Facile Aerobic Photo-Oxidative Synthesis of Sulfinic Esters

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Abstract: A mild and efficient one-pot visible light-induced method has been developed for the synthesis of sulfinic esters. Sulfinic esters are important structural elements that are frequently found in pharmaceutical agents and biologically active natural products. The routine procedure in the drug discovery and development process to prepare and fully characterize sulfinic esters make them a drug candidate for biological evaluation.

Keywords: eosin Y, photoredox, sulfinic esters, SET, aerobic.

INTRODUCTION

SULFONIC esters constitute an important class of organic compound and its application have evoked considerable attention during past decades because of their wide range of industrial pharmaceutical and biological activities such as regulating them mitochondrial function of the Parkinsonism protein DJ-1 and stimulating the glucose uptake in muscle cells. Furthermore, sulfinic esters act as both electrophiles and nucleophiles, which have been extensively employed for the synthesis of a variety of functional products such as, α,β-unsaturated ketones, sulfonamides and sulfonamides, sulfoxides, sulfonimidamides, and sulfonyl allenes. Due to the interesting applications, the development of alternative approaches to access sulfinic esters is of high importance in synthetic chemistry. A wide array of sulfinic esters were efficiently afforded in an exclusive chemoselective manner.

The challenge in chemistry to develop practical process, reaction media, conditions and/or utility of materials based on the idea of integrated chemical process is one of the important issues in scientific society. The development of environmentally benign processes is the goal of synthetic organic chemistry. Rational approach involving increasing focus on the utilization of visible light energy is due to its chief, easily available, abundant nature and its impeccable tolerance towards the environment. Harvesting visible light and performing chemical reactions via photocatalysis is one of the emerging strategies to meet the increasing demand for more sustainable chemical processes. Visible light photoredox catalysis (VLPC) has been successfully applied to various organic transformations, including aza-Henry reaction, cycloaddition, asymmetric alkylation, Diels-Alder reaction, oxidations, reductive dehalogenation etc. Photoredox catalysis is an attractive approach to activating organic molecules by translating visible light energy via single-electron transfer (SET). Some pioneering researchers have dedicated to converting solar energy into chemical energy for chemical transformations which includes a promising strategy for the application of photoredox catalysts to initiate single electron transfer processes have been developed. Previously, transition metal based photocatalysts were widely used, which exhibit any one or more disadvantages such as high cost, low sustainability and potential toxicity. In recent year, eosin Y, fluorescein, rose bengal, nile red, perylene and rhodamine B have been used as superior alternative to transition metal photoredox catalyst Ru (II) and Ir(II) complexes as economically and ecologically...
superior surrogates in visible-light promoted organic transformations involving SET\textsuperscript{26–29} (single electron transfer). These organic dyes have got much more attention because of ease of handling, eco-friendly and have great potential for applications in visible-light-mediated organic synthesis\textsuperscript{30–33} which fulfills the basic principle of green chemistry.

Oxidation is the foundation of synthetic organic chemistry, and recent methodology using molecular oxygen is one way consistent with this notion due to its high atomic effect or low E-factor as an oxidant. With this background in mind, and in continuation of our research work\textsuperscript{34–41} for the development of new synthetic methodology, we have developed visible light promoted an aerobic photoredox catalysis for the oxidative esterification of (hetero) aryl and alkyl thiols with alcohols using Eosin Y at room temperature with merits of oxidative esterification of (hetero) aryl and alkyl thiols with alcohols using Eosin Y at room temperature with merits of

In order to work out the envisaged protocol, a key reaction was conducted with thiol 1(a–r) and alcohol 2(a–r) in 2 mol % of eosin Y under an aerobic atmosphere (without air bubbling) by irradiation with visible light (green light-emitting diodes (LEDs), \( \lambda_{\text{max}} = 535 \text{ nm} \)) at rt.

