined ruthenium polypyridine complexes (*e.g.*, $[Ru(bpy)_3]^{2+}$: bpy = 2,2′-bipyridine) has become a powerful tool for redox reaction in synthetic chemistry because it can easily promote single-electron-transfer (SET) processes under visible light irradiation [10,11]. Our group has extensively developed photoredox-catalyzed trifluoromethylation of olefins using electrophilic CF_3 reagents such as Umemoto's reagent **1a** and Togni's reagent **1b** [12]. Electrophilic CF_3 reagents can serve both as an electron acceptor and as a CF_3 radical source by photoredox catalysis. Herein we will disclose photoredox-catalyzed trifluoromethylation of aromatic alkenes, in particular α-alkylstyrenes, using Umemoto's reagent **1a** as a CF_3 source. This protocol is the first example to access CF_3-allyl compounds directly from aromatic alkenes. In addition, further trifluoromethylation of the CF_3-allyl compounds allows us an opportunity to readily construct 1,3-bis(trifluoromethyl)-1-propenyl scaffolds (Scheme 1(c)) [13].

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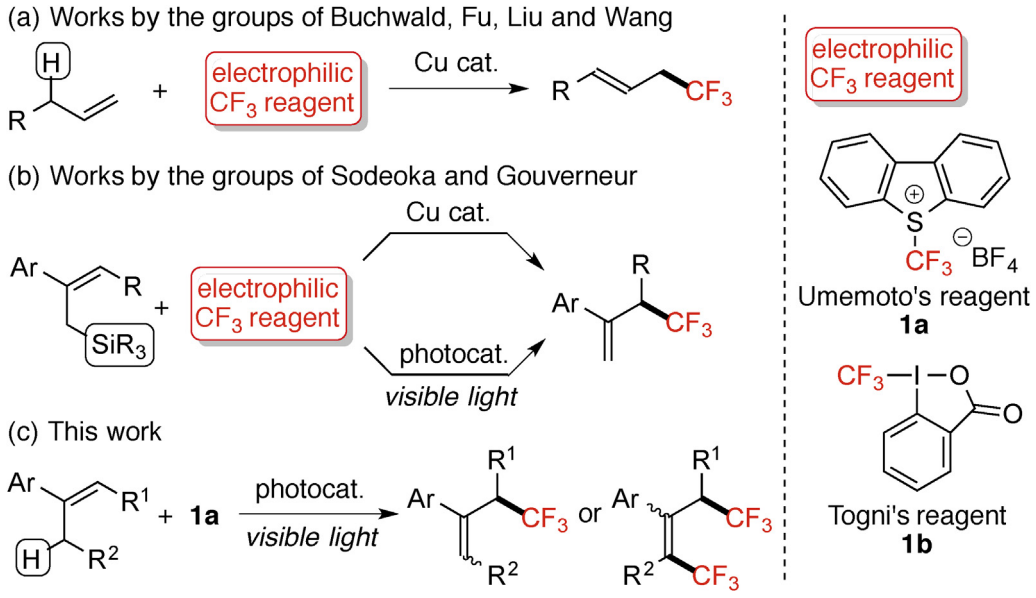


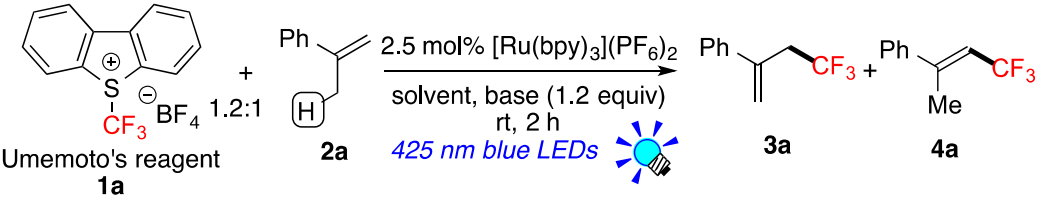
Scheme 1. Transition-metal-catalyzed trifluoromethylations of alkenes: synthesis of alkenes bearing a CF_3 group at the allylic position.

