Trifluoroethoxy-Coated Subphthalocyanine affects Trifluoromethylation of Alkenes and Alkynes even under Low-Energy Red-Light Irradiation

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Photoredox chemical reactions induced by visible light have undergone a renaissance in recent years. Polypyridyl dyes such as Ir(ppy)$_2$ and Ru(bpy)$_3$ are key catalysts in this event, and blue- or white-light irradiation is required for the chemical transformations. However, it remains a challenge to achieve reactions under the lower energy of red light. We disclose, herein, that trifluoroethoxy-coated subphthalocyanine realizes the red-light-driven trifluoromethylation of alkenes and alkynes with trifluoromethyl iodide in good-to-high yields. Perfluoroalkylations were also achieved under red light. The reaction mechanism is discussed with the support of UV/Vis spectroscopy and cyclic voltammetry of trifluoroethoxy-coated subphthalocyanine. Light irradiation/dark study also supports the proposed mechanism.

Visible-light-mediated chemical transformations of organic molecules under photoredox catalysis has dramatically changed the realm of photochemical reactions in organic synthesis. Classical photochemical reactions under ultraviolet (UV)-light irradiation often damage substrates/products, resulting in undesired complex mixtures.[1] Owing to the high energy of UV irradiation (290–366 nm), control of the reaction is problematic, and thus careful and strict design of substrates/reactions is required.[2] More importantly, UV light is toxic. On the other hand, visible light is a longer wavelength light with lower energy (380–780 nm), and chemical transformations proceed efficiently under mild conditions in the presence of photoredox catalysts.[2] Polypyridyl dyes complexed with transition metals, such as Ir(ppy)$_2$ and Ru(bpy)$_3$, are the most powerful catalysts when irradiated by visible light. Although these photoredox systems are mild, high-energy photon sources such as blue light (400–500 nm) are still necessary for the chemical transformations.[2] In addition, there is a risk of photo-oxidative damage to eyes (retina) by the blue light.[3] Green light (500 nm), however, is one-tenth as hazardous to the retina as blue light.[4]

The move towards an “all-green” process by using lower power light for chemical reactions remains a challenge to achieve non-toxic, eco-friendly, mild, and selective transformations. In this context, red light has gained attention for its application in “greener” visible-light photoredox reactions.[5] Red light has the benefits of low power (600–700 nm), no risk of light hazard, and cheap lamps. More interestingly, it penetrates even bulk turbid media. Although versatile photocatalytic systems have been well researched to date, there are very few examples of the application of red light for organic synthesis, owing to a poor range of absorption windows for general photocatalysts [5] (e.g. maximum excitation wavelengths of $\lambda_{\text{max}} = 452$ nm for Ru(bpy)$_3$,[6] 375 nm for fac-Ir(ppy)$_3$[7] and 539 nm for eosin Y).[8] To expand the utilizable wavelength range of visible light for photochemical reactions, an Os$^2$/Re$^2$ supramolecular complexed photosensitizer was designed for red-light-driven photoredox catalytic reactions.[9] This system is limited to the reduction of CO$_2$ and the catalyst requires a multi-step synthesis.

Phthalocyanines 1 are dyes with the most potential to be red-light-driven photocatalysts, owing to their absorption bands at around 600–700 nm,[10] followed closely by subphthalocyanines 2 at 500–600 nm.[11] However, the poor solubility of 1 and the instability of 2 strictly limit their utility in organic reactions.[12] Our group has researched a series of trifluoroethoxy-coated phthalocyanines and subphthalocyanines for the photodynamic therapy of cancer and electronic materials (Figure 1a).[13] Drawing motivation from this background, we decided to develop a new utility of 1 and 2 for the photoredox catalytic system, especially under the low energy of red light. Trifluoromethylation is an attractive target reaction under a photoredox system.[14] Indeed, trifluoromethylation reactions induced by visible light constitute a recent breakthrough in organic chemistry.[15] However, all of the reported methods for trifluoromethylation reactions strictly require high-energy photon sources such as blue light-emitting diode (LED) photoradiation (Figure 1b). Before the completion of our research, You and co-workers reported the first attempt at the photoredox catalytic generation of trifluoromethyl radicals under low-energy photoradiation.[16] Metal–porphyrins were selected for the trifluoromethylation of alkenes with trifluoromethyl iodide (CF$_3$I) by using LEDs. In the presence of oxalate, Pt–porphyrin was best for this transformation under green LEDs, but the substrate scope was narrow and limited, yields were low to...
We, herein, disclose that trifluoroethoxy-coated subphthalocyanine 3a dramatically catalyzes the trifluoromethylation of alkenes 3, including alkynes with CF3I, under red-light-driven photoredox conditions to provide the corresponding trifluoromethylated iodides 4 in a short space of time and with very high yields (Figure 1c). The reaction mechanism is discussed based on cyclic voltammetry and the absorption spectra of 2a.

