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Metal-Free Visible Light Hydroperfluoroalkylation of Unactivated Alkenes Using Perfluoroalkyl Bromides

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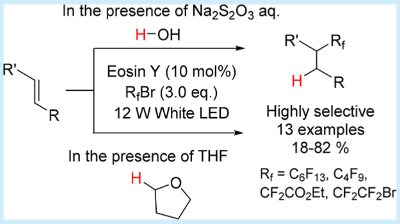
Supporting Information

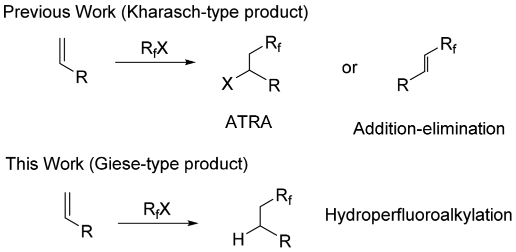
ABSTRACT: Organic dye-catalyzed visible light induced hydroperfluoroalkylation of unactivated alkenes is described. Hydroperfluoroalkylation proceeds selectively and is applicable for various perfluoroalkyl bromide and alkenes including internal alkenes. The reaction mechanism is discussed, and it is shown that the hydrogen source varies with reaction conditions.



The incorporation of perfluoroalkyl groups to organic compounds can confer unique properties such as increased lipophilicity, high chemical and thermal stability, high water repellency, and so on.[1] Owing to their behavior, perfluoroalkylated compounds have been widely used not only for pharmaceuticals but also for materials, and the development of efficient perfluoroalkylation reactions is a significant challenge. Therefore, many general and mild perfluoroalkylations have been reported,[2] among which radical perfluoroalkylation is one of the most convenient and direct methods to introduce perfluoroalkyl groups into organic compounds.[3] More specifically, the radical reaction using perfluoroalkyl halides can provide a general method for the introduction of many kinds of perfluoroalkyl groups, especially because a variety of perfluoroalkyl halides are commercially available and easy to obtain.[4] Recently, radical reaction using photoredox catalysis has emerged as an active, sustainable, and promising field of research.[5] Photoredox-catalyzed perfluoroalkylations have been reported previously;[6] however, there are limited examples using perfluoroalkyl halides as the perfluoroalkyl source.

There are two well-known types of reactions for the radical addition to alkenes: the Kharasch-type reaction,[7] which gives an atom transfer radical addition (ATRA) product, and the Giese-type reaction,[8] which gives a hydrogen transfer product (Scheme 1). The Kharasch-type reaction is well-known for the reaction using perfluoroalkyl halides;[9] however, the Giese-type reaction is not suitable for the radical perfluoroalkylation, because the hydrogen donor used for the reaction reacts preferentially with electron-poor perfluoroalkyl radicals and the desired adduct is difficult to obtain.[10] Furthermore, the reaction must compete with ATRA or addition−elimination reactions, and achieving selective hydroperfluoroalkylation is problematic.[11] Recently, iridium-catalyzed visible-light-induced hydrofluoroalkylations of unactivated terminal olefins using a Hantzsch ester[6m] or an amine[6i] as the hydrogen donor have been reported. However, in these cases, ATRA or addition−elimination products are also produced, and the examples of selective hydroperfluoroalkylation are limited.

Scheme 1. Perfluoroalkylation of Olefins



In the previous work, we studied organic dye-catalyzed perfluoroalkylation using perfluoroalkyl iodide and reported that a Kharasch-type iodoperfluoroalkylation reaction proceeded with various unactivated terminal alkenes and alkynes.[6n] In this study, we have investigated an Eosin Y catalyzed visible light induced reaction using perfluoroalkyl bromide and found that the reaction gave the hydroperfluoroalkylation product selectively. Herein, we report a metal-free selective hydroperfluoroalkylation of unactivated olefins, which is the first example of organic dye-catalyzed perfluoroalkylation using perfluoroalkyl bromide.