2. Results and discussion

We initially examined the reaction of α-methylstyrene **2a** with Umemoto's reagent **1a** in the presence of 2.5 mol% $[Ru(bpy)_3](PF_6)_2$ in DMSO-d_6 at room temperature under visible light irradiation (λ_{max} = 425 nm). As a result, 4,4,4-trifluoro-2-phenyl-1-butene **3a** was formed in a 53% yield together with α-methyl-β-trifluoromethylstyrene **4a** as a by-product (entry 1 in Table 1). Exploration of the solvent showed that DMSO was the best solvent with respect to the yield of **3a** (entries 1–4). To improve the yield of **3a**, addition of base (1.2 equiv.), K_2CO_3, pyridine and 2,6-di-*tert*-butylpyridine, was tested (entries 5–7). Bulkier base, 2,6-di-*tert*-butylpyridine, resulted in slightly improvement of the yield of **3a** (60% yield). The selectivity of products **3a** and **4a** is determined at the stage of the deprotonation process (see below). In addition, the present photocatalytic reaction did not proceed at all either in the dark or in the absence of photocatalyst (entries 8 and 9). The photoexcited catalyst plays a key role in the present reaction.

The result of the present photocatalytic trifluoromethylation in preparative scales is summarized in Table 2. The yield of **3a** of the preparative scale was lower than that of the NMR experiment due to volatility of **3a** (entry 1 in Table 2 and entry 7 in Table 1). Then, the reactions of heavier α-methylstyrene derivatives bearing functional groups were examined. Reactions of terminal alkenes such as α-methylstyrene bearing Br (**2b**) and ^{t}Bu (**2c**) groups on the benzene ring and 2-(α-methylvinyl)naphthalene (**2d**) afforded the corresponding CF_3-allyl products (**3b–d**) in moderate yields (44–49% NMR yields) together with CF_3-alkenes **4** (entries 2–4 in Table 2). Electron-rich α-methylstyrenes bearing MeO (**2e**) and methylenedioxy (**2f**) groups on the benzene ring gave the allyl products in low yields (**3e**: 24%, **3f**: 11% NMR yields) because of not only formation of CF_3-alkenes **4** but also further

Table 1
Photocatalytic trifluoromethylation of α-methylstyrene.[a]



Entry	Solvent	Base (1.2 equiv of **2a**)	% Yield of **3a**[b]	**3a**:**4a**[b]
1	DMSO-d_6	–	53	2.1:1
2	Acetone-d_6	–	32	6.4:1
3	CD_2Cl_2	–	7	2.3:1
4	CD_3CN	–	0	–
5	DMSO-d_6	K_2CO_3	47	2.9:1
6	DMSO-d_6	Pyridine	46	1.3:1
7	DMSO-d_6	2,6-di-*tert*-butylpyridine	60	2.5:1
8[c]	DMSO-d_6	2,6-di-*tert*-butylpyridine	0	–
9[d]	DMSO-d_6	2,6-di-*tert*-butylpyridine	0	–

[a] Reaction conditions: a mixture of $[Ru(bpy)_3](PF_6)_2$ (1.3 μmol, 2.5 mol%), **1a** (60 μmol, 1.2 equiv), **2a** (50 μmol, 1.0 equiv), base (60 μmol, 1.2 equiv) and $SiEt_4$ (an internal standard) in a solvent (0.5 mL) was irradiated by 3 W blue LEDs (λ = 425 ± 15 nm) at room temperature.
[b] Determined by ^{1}H NMR spectroscopy.
[c] In the dark.
[d] No photocatalyst.

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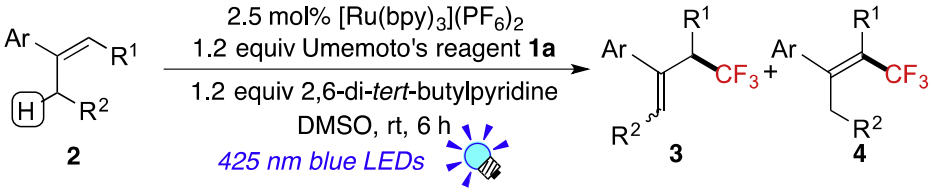
Table 2
Scope of the present trifluoromethylation of alkenes in preparative scales.[a]