![Figure 1](image)

**Figure 1.** a) Structures of phthalocyanines 1 and subphthalocyanines 2. b) Photoredox trifluoromethylation under visible light (previous reports). c) This work of photoredox trifluoromethylation under red light.

We first investigated the trifluoromethylation of hex-5-en-1-ol (3a) with CF3I by using various photocatalysts under red-light irradiation (Table 1). Following an earlier report by Stephenson and co-workers, a catalytic amount of sodium l-ascorbate (35 mol%) was used as the initial reductant in a MeCN/MeOH system.15b,17 Apparently, in the initial reductant and red-light-driven photoredox conditions to provide the corresponding trifluoromethylation iodides 4 in a short space of time and with very high yields (Figure 1c). The reaction mechanism is discussed based on cyclic voltammetry and the absorption spectra of 2a.

| Run | Catalyst | LED | Additive | Time [h] | Yield [ %] |
|-----|----------|-----|----------|---------|-----------|
| 1   | [Ru(bpy)3]2⁺(PF6)6 | red | – | 6 | <5 |
| 2   | Eosin Y | red | – | 6 | <5 |
| 3   | Methylene blue | red | – | 6 | <5 |
| 4   | 1a | red | – | 6 | 12 |
| 5   | 1b | red | – | 6 | <5 |
| 6   | 2a | red | – | 6 | 92 |
| 7   | 2a | red | – | 3 | 62 |
| 8   | 2a | red | – | 1 | 35 |
| 9   | 2b | red | – | 6 | <5 |
| 10  | 2a | red | LiBr | 1 | 65 |
| 11  | 2a | red | NaOAc | 1 | 99 |
| 12  | 2a | red | LiOAc | 1 | 99 |
| 13  | 2a | red | CsOAc | 1 | 99 |
| 14  | 2a | red | NaOAc | 1 | 96 |
| 15  | – | | NaOAc | 3 | <5 |
| 16  | 2a | red | NaOAc | 3 | <5 |
| 17  | 2a | – | NaOAc | 3 | <5 |
| 18  | 2a | white | – | 0.5 | 90 |

[a] The reaction of alkene 3a (0.25 mmol) with CF3I (excess) was carried out in the presence of 1 or 2 (0.0025 mmol) and sodium l-ascorbate (0.0875 mmol) in MeCN (1.0 mL) and MeOH (0.75 mL) at room temperature. [b] Yields were determined by using 19F NMR spectra of the crude product with PhCF3 as an internal standard. [c] 5 mol% of Na ascorbate was used. [d] 20 mol% of NaOAc was used. [e] In the absence of Na ascorbate. [f] The reaction was carried out in the dark.

Although the effect of light was clear (Table 1, run 17), a further investigation was attempted to confirm the necessity of light to maintain the transformation or whether it was only required to initiate a reaction, according to a light irradiation/dark study (Scheme S1). These results clearly indicate that the light must be maintained during the transformation as well.
The effectiveness of 2a rather than 1a, 1b, or 2b, can be explained by the UV/Vis spectra of catalysts and LED lights. The UV/Vis spectra of 1 and 2 were recorded in MeCN/MeOH and/or 1,4-dioxane at a concentration of 1 × 10⁻⁴ M, depending on the solubility (Figure 2, also see Figure S1). Their Q bands were slightly blue shifted in MeCN/MeOH compared to 1,4-dioxane, but the differences were small. These spectra indicate that all phthalocyanines 1 and subphthalocyanines 2 were present solely as monomers and were characterized by sharp absorption bands in the Q-band region. Strong absorption peaks were observed at 710 or 703 nm for 1a, 666 nm for 1b, 603 and 598 nm for 2a, and 563 nm for 2b. On the other hand, white LEDs showed broad spectrum of 430–700 nm with two peaks, and red LEDs displayed a sharp absorption at 600–650 nm. These results suggest that the absorption of 2a shows a suitable overlap with red LEDs, resulting in a 99% yield of 4a, whereas catalysts 1b and 2b were useless, owing to the lack of overlapping spectra. The 12% formation of 4a from 1a is reasonable, as 1a has an overlapping shoulder peak at 638 or 632 nm. White LEDs are effective for the activation of 2a with wide range of overlapping spectra.