We initially examined the reaction between fluoroalkyl bromide and decene (**1**) (Table 1). First, the reaction of decene with 3.0 equiv of perfluorohexyl bromide using 10 mol % of Eosin Y (**3a**) with photoirradiation for 17 h using a 12 W white LED in CH_3CN in the presence of aqueous $Na_2S_2O_3$ was tested according to our previous report (Table 1, entry 1).[6n] As a result, the corresponding hydroperfluorohexylated product **2a** was obtained in 10% yield. We tried the reaction in THF and found that the reaction yield was increased up to 48% (Table 1, entry 2). Then we screened organic dyes (Table 1, entries 3−5). The reactions using Phloxine B (**3c**) and Rose

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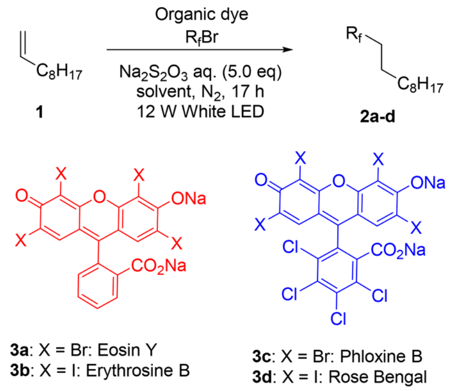
Table 1. Optimization of the Reaction Conditions[a]



entry	organic dye (mol %)	R_fBr (equiv)	solvent	prod	yield (%)
1	**3a** (10)	$C_6F_{13}Br$ (3.0)	CH_3CN	**2a**	10
2	**3a** (10)	$C_6F_{13}Br$ (3.0)	THF	**2a**	48
3	**3b** (10)	$C_6F_{13}Br$ (3.0)	THF	**2a**	4
4	**3c** (10)	$C_6F_{13}Br$ (3.0)	THF	**2a**	33
5	**3d** (10)	$C_6F_{13}Br$ (3.0)	THF	**2a**	38
6	**3a** (10)	$C_6F_{13}Br$ (3.0)	THF/CH_3CN[b]	**2a**	82
7[c]	**3a** (10)	$C_6F_{13}Br$ (3.0)	THF/CH_3CN[b]	**2a**	77
8	**3a** (5)	$C_6F_{13}Br$ (3.0)	THF/CH_3CN[b]	**2a**	67
9	**3a** (10)	$C_6F_{13}Br$ (2.5)	THF/CH_3CN[b]	**2a**	69
10[d]	**3a** (10)	$C_6F_{13}Br$ (3.0)	THF/CH_3CN[b]	**2a**	64
11	**3a** (10)	C_4F_9Br (3.0)	THF/CH_3CN[b]	**2b**	61
12	**3a** (10)	$EtCO_2CF_2Br$ (3.0)	THF/CH_3CN[b]	**2c**	82
13	**3a** (10)	$BrCF_2CF_2Br$ (1.5)	THF/CH_3CN[b]	**2d**	66
14	**3a** (10)	$BrCF_2CF_2Br$ (0.5)	THF/CH_3CN[b]	**2d**	34

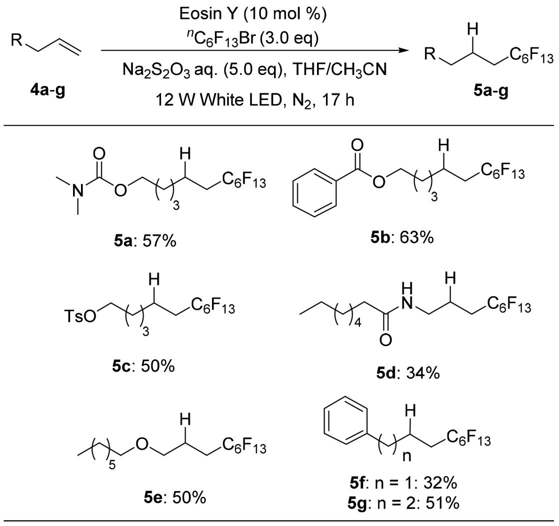
[a] Reaction conditions: **1** (0.20 mmol), R_fBr, **3**, solvent (5 mL), $Na_2S_2O_3$ aq. (1.00 mmol in 1 mL of H_2O) at rt for 17 h irradiated with 12 W white LED under N_2 unless otherwise noted. [b] 1:1 mixture. [c] 8 h irradiation. [d] In the absence of $Na_2S_2O_3$ aq.