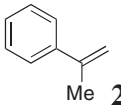
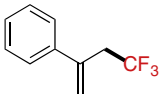
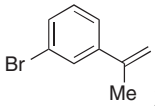
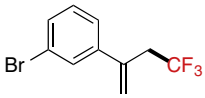
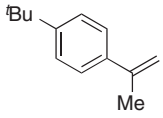
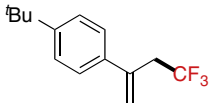
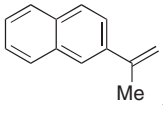
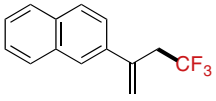
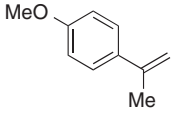
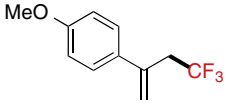
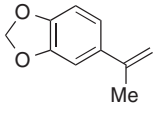
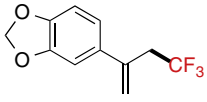
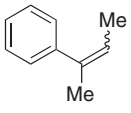
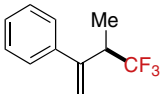
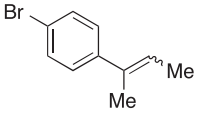
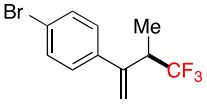
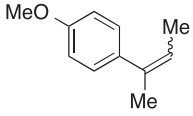
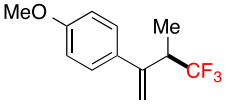
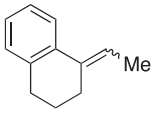
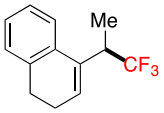
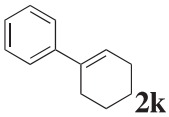
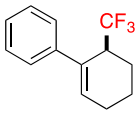
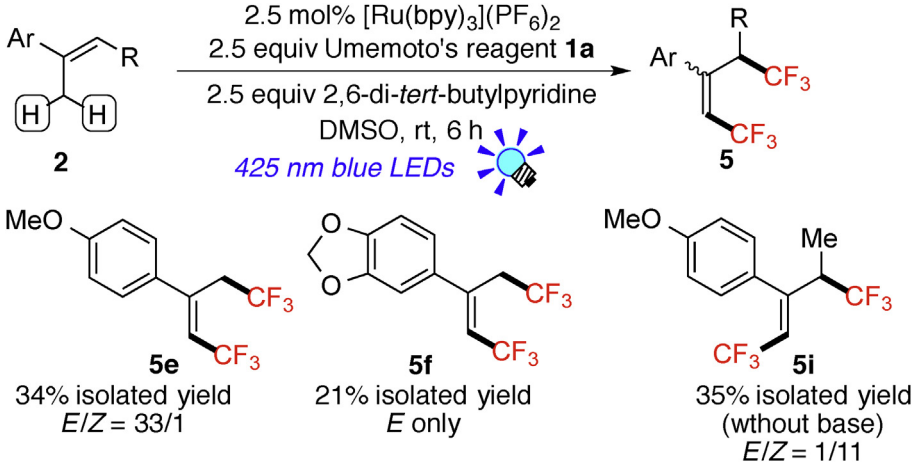
Entry	Substrate **2**	Product **3**	% Yield of **3**	**3**:**4**[b]
1	 **2a**		**3a**: 42[b]	2.5:1
2	 **2b**		**3b**: 49[b]	2.6:1
3	 **2c**		**3c**: 44[b]	2:1
4	 **2d**		**3d**: 44[b]	2.4:1
5	 **2e**		**3e**: 24[b]	1:1.1
6	 **2f**		**3f**: 11[b]	1:1.4
7	 **2g** (*E*/*Z* = 1/4.5)		**3g**: 48[b,d]	Only **3**
8	 **2h** (*E*/*Z* =1.1/1)		**3h**: 30[d](58[c,d,e])	Only **3**
9	 **2i** (*E*/*Z* = 1/3.8)		**3i**: 10[b,d]	Only **3**
10	 **2j** (*E*/*Z* = 1.4/1)		**3j**: 23[d] (60[d,e])	Only **3**

