EXTENDED ABSTRACT

Photo-Induced Oxidative Coupling *via* C-H/S-H Functionalization

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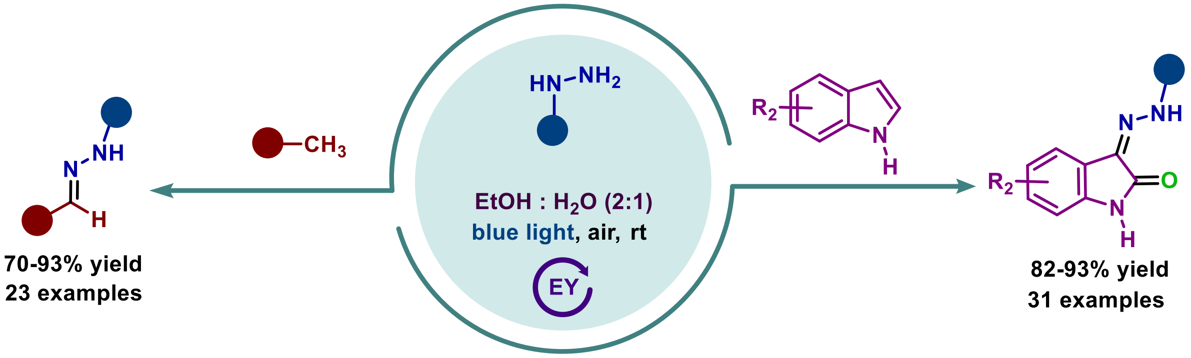
Extended Abstract

The main goal of this thesis is to design new synthetic methods for oxidative coupling utilizing visible light as a clean, eco-friendly, and renewable source of energy. Visible light photons are a traceless source of energy that carry out the reaction along with enhanced atom economy and green catalysis. The field of photoredox catalysis for C-H/S-H bond functionalization is rapidly expanding and has emerged as one of the extensively investigated areas for synthetic chemists. This thesis work focuses on developing novel photo-induced oxidative coupling methodologies for organic transformations via C-H/S-H functionalization in distinct ways.

The effective synthetic strategies for C-H/S-H functionalization are embodied in the thesis titled **" Photo-Induced Oxidative Coupling via C-H/S-H Functionalization ".** The thesis is divided into six chapters.

Chapter 1 provides an intricate elucidation of the significance of visible light in photochemical reactions, along with an exploration of the mechanisms governing these photochemical reactions. It also demonstrates several oxidative coupling reactions facilitated by photo-induced C-H/S-H functionalization. The subsequent four chapters outline the studies conducted and the resulting conclusions. Each chapter is self-contained and comprises an introduction, results and discussion, mechanism, experimental section, and references.

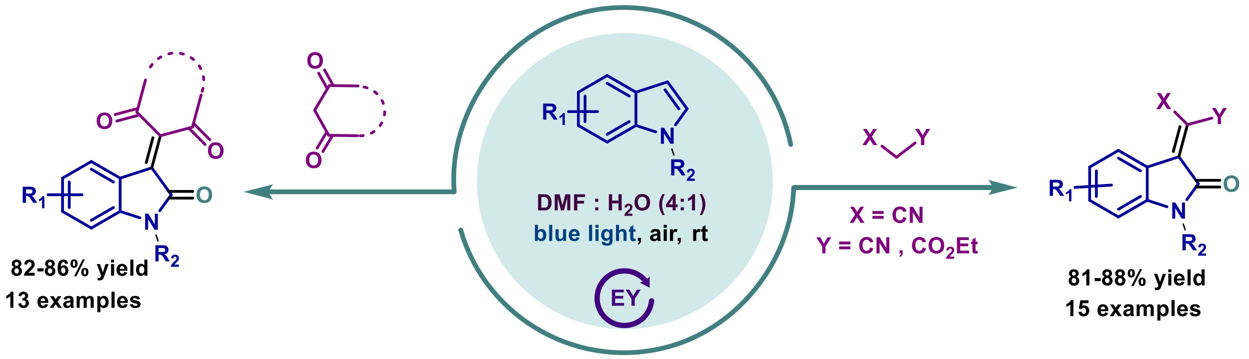
Chapter 2 describes a highly efficient, green, and metal-free method for synthesizing aryl hydrazones through oxidative $C(sp^2)-H$ and $C(sp^3)-H$ functionalization of indole and methylarene to form C–N bonds under ambient air using organic photoredox catalysis at room temperature. With the aid of eosin Y, the C–H bonds of indole and methyl arenes were activated, and the arylhydrazines were coupled. The absence of metals, low cost, environmental friendliness, green solvent, non-toxicity, ease of handling, and utilization of renewable energy sources like visible light are some of this method's primary advantages **(Scheme A)**.