Bengal (**3d**) also proceeded, but the yields were slightly lower than that of the reaction with Eosin Y. We then tried the reaction using a 1:1 mixture of CH_3CN/THF as a solvent and found that the yield improved to 82% (Table 1, entry 6). The reaction was clean, and no side products were observed (SI, Figure S1). The reactions having a shorter reaction time or a reduced amount of catalyst or perfluorohexyl bromide exhibited lower yields (Table 1, entry 7−9). In the absence of aqueous $Na_2S_2O_3$, the reaction proceeded, but the yield was lower (Table 1, entry 10). The reactions using perfluorobutyl bromide and ethyl bromodifluoroacetate were investigated and gave their respective fluoroalkylated products in good yield (Table 1, entries 11 and 12). The reaction with 1,2-dibromoperfluoroethane was also tested and gave the 1:1 adduct as a single product (Table 1, entries 13 and 14).

Next, we tried the reaction with various unactivated terminal olefins with perfluorohexyl bromide under the optimized reaction conditions (Table 1, entry 8) (Scheme 2). The substrates containing amide (**5a**), ester (**5b**), sulfonyl (**5c**), and ether groups (**5e**) proceeded to give the corresponding hydroperfluoroalkylated product in moderate yield. The substrate possessing an amide proton (**5d**) lowers the yield, but the reaction proceeded. The reactions with aromatic rings (**5f**, **5g**) also proceeded, and the perfluoroalkylation of the phenyl group did not occur. We also attempted the reaction with styrene,[12] but the desired product was not obtained.

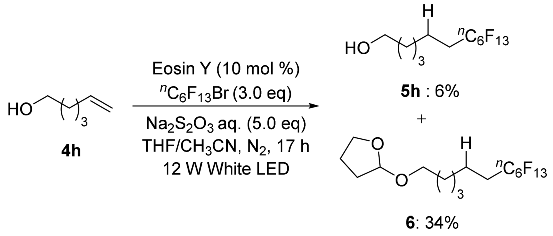
Interestingly, perfluoroalkylation also proceeded with unprotected alcohol **4h**; however, the THF adduct **6** was formed as a major product together with perfluoroalkylated alcohol **5h** (Scheme 3).

Scheme 2. Hydroperfluoroalkylation of Terminal Alkenes

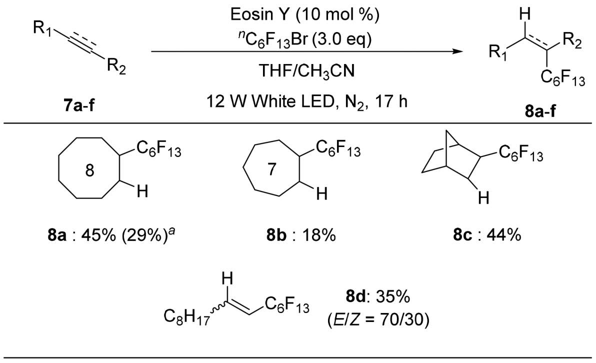


Using internal alkenes in the reaction was also investigated (Scheme 4). The reaction with cyclohexene did not proceed, but the reaction with cyclooctene gave the corresponding hydroperfluoroalkylated product **8a**. The reaction in the absence of water gave a higher yield than in the presence of water in this case. The reaction with cycloheptene gave the product **8b** in 18% yield, and the reaction with 2-norbornene gave a 44% yield of **8c**. The hydroperfluoroalkylation also proceeded with distorted internal olefins, although the yield