Table 2 (*Continued*)

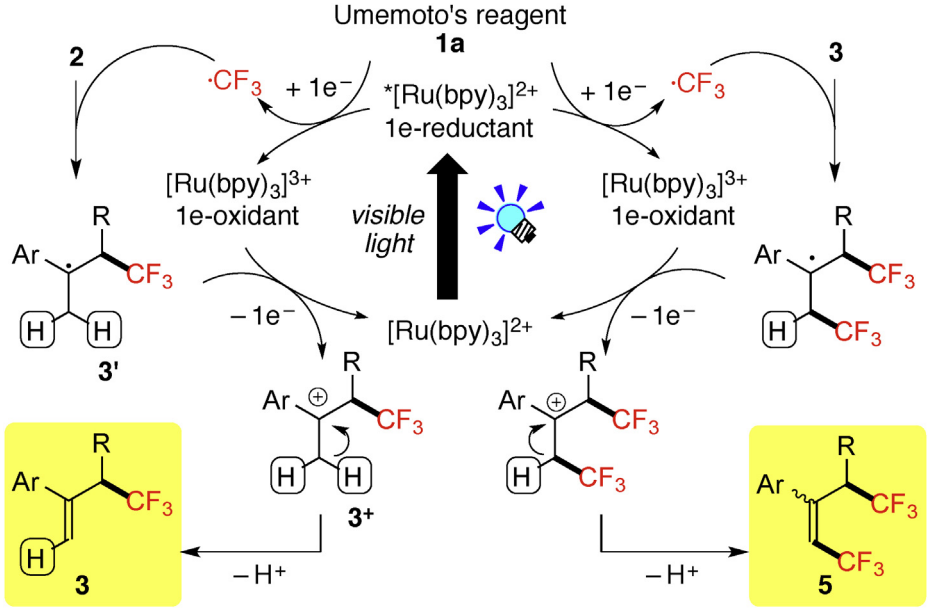
Entry	Substrate **2**	Product **3**	% Yield of **3**	**3**:**4**[b]
11	 **2k**		**3k**: 58[d] (83[d,e])	Only **3**

[a] Reaction conditions for preparative scales: see Section 4 and Supporting Information. Yields are lower than those obtained by NMR experiments because of the volatility of the products. Products **3** and **4** were not separable by column chromatography.
[b] Determined by ^{19}F NMR spectroscopy using $CF_3C_6H_5$ or $(CF_3O)C_6H_5$ as an internal standard.
[c] Reaction time = 4 h.
[d] In the absence of base.
[e] Experiments of NMR scale were conducted (reaction conditions, see the footnote in Table 1) and yields were determined by ^1H NMR spectroscopy using $SiEt_4$ as an internal standard.

trifluoromethylation of the formed CF_3-allyl products **5** (**5e**: 24% NMR yield and **5f**: 28% NMR yield, *vide infra*) (entries 5 and 6). Reactions of internal alkenes, α,β-dimethylstyrenes (**2g–i**), dramatically suppressed formation of CF_3-alkenes **4**, but further trifluoromethylation of the products **3** occurred to some extent, resulting in low to moderate yields of **3** (**3g**: 48% NMR yield, **3h**: 30% isolated yield, **3i**: 10% NMR yield [14]) (entries 7–9). Probably, terminal C=C bonds in the CF_3-ally products (**3g–i**) are more reactive toward trifluoromethylation, compared to the starting internal alkenes (**2g–i**). As expected, alkenes **2**, which were designed so as to give CF_3-allyl products **3** bearing internal C=C bond, suppressed further trifluoromethylation and formation of CF_3-alkene **4**. Reactions of (*E*)-1-ethylidene-1,2,3,4-tetrahydronaphthalene (**2j**) and 1-phenylcyclohexene (**2k**) afforded the



Scheme 2. Double trifluoromethylation of alkenes *via* CF_3-allyl compound **3**.



Scheme 3. A plausible reaction mechanism.