Scheme A

To achieve the highest yield, several reaction parameters such as type of photocatalyst, solvent effect, molar ratio of photocatalyst, and light source were examined, taking indole and phenylhydrazine as model reactants under blue LED irradiation in ambient air at room temperature. The desired hydrazone was obtained with an excellent yield of 88% using 3 mol% of eosin Y in EtOH:H_2O (1:2) as solvent under blue light irradiation. This protocol can tolerate a wide range of functional groups on indoles, methylarenes, and arylhydrazines, and several aryl hydrazones were synthesized in good to moderate yields (70-93%). Several control experiments were performed, such as the detection of various intermediates by TEMPO adduct (which were confirmed by HRMS), quantum yield, fluorescence quenching, and light ON-OFF, and based on that, a reaction mechanism was proposed. Finally, the structure of the products was determined through ^{1}H NMR, ^{13}C NMR, ^{19}F NMR, and HRMS analysis of all the products.

Chapter 3 describes a visible-light-mediated oxidative coupling of indoles and active methylene compounds, including malononitrile, ethylcyanoacetate, dimedone, and barbituric acid for the formation of C-C unsaturated bonds using eosin Y as a metal-free photocatalyst. This new approach generates isatin *in situ* via a photochemical oxidation of indole using ambient air; then accomplishing comparable coupling reactions. In this work, only one molecule of malononitrile, ethyl acetoacetate, or dimedone reacts with one molecule of indole, but, in contrast, two molecules of barbituric acid react with one molecule of indole. **(Scheme B)**.

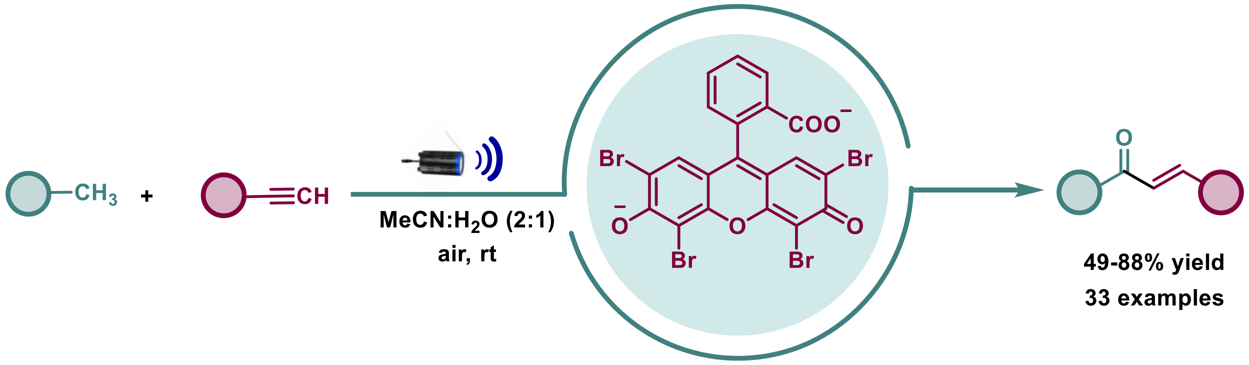


Scheme B

A systematic study was carried out to optimize the reaction to obtain the best yield for the products. The best result for synthesizing C-C unsaturated was obtained using DMF:H_2O (4:1) as solvent under blue light for 24 h. Under optimized conditions, sufficient substrates were tested to provide products in good to excellent yields (81-88%). Control experiments demonstrated that water, oxygen, and continuous light irradiation are necessary for this transformation. Based on the control experiments and reported literature, the mechanism of the reaction was proposed. All the products have been fully characterized based on their physicochemical and spectroscopic (^{1}H NMR, ^{13}C NMR, ^{19}F NMR, and HRMS) studies.

Chapter 4 describes the first method for hydroacylating terminal alkynes employing C(sp^{3})-H functionalized methyl arenes as the acylating agent using metal-free photoredox catalysis in a more environmentally friendly solvent. This protocol synthesizes α, β-unsaturated ketones i.e.

