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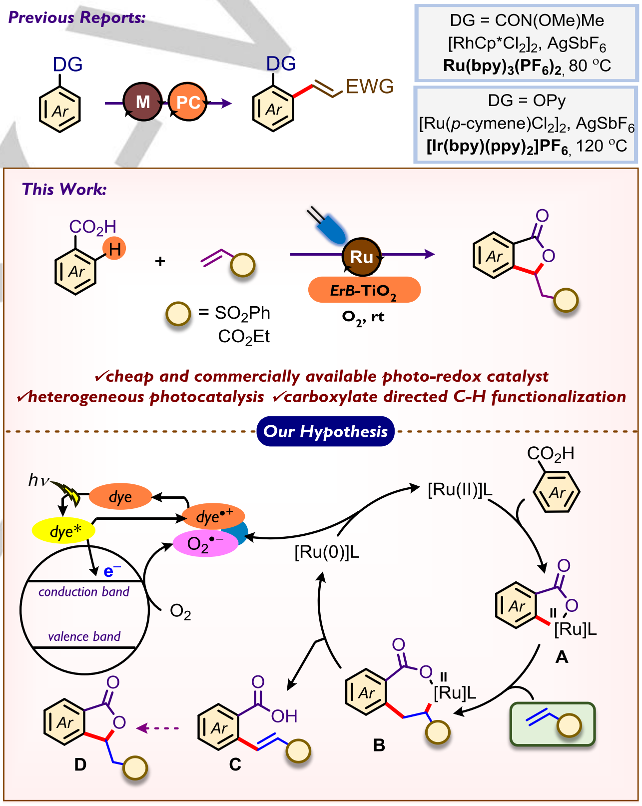
Enhancing Ru(II)-Catalysis with Visible-Light Mediated Dye-Sensitized TiO_2 Photocatalysis for Oxidative C–H Olefination of Arene Carboxylic Acids at Room Temperature

Suman Dana,[a] Purusattam Dey,[a] Siddappa A. Patil,[b] and Mahiuddin Baidya*[a]

Abstract: Erythrosine B sensitized TiO_2 photocatalysis has been combined with Ru(II)-catalysis to accomplish an oxidative olefination/annulation of benzoic acids with activated olefins under mild conditions that tolerates useful functionalities such as halides, free hydroxy, acetamido etc. The morphology of the photocatalyst is unaffected during the reaction and it can be reused. Mechanistic studies favor the involvement of a photo-induced single electron transfer process.

Transition-metal catalyzed direct C–H bond functionalization reactions have reigned supreme as a sustainable complementary approach to conventional synthetic processes due to their step- and atom-economy.[1-2] However, in most of the cases, stoichiometric amounts of sacrificial oxidants are necessary for manipulating the oxidation-state of the active transition-metal catalyst to enable the crucial redox events in the catalytic cycle.[3,4a-b] Recently, visible-light photo-redox catalysis has emerged as an alternative catalytic mode of redox manipulation[4] and the groups of Sanford, Rueping, and others have showcased its utility as catalytic internal as well as terminal oxidants in C–H bond activation reactions.[5,6] Generally, transition-metal based polypyridyl complexes, due to their high redox potentials and long excited-state life-times, are found effective to accomplish redox manipulation with high precision. However, less abundance and high cost of these catalysts are the major issues towards their broad utility. Organic dyes are also found ineffective and only sporadic examples are reported in this direction.[5c,d,f,g,h] Thus, the introduction of readily available inexpensive photo-redox catalysts with good chemical stability can fulfil the available synthetic space in metallaphotoredox catalyzed C–H bond activation reactions.

Meanwhile, metal-oxide semiconductors, such as TiO_2, have found widespread application in visible-light induced water-splitting, dye-degradation reactions, and synthetic transformations.[7,8] We questioned whether TiO_2 nanoparticles, which is well recognized for its oxygen reduction properties, could be engaged as an efficient photo-redox catalyst in metallaphotoredox catalyzed C–H activation reactions. The features of TiO_2 complements suitably with the necessities of an ideal photocatalyst. It is a low-cost material with high chemical stability and reusable. Although photoreduction efficiency of TiO_2 is maximum in the UV-region due to its large band gap (~3.2 eV), surface-modification with organic or inorganic dyes can shift the light absorption from UV to visible region. Recently, this manoeuvre has been perceived as a strong impetus to execute organic reactions under visible-light, as heterogeneous photocatalysis embodies a sustainable means for organic synthesis.[9] Nevertheless, to the best of our knowledge, dye-sensitized TiO_2 has been rarely explored for redox manipulation of the active transition-metal catalyst in C–H activation reactions.