CF_3-allyl products (**3j**, **k**) in 23 and 58% isolated yields, respectively. These results suggest that preferable formation of the CF_3-allyl product **3** can be attributed to (i) facile deprotonation of protons at the allylic position of **2**, which are less sterically hindered and (ii) large steric hindrance of the C=C bond on the formed CF_3-allyl product **3**.

As mentioned above, further trifluoromethylation of CF_3-allyl products **3** was observed, especially for the reactions of electron-rich alkenes (**2e**, **2f**, **2i**). Therefore, reactions using an excess amount of Umemoto's reagent **1a** were examined to attempt double trifluoromethylation (Scheme 2). As a result, double trifluoromethylation proceeded smoothly to yield new bis(trifluoromethylated) products, 1,1,1,5,5,5-hexafluoro-3-phenyl-2-pentene derivatives (**5e**: 34%, **5f**: 21%, **5i**: 35% [15] isolated yields). Remarkably, the reactions of terminal alkenes **2e** and **2f** exhibited high *E* selectivity. In contrast, predominant formation of *Z* isomer was observed in the reaction of internal alkene **2i** possibly due to steric hindrance of the $CHMeCF_3$ group.

A plausible reaction mechanism is shown in Scheme 3. First, Ru photocatalyst, $[Ru(bpy)_3]^{2+}$, is excited by irradiation with visible light to form the excited state, $^*[Ru(bpy)_3]^{2+}$, which undergoes SET to Umemoto's reagent **1a** to give a CF_3 radical ($\cdot CF_3$) and the highly oxidized Ru species, $[Ru(bpy)_3]^{3+}$. The generated CF_3 radical ($\cdot CF_3$) reacts with alkene **2** to afford the trifluoromethylated radical intermediate **3′**. The second SET event between the highly oxidized Ru species, $[Ru(bpy)_3]^{3+}$, and the trifluoromethylated radical intermediate **3′** generates α-CF_3-substituted carbocationic intermediate $\mathbf{3}^+$, which subsequently undergoes deprotonation. Steric factors might induce selective deprotonation from the intermediate $\mathbf{3}^+$, leading to preferable formation of the CF_3-allyl product **3** (the left cycle in Scheme 3). The CF_3-allyl product **3,** especially alkene with an electron donating group and a terminal C=C bond, is further susceptible to the trifluoromethylation and deprotonation process, [12f] leading to the bis(trifluoromethylated) product **5** (the right cycle in Scheme 3).

3. Conclusions

In conclusion, we have developed the photoredox-catalyzed trifluoromethylation of alkenes using Umemoto's reagent, leading to preferable formation of 3-trifluoromethyl-1-propenyl derivatives. In particular, this method is useful for synthesis of the CF_3-allyl product from branched and internal aromatic alkenes. In addition, use of an excess amount of Umemoto's reagent induces the double trifluoromethylation of electron-rich alkenes, resulting in 1,3-bis(trifluoromethyl)-1-propenyl derivatives. Further development of this protocol in the synthesis of organofluorine molecules is a continuing effort in our laboratory.

4. Experimental

Details of experimental procedures and spectral data for new compounds (**3h**, **3j**, **3k**, **5e**, **5f** and **5i**) are summarized in the Supporting Information.

4.1. Typical NMR experimental procedure (reaction conditions in Table 1)

Under N_2, Umemoto's reagent (**1a**) (20.0 mg, 60 μmol), α-methylstyrene (**2a**) (6.5 μL, 50 μmol), $[Ru(bpy)_3](PF_6)_2$ (1.1 mg, 1.3 μmol), 2,6-di-*tert*-butylpyridine (13 μL, 60 μmol), $SiEt_4$ (2.0 μL) as an internal standard, and dry DMSO-d_6 (0.50 mL) were added to an NMR tube. Then, the mixture was degassed by three freeze-pump-thaw cycles and refilled with N_2. The mixture was irradiated by blue LED lamps (placed at a distance of ~3 cm from blue LED lamp: $h\nu = 425 \pm 15$ nm) at room temperature (water bath) for 2 h.