The reaction gave the desired thioester 3(a–r) and following this methodology, a series of control experiments were performed, which indicates that the aerobic condition is essential to give the desired product with high yield (97 %) (Table 1, entry 1). There was no product formation or it was formed in traces in the absence (–) of any one of the reagents / catalyst (Table 1, entries 2–4). The reaction did not proceed satisfactorily when a household 20 W fluorescent lamp was used instead of green LEDs (Table 1, entries 5 versus 1). Notably, the same result was obtained on using O\textsubscript{2} (balloon) instead of an air atmosphere (Table 1, entry 7 versus 1), where as in the absence of any gas or under a nitrogen atmosphere no product formation was detected (Table 1, entry 4, 6). These results establish that visible light, photocatalyst and air all are essential (+) for the reaction and support the visible light promoted photocatalytic model of the reaction.

The substituents on the aryl ring of aryl thiols influenced the desired product yields to some extent. In general, substrates 1 bearing an electron-donating group are able to afford relatively higher yields than those of electron-deficient ones due to the fact that electron-rich aryl thiols are beneficial to form more stable radical intermediates, thus favoring the coupling process. Interestingly, the less-reactive heterocyclic substrates such as furan-3-thiol 1k and thiophene-2-thiol 1l were also amenable to the transformation to afford the desired products in good yields (3k, 3l). Further, the change of methanol to ethanol, propyl alcohol, butyl alcohol, isopropanol and benzyl alcohol also led to the generation of desired sulfinic ester products at slightly different time duration (3m, 3n, 3o, 3p, 3q and 3r). Furthermore, a variety of functional groups such as –Me, OMe, iso-propyl, –F, –Cl and –Br are well tolerated in the transformation, which would offer the potential for molecular complexity via further transformations.

On the basis of the above observations and the literature precedents, a plausible mechanism involving photoredox catalysis for the oxidative esterification to form sulfinic ester is depicted in Scheme 1. On absorption of visible light, the organophotoredox catalyst eosin Y (EY) is excited to its singlet state 1EY\textsuperscript{*} which through inter system crossing (ISC) comes to its more stable triplet state 3EY\textsuperscript{*} and undergoes a single electron transfer (SET),\textsuperscript{32} 3EY\textsuperscript{*} may undergo both reductive and oxidative quenching\textsuperscript{42–46} to generate RS\textsuperscript{•−}, which undergo SET to give RSO\textsuperscript{•−}. The coupling of A and B gave the desired product. The single electron transfer that generate the sulfur radicals were supported by trapping of this radical by 2,2,6,6-tetramethylpiperidinyl 1-oxyl (TEMPO) as a radical scavenger.\textsuperscript{45} The formation of superoxide radical anion (O\textsubscript{2}–\textsuperscript{−}) during the reaction was confirmed by the detection of the resulting H\textsubscript{2}O\textsubscript{2} using KI/starch indicator.\textsuperscript{46}
Table 2. Scope of the reaction.

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EXPERIMENTAL

All chemicals used were reagent grade and were used as received. $^1$H NMR and $^{13}$C NMR spectra were recorded on a Bruker AVANCE DPX (400 MHz and 75 MHz) FT spectrometer in chloroform using TMS as an internal reference (chemical shift in $\delta$, ppm).

General Procedure for the Photocatalysed Synthesis of Sulfinic Ester (3a–r)

A round bottom flask was charged with thiol RSH 1(a–r) (1.0 mmol), eosin Y (2 mol %), alcohol (R’OH) 2a–f (3 mL) and the contents were stirred in open air under irradiation with Luxeon Rebel high power green LEDs [2.50 W, $\lambda = 535$ nm] at room temperature for the time specified in (Table 1). After the completion of reaction as monitored by TLC (preparative TLC), the resulting mixture was filtered and washed with ethyl acetate, and then concentrated to remove the excess of solvent under vacuum. The organic phase was dried over anhydrous magnesium sulfate and purified with TLC (preparative TLC silica gel). The eluent used was petroleum ether: ethyl acetate (20 : 1; v/v) to gave the desire product 3a–r with excellent yields (75–95 %).

CONCLUSION

In conclusion, we have developed a novel, one-pot procedure for the synthesis of substituted sulfinic ester from substituted thiol and alkanol via photoredox catalyst at room temperature. This protocol involves the use of visible light as the cheapest and eco-sustainable reagents as well as eosin Y as an organophotoredox catalyst at room temperature. Thus, it is a superior alternative to the existing method with respect to green and sustainable chemistry (better atom- and step-economy) for redox reactions.

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REFERENCES