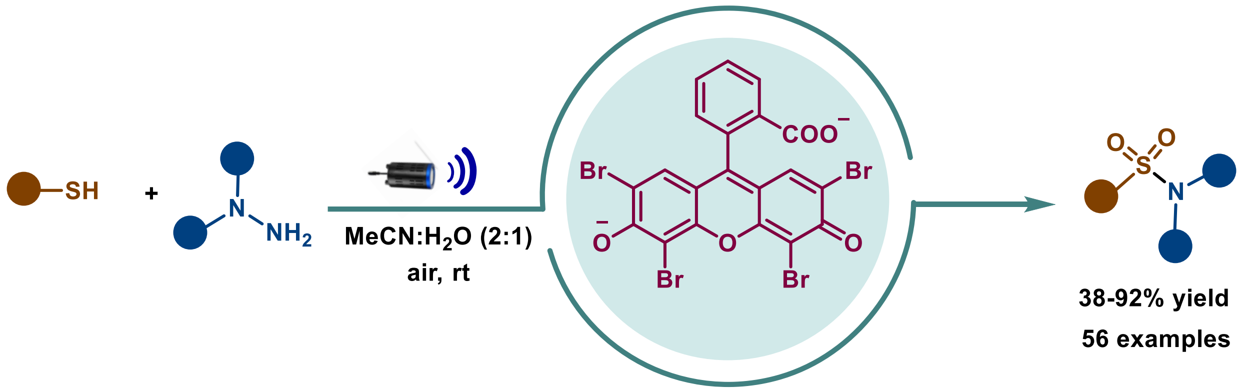
chalcones, using eosin Y as an organic photocatalyst and ambient air as an oxidant under blue LED irradiation. This visible-light-mediated aerobic oxidation showcases atom economy and conforms to the green chemistry concept **(Scheme C)**.



Scheme C

We screened the transformation parameters of photocatalyzed C(sp^3)−H activation for the hydroacylation of terminal alkynes. The reaction was conducted by taking toluene and phenylacetylene and found the best reaction conditions with 81% yield of the desired product using MeCN:H_2O (2:1) as a solvent, ambient air as oxidant at room temperature for 18 h. This strategy effectively transformed a variety of methyl arenes and aromatic alkynes into the desired product with 49-88% yields. With high atom efficiency, use of green solvents, metal-free nature, environmental friendliness, and visible light as a renewable energy source, this method is compatible with biologically active molecules. A mechanistic investigation indicated that the protocol followed radical pathways. Some control experiments like fluorescence quenching studies, isotope-labeling experiments, and deuterium labeling experiments were carried out to establish the reaction mechanism. Based on control experiments and mechanistic investigations, product isolation, and reported literature, the mechanism of the reaction was proposed. All the products were characterized by ^{1}H NMR, ^{13}C NMR, ^{19}F NMR, and HRMS studies.

Chapter 5 describes a metal-free, environment-friendly photoredox-catalyzed sulfonylation of phenylhydrazines using thiols, employing MeCN:H_2O as a green solvent and eosin Y as a photoredox catalyst. Compared to the conventional synthetic methods of sulfonamides, the appealing part of the current method is the employment of thiols instead of sulfonyl chlorides as the sulfur sources, which is more step-economical **(Scheme C)**.



Scheme D

Various parameters were investigated to find the optimum reaction condition with different solvents under visible light conditions using benzenethiol and phenylhydrazine as a model reaction. It was found that the excellent yield of the product (85%) was obtained using 3 mol% of eosin Y, air as oxidant under blue light at room temperature. Under carefully optimized conditions, the reaction exhibits a broad substrate scope with 38-92% yield and good functional group compatibility, including hetero(aryl) as well as aliphatic phenylhydrazines, including a wide range of biologically active compounds. The protocol has shown gram scale synthesis by utilizing the optimized conditions. Some control experiments were carried out, like UV-visible spectroscopy, fluorescence quenching studies, deuterium labeling experiments, and reaction with radical scavenger TEMPO. Finally, all the compounds were characterized and identified by ^{1}H NMR, ^{13}C NMR, ^{19}F NMR, HRMS studies, and single crystal XRD.

Chapter 6 describes the summary and conclusions of the present research work and its future scope.