4.2. General procedure for the photocatalytic trifluoromethylation of alkenes (reaction conditions in Table 2)

A 20 mL Schlenk tube was charged with $[Ru(bpy)_3](PF_6)_2$ (5.4 mg, 6.3 μmol), Umemoto's reagent (**1a**) (1.0×10^2 mg, 0.30 mmol), alkenes **2** (0.25 mmol), 2,6-di-*tert*-butylpyridine (65 μL, 0.30 mmol) and dry DMSO (2.5 mL) under N_2. Then, the mixture was degassed by three freeze-pump-thaw cycles and refilled with N_2. The tube was irradiated for 6 h at room temperature (water bath) with stirring by 3 W blue LED lamps ($h\nu = 425$ nm ± 15 nm) placed at a distance of 2–3 cm. Then, H_2O was added to the reaction mixture, which was then extracted with Et_2O. The organic layer was washed with H_2O, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo*. The residue was treated by mCPBA (0.18 g, *ca.* 0.72 mmol) in CH_2Cl_2 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 $Na_2S_2O_3{\cdot}5H_2O$ was added to the solution, and the products were extracted with CH_2Cl_2. The organic layer was washed with H_2O, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo*. The residue was purified by chromatography on silica gel (eluent: pentane) and further purification was conducted by GPC. Yields of **3a**–**3g** and **3i** were determined by ^{19}F NMR spectroscopy using $CF_3C_6H_5$ or $(CF_3O)C_6H_5$ as an internal standard before treatment with mCPBA in the above-mentioned procedure.

4.3. General procedure for the photocatalytic double trifluoromethylation of alkenes

A 20 mL Schlenk tube was charged with $[Ru(bpy)_3](PF_6)_2$ (5.5 mg, 6.3 μmol), Umemoto's reagent (**1a**) (2.0×10^2 mg, 0.63 mmol), alkenes **2** (0.25 mmol), 2,6-di-*tert*-butylpyridine (1.4×10^2 μL, 0.63 mmol) and dry DMSO (2.5 mL) under N_2. Then, the mixture was degassed by three freeze-pump-thaw cycles and refilled with N_2. The tube was irradiated for 6 h at room temperature (water bath) with stirring by 3 W blue LED lamps ($h\nu = 425$ nm ± 15 nm) placed at a distance of 2–3 cm. Then, H_2O was added into the reaction mixture, and the reaction mixture was extracted with Et_2O. The organic layer was washed with H_2O, dried (Na_2SO_4), and filtered. The filtrate was concentrated *in vacuo*. The residue was purified by chromatography on silica gel and further purification was conducted by GPC if necessary.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jfluchem.2015.07.020.

References

[1] For selected recent reviews on trifluoromethylation of alkenes, see:
(a) E Merino, C. Nevado, Chem. Soc. Rev. 43 (2014) 6598–6608;
(b) T. Besset, T. Poisson, X. Pannecoucke, Chem. Eur. J. 20 (2014) 16830–16845;
(c) H. Egami, M. Sodeoka, Angew. Chem. Int. Ed. 53 (2014) 8294–8308;
(d) J. Xu, X. Liu, Y. Fu, Tetrahedron Lett. 55 (2014) 585–594;
(e) T. Koike, M. Akita, J. Fluor. Chem. 167 (2014) 30–36.
[2] For selected reviews on synthesis of organofluorine compounds, see:
(a) J-A. Ma, D. Cahard, Chem. Rev. 104 (2004) 6119–6146;
(b) M. Shimizu, T. Hiyama, Angew. Chem. Int. Ed. 44 (2005) 214–231;
(c) J.-A. Ma, D.D. Cahard, J. Fluor. Chem. 128 (2007) 975–996;
(d) J.-A. Ma, D. Cahard, Chem. Rev. 108 (2008) PR1–PR43;
(e) J. Hu, W. Zhang, F. Wang, Chem. Commun. (2009) 7465–7478;
(f) O.A. Tomashenko, V.V. Grushin, Chem. Rev. 111 (2011) 4475–4521;