Scheme 1. Ru(II)/photo-redox catalyzed C–H bond activation.

With our continuous interest in carboxylate-assisted Ru(II)-catalysis,[10] we herein envisaged to demonstrate dye-sensitized TiO_2 as a state-of-the-art photocatalytic oxidant for transition-metal catalyzed C–H bond activation reactions and considered the cross-dehydrogenative olefination of arene carboxylic acids as a model reaction, where dye-sensitized TiO_2 can be utilized as a terminal oxidant. Recently, Rueping et al. reported Weinreb amide directed Rh(III)-catalyzed olefination of arenes[6a] using $Ru(bpy)_3(PF_6)_2$ and pyridine directed Ru(II)-catalyzed olefination of phenols[6b] using $Ir(ppy)_2(bpy)PF_6$ (Scheme 1). During our investigation, the same group has also disclosed that these reactions can also be achieved

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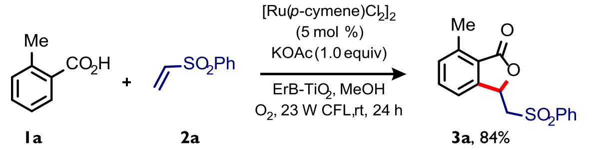
Supporting information for this article is given via a link at the end of the document.((Please delete this text if not appropriate)) using metal-oxide semiconductor materials as photocatalytic oxidants.[6c] However, weakly coordinating carboxylic acids have never been examined in this scenario. We hypothesized that the dye adsorbed on the surface of the TiO_2 can absorb visible-light and goes to its excited electronic state. The excited dye molecule can donate one electron to the conduction band of TiO_2, forming a radical cation of the dye. Then the electron in the conduction band can be donated to oxygen molecule forming superoxide anion radical (Scheme 1). Simultaneously, arene carboxylic acid can undergo Ru(II)-catalyzed C–H bond activation followed by migratory insertion to generate intermediate **B**. After β-hydride elimination, the intermediate **B** delivers the vinylated product **C** and Ru(0) species. Finally, Ru(II)-catalyst can be regenerated from Ru(0) species through electron transfer with the superoxide anion radical and cationic dye radical to continue the catalytic cycle.

To verify our hypothesis, we performed the bench-mark reaction between commercially available 2-toluic acid (**1a**) and phenyl vinyl sulfone (**2a**). Delightfully, when the mixture of **1a** and **2a** in methanol was irradiated under 23 W CFL at room temperature in presence of $[Ru(p\text{-cymene})Cl_2]_2$ (5 mol %), KOAc (1.0 equiv), and erythrosine B (ErB) modified TiO_2 for 24 h, the oxidative *Heck*-coupling followed by *oxa*-Michael addition proceeded smoothly and the desired phthalide[11] product **3a** was obtained in 84% isolated yield (Table 1, entry 1). Control experiments clearly indicated that all the components, Ru(II)-catalyst, KOAc base, visible-light, and erythrosine B-modified TiO_2 photocatalyst, are crucial to achieve high yield (entries 2–5). In the absence of photocatalyst, **3a** was isolated only in 44% yield (entry4). Similar diminished yield of **3a** was obtained in the absence of light source even under reflux conditions (entry 5). These experiments clearly demonstrate that ErB-TiO_2 is the active photocatalyst (not ruthenacycle intermediates) responsible for the regeneration of the Ru(II)-active catalyst. When Eosin Y-sensitized TiO_2 was used, **3a** was isolated in 65% yield (entry 6). Change of reaction solvent from MeOH to DMF or MeCN