Scheme 3. Hydroperfluoroalkylation of 4h



Scheme 4. Hydroperfluoroalkylation of Internal Alkenes and Alkynes



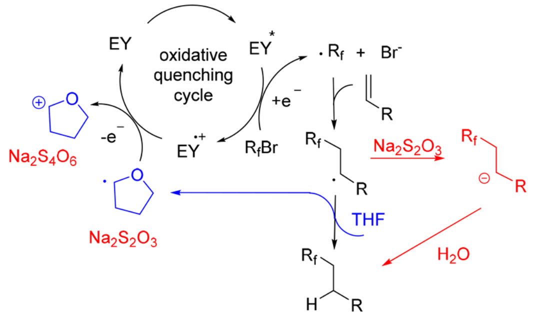
[a] In the presence of aq. $Na_2S_2O_3$ (5.0 equiv).

was not unsatisfactory. The reaction with a terminal alkyne gave the corresponding hydroperfluoroalkylated alkene **8d** as a stereoisomeric mixture.

Based on these results, we propose the reaction mechanism as shown in Scheme 3. The photoexcited Eosin Y reacted with perfluoroalkyl bromide to give a perfluoroalkyl radical and bromonium ion. The radical was then added to the olefin to give the intermediate radical, at which point there are two possible reaction pathways for the intermediate radical.

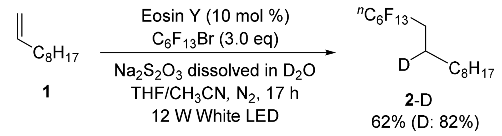
The first pathway is possible when the reaction is performed in the presence of aqueous $Na_2S_2O_3$ (Scheme 5, red line route). The intermediate radical is reduced to the carbanion by $Na_2S_2O_3$ and reacts with water to give a hydroperfluoroalkylated product. To confirm that hydrogen originated from water, a labeled experiment using D_2O was performed (Scheme 6). As expected, the reaction gave a deuterated product.

Scheme 5. Proposed Mechanism[a]



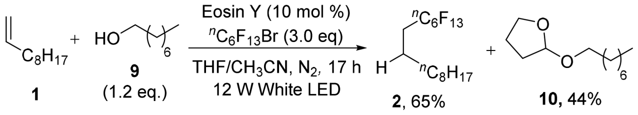
[a] In the presence of aq. $Na_2S_2O_3$: red line route. In the presence of THF: blue line route.

Scheme 6. Labeled Experiment



However, the reaction also proceeded in the absence of aqueous $Na_2S_2O_3$. Therefore, the second pathway in which hydrogen comes from THF has been proposed (Scheme 5, blue line route). The intermediate radical receives hydrogen from THF, forming a THF radical. Then the THF radical reacts with the radical cation of Eosin Y, and the catalytic cycle of Eosin Y is thereby completed. The reacted THF radical is converted to a carbocation, and when the substrate is alcohol, as shown in Scheme 2, the THF cation reacts with the hydroxyl group of alcohol. In order to verify this route, alcohol was added to the reaction mixture (Scheme 7). Reaction in the presence of decanol gave the THF adduct, **10**, as we expected. These experiments demonstrated that the reaction presents two pathways, wherein the hydrogen is derived from either water or THF.

Scheme 7. In the Presence of Alcohol



In summary, we have developed metal-free Eosin Y-catalyzed visible light induced perfluoroalkylations of unactivated olefins. Selective hydroperfluoroalkylation was achieved with the use of perfluoroalkyl bromides. We also revealed that the reaction can proceed via two different pathways: one in which the hydrogen is derived from water, and another in which hydrogen is derived from THF. Furthermore, the reaction permits various bromides and olefins including internal olefins, which are inappropriate according to the previously reported iodoperfluoroalkylation. The reaction is very sustainable and enables the synthesis of various perfluoroalkyl compounds.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.8b03596.

Experimental procedures, and characterization of all new products, including ^1H, ^{13}C and ^{19}F NMR spectra (PDF)

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Notes

The authors declare no competing financial interest.

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