(g) T. Furuya, A.S. Kamlet, T. Ritter, Nature 473 (2011) 470–477;
(h) T. Besset, C. Schneider, D. Cahard, Angew. Chem. Int. Ed. 51 (2012) 5048–5050;
(i) A. Studer, Angew. Chem. Int. Ed. 51 (2012) 8950–8958;
(j) C. Hollingworth, V. Gouverneur, Chem. Commun. 48 (2012) 2929–2942;
(k) Y. Macé, E.E. Magnier, Eur. J. Org. Chem. (2012) 2479–2494;
(l) H. Liu, Z. Gu, X. Jiang, Adv. Synth. Catal. 355 (2013) 617–626;
(m) T. Liang, C.N. Neumann, T. Ritter, Angew. Chem. Int. Ed. 52 (2013) 8214–8264;
(n) S. Barata-Vallejo, B. Lantaño, A. Postigo, Chem. Eur. J. 20 (2014) 16806–16829;
(o) C. Alonso, E.M. de Marigorta, G. Rubiales, F. Palacios, Chem. Rev. 115 (2015) 1847–1935;
(p) X. Liu, C. Xu, M. Wang, Q. Liu, Chem. Rev. 115 (2015) 683–730;
(q) C. Ni, M. Hu, J. Hu, Chem. Rev. 115 (2015) 765–825.

[3] (a) T. Umemoto, S. Ishihara, Tetrahedron Lett. 31 (1990) 3579–3582;
(b) T. Umemoto, S. Ishihara, J. Am. Chem. Soc. 115 (1993) 2156–2164;
(c) T. Umemoto, Chem. Rev. 96 (1996) 1757–1777;
(d) C. Zhang, Org. Biomol. Chem. 12 (2014) 6580–6589.

[4] (a) P. Eisenberger, S. Gischig, A. Togni, Chem. Eur. J. 12 (2006) 2579–2586;
(b) I. Kieltsch, P. Eisenberger, A. Togni, Angew. Chem. Int. Ed. 46 (2007) 754–757;
(c) J. Charpentier, N. Früh, A. Togni, Chem. Rev. 115 (2015) 650–682.

[5] (a) A.T. Parsons, S.L. Buchwald, Angew. Chem. Int. Ed. 50 (2011) 9120–9123;
(b) J. Xu, Y. Fu, D.-F. Luo, Y.-Y. Jiang, B. Xiao, Z.-J. Liu, T.-J. Gong, L. Liu, J. Am. Chem. Soc. 133 (2011) 15300–15303;
(c) X. Wang, Y. Ye, S. Zhang, J. Feng, Y. Xu, Y. Zhang, J. Wang, J. Am. Chem. Soc. 133 (2011) 16410–16413.

[6] More recently, Qing and co-worker reported trifluoromethylation of alkenes using CF_3TMS as a CF_3 source, see:
L Chu, F.-L. Qing, Org. Lett. 14 (2012) 2106–2109.

[7] (a) R. Shimizu, H. Egami, Y. Hamashima, M. Sodeoka, Angew. Chem. Int. Ed. 51 (2012) 4577–4580;
(b) S. Mizuta, O. Galicia-López, K.M. Engle, S. Verhoog, K. Wheelhouse, G. Rassias, V. Gouverneur, Chem. Eur. J. 18 (2012) 8583–8587.

[8] S. Mizuta, K.M. Engle, S. Verhoog, O. Galicia-López, M. O'Duill, M. Médebielle, K. Wheelhouse, G. Rassias, A.L. Thompson, V. Gouverneur, Org. Lett. 15 (2013) 1250–1253.

[9] (a) R.T. Jacobs, P.R. Bernstein, L.A. Cronk, E.P. Vacek, L.F. Newcomb, D. Aharony, C.K. Buckner, E.J. Kusner, J. Med. Chem. 37 (1994) 1282–1297;
(b) C.-J. Wang, X. Sun, X. Zhang, Angew. Chem. Int. Ed. 44 (2005) 4933–4935;
(c) M.M. Lerch, B. Morandi, Z.K. Wickens, R.H. Grubbs, Angew. Chem. Int. Ed. 53 (2014) 8654–8658.