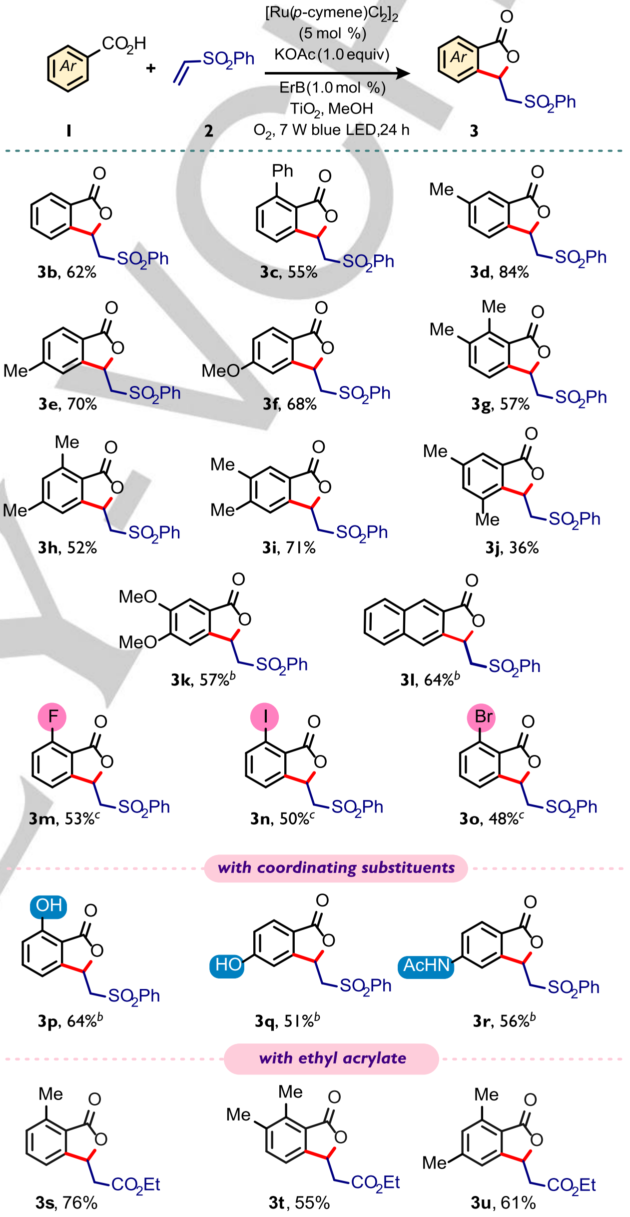
Table 1. Optimization of reaction conditions[a]



entry	deviation from final conditions	**3a** (%)
1	none	84
2	without $[Ru(p\text{-cymene})Cl_2]_2$	–
3	without KOAc	trace
4	without ErB-TiO_2	44
5	without light (without PC)	47(58)[b]
6	with Eosin Y-TiO_2 instead of ErB-TiO_2	65
7	DMF instead of MeOH	trace
8	MeCN instead of MeOH	21
9	$Cu(OAc)_2.H_2O$ instead of KOAc	19[b]
10	7 W White LED instead of 23 W CFL	58
11	7 W Blue LED instead of 23 W CFL	91
12	TiO_2 (6 mg) and ErB (1 mol %)	90
13	only ErB (2.5 mol %)(without TiO_2)	45
14	ZnO instead of TiO_2	38
15	$BiVO_4$ instead of TiO_2	29
16	air instead of O_2 balloon	36

[a]Reaction conditions: **1a** (0.15 mmol, 1.0 equiv), **2a** (2.0 equiv), $[Ru(p\text{-cymene})Cl_2]_2$ (5 mol %), KOAc (1.0 equiv), ErB-TiO_2 (50 mol %, 6 mg), MeOH (0.5 mL), oxygen balloon at room temperature for 24 h. [b]Reaction was perfomed under reflux conditions. Catalytic turn over number (TON) based on entry 11 = 1.8.