With the optimized conditions under red light in hand, the substrate scope of 3 was investigated (Table 2). Terminal olefin-like 3a–j finely reacted with CF₃I to afford the desired adducts 4a–j under the red-light-induced photocatalytic system by using 2a. Common functional groups such as tosyl 3d, ester 3e, alkyl- and aryl-halide 3f, h, i, carbonate 3m, and electron-rich aromatic groups 3g were tolerated under these conditions. Internal olefin 3k and exo-olefin 3l also gave good yields. The alkene 3n, appending a β-keto ester functionality, reacted selectively with CF₃I at the olefinic moiety to provide 4n (66% ¹⁹F NMR yield and 59% isolated yield), whereas the active methylene of 3n was touched with only 2% ¹⁹F NMR yield. The result is worth noting, because the β-keto esters reacted with CF₃I under white LEDs or radical conditions. [19] Not only alkene 3i, but also alkyne 3o and 3p, were converted into the corresponding adducts 4o and 4p in 70 and 44% yield, respectively. In all cases, the regioselectivity was almost perfect and only a trace amount of regioisomers, such as 4b', were observed in the ¹⁹F NMR (< 4 % as a doublet at around △- 70 ppm in the ¹⁹F NMR analysis). The red-light methodology was extended to the perfluoroalkylation of 2a using nC₆F₅-I and nC₆F₅-I to give perfluoroalkylation adducts 5a and 6a in 92 and 85%, respectively. Although the reaction has a wide scope, electron-deficient alkenes and styrene were not accepted.

A plausible reaction mechanism involving both a closed catalytic cycle A and chain propagation cycle B was proposed (Scheme 1) with the support of cyclic voltammetry of 2a (Figure S2). Earlier reports of CF₃-I ATRA reactions have shown that the reaction is based on an effective radical chain reaction that can be initiated through visible-light irradiation even without photocatalysts; however, our system requires both photocatalyst 2a (run 15, Table 1) and light (run 17, Table 1). Thus, in the initial step, photo-excited trifluoroethoxy subphthalocyanine 2a receives one electron from sodium ascorbate to form an anion radical of 2a. [11b,17] The anion radical (⁻[2a/2a⁻]) = −0.69 V vs. SCE) should reduce CF₃I (E° = −1.22 V vs. SCE) [21] to generate the CF₃ radical (CF₃) (Scheme S3). Although this reduction process is a thermodynamically unfavorable electron transfer [22] from the reduced photocatalyst to CF₃I (about
In conclusion, we have disclosed that trifluoroethoxy-coated subphthalocyanine 2a is an efficient photocatalyst for the trifluoromethylation of alkenes and alkynes 3 under red light. Although a variety of photocatalysts have been reported, they require blue- or white-light irradiation for chemical transformation, and are unreactive under the low energy of red light. Trifluoroethoxy-subphthalocyanine 2a is activated under either red or white light. As red light is much “greener” than white light, Trifluoroethoxy-subphthalocyanine formation, and are unreactive under the low energy of red light. They require blue- or white-light irradiation for chemical transformation.

Further mechanistic studies should be required to elucidate the mechanism.

In conclusion, we have disclosed that trifluoroethoxy-coated subphthalocyanine 2a is an efficient photocatalyst for the trifluoromethylation of alkenes and alkynes 3 under red light. Although a variety of photocatalysts have been reported, they require blue- or white-light irradiation for chemical transformation, and are unreactive under the low energy of red light. Trifluoroethoxy-subphthalocyanine 2a is activated under either red or white light. As red light is much “greener” than white or blue light, this strategy is likely to be increasingly used in the future.

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Conflict of Interest

The authors declare no conflict of interest.

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