[10] For selected reviews on photoredox catalysis, see:
(a) TP. Yoon, M.A. Ischay, J. Du, Nat. Chem. 2 (2010) 527–532;
(b) J.M.R. Narayanam, C.R.J. Stephenson, Chem. Soc. Rev. 40 (2011) 102–113;
(c) J. Xuan, W.-J. Xiao, Angew. Chem. Int. Ed. 51 (2012) 6828–6838;
(d) D.P. Hari, B. König, Angew. Chem. Int. Ed. 52 (2013) 4734–4743;
(e) C.K. Prier, D.A. Rankic, D.W.C. MacMillan, Chem. Rev. 113 (2013) 5322–5363;
(f) M.N. Hopkinson, B. Sahoo, J.-L. Li, F. Glorius, Chem. Eur. J. 20 (2014) 3874–3886;
(g) T. Koike, M. Akita, Inorg. Chem. Front. 1 (2014) 562–576.

[11] For a review on photoredox-catalyzed trifluoromethylation, see:
T Koike, M. Akita, Top. Catal. 57 (2014) 967–974.

[12] (a) Y. Yasu, T. Koike, M. Akita, Angew. Chem. Int. Ed. 51 (2012) 9567–9571;
(b) Y. Yasu, T. Koike, M. Akita, Org. Lett. 15 (2013) 2136–2139;
(c) Y. Yasu, T. Koike, M. Akita, Chem. Commun. 49 (2013) 2037–2039;
(d) T. Koike, M. Akita, Synlett 24 (2013) 2492–2505;
(e) Y. Yasu, Y. Arai, R. Tomita, T. Koike, M. Akita, Org. Lett. 16 (2014) 780–783;
(f) R. Tomita, Y. Yasu, T. Koike, M. Akita, Beilstein J. Org. Chem. 10 (2014) 1099–1106;
(g) R. Tomita, Y. Yasu, T. Koike, M. Akita, Angew. Chem. Int. Ed. 53 (2014) 7144–7148.

[13] (a) M. Zhang, A. Porte, G. Diamantidis, K. Sogi, D. Kubrak, L. Resnick, S.C. Mayer, Z. Wang, A.F. Kreft, B.L. Harrison, Bioorg. Med. Chem. Lett. 17 (2007) 2401–2403;
(b) S.C. Mayer, A.F. Kreft, B. Harrison, M. Abou-Gharbia, M. Antane, S. Aschmies, K. Atchison, M. Chlenov, D.C. Cole, T. Comery, G. Diamantidis, J. Ellingboe, K. Fan, R. Galante, C. Gonzales, D.M. Ho, M.E. Hoke, Y. Hu, D. Huryn, U. Jain, M. Jin, K. Kremer, D. Kubrak, M. Lin, P. Lu, R. Magolda, R. Martone, W. Moore, A. Oganesian, M.N. Pangalos, A. Porte, P. Reinhart, L. Resnick, D.R. Riddell, J. Sonnenberg-Reines, J.R. Stock, S.-C. Sun, E. Wagner, T. Wang, K. Woller, Z. Xu, M.M. Zaleska, J. Zeldis, M. Zhang, H. Zhou, J.S. Jacobsen, J. Med. Chem. 51 (2008) 7348–7351;
(c) A. Alimardanov, J. Schmid, J. Afragola, G. Khafizova, Org. Process Res. Dev. 12 (2008) 424–428;
(d) D. Wang, P.-C. Chu, C.-N. Yang, R. Yan, Y.-C. Chuang, S.K. Kulp, C.-S. Chen, J. Med. Chem. 55 (2012) 3827–3836.

[14] Under these reaction conditions, double trifluoromethylated product **5i** was formed in 25% NMR yield.

[15] An NMR experiment gave a 69% yield of **5i**, indicating that isolated yield was reduced through purification process. Double trifluoromethylation of **2i** gave a better yield than reactions of **2e** and **2f** because the reaction of **2i** did not produce by-product **4**. Reaction conditions for NMR experiment of double trifluoromethylation of **2i**: A mixture of $[Ru(bpy)_3](PF_6)_2$ (1.3 μmol, 2.5 mol%), **1a** (0.13 mmol, 2.5 equiv), **2i** (50 μmol, 1.0 equiv) and $SiEt_4$ (an internal standard) in DMSO-d_6 (0.5 mL) was irradiated by 3 W blue LEDs ($\lambda = 425 \pm 15$ nm) at room temperature for 4 h.

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