Scheme 2. Scope of the oxidative annulation with olefins[a]

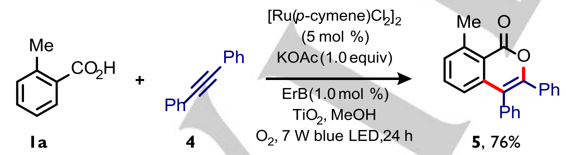


[a]Reaction conditions: **1** (0.15 mmol, 1.0 equiv), **2** (2.0 equiv), $[Ru(p\text{-cymene})Cl_2]_2$ (5 mol %), ErB (1 mol %), TiO_2 (50 mol %, 6 mg), MeOH (0.5 mL), oxygen balloon under 7 W blue LED irradiation at room temperature; [b]Reactions were performed at 50 °C with two 7 W blue LEDs. Unreacted aromatic acids were recovered; [c]Reaction time was 36 h and unreacted aromatic acids were also recovered.

and replacement of KOAc with $Cu(OAc)_2.H_2O$ gave inferior results (entries 7–9). Altering the light source to white LED displayed a deleterious effect, whereas blue LED provided improved yield of 91% (entries 10–11). Interestingly, the use of TiO_2 and ErB instead of the preformed ErB-TiO_2 was equally effective to promote the transformation (entry 12). As expected, ErB alone did not show any impact in the reaction outcome (entry 13) and the product yield was similar to the reactions performed without light/photocatalyst (entries 4–5). Other semiconductor materials such as ZnO and $BiVO_4$ were inefficient to provide increased yields (entries 14–15). The use of ambient air instead of oxygen balloon also gave diminished yield of the desired product (entry 16).

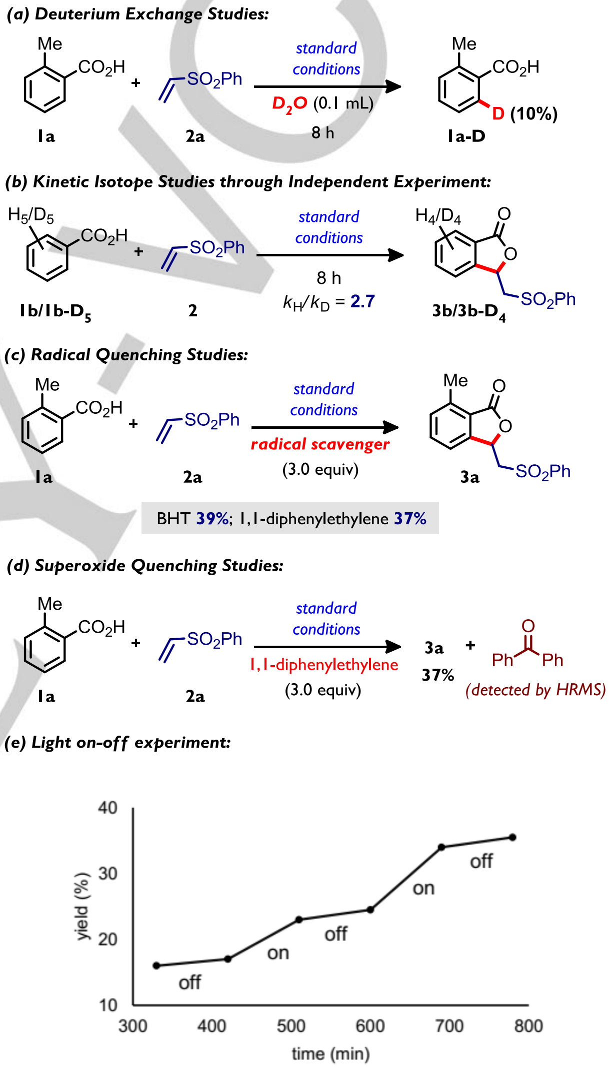
With the optimal conditions in hand, we next intended to explore the breadth of substrate compatibility (Scheme 2). The protocol was found quite general with a series of benzoic acids consisting of electron-donating or -withdrawing substituents. Benzoic acids with aryl and alkyl substitutions underwent smooth transformation, producing **3b–e** in 55–84% yields. Reaction of electron-rich 4-methoxy benzoic acid proceeded efficiently, bestowing annulated product **3f** in 68% yield. The oxidative annulation process was also fruitful with various difunctionalized benzoic acids (**3g**–**k**). However, sterically hindered 3,5-disubstituted benzoic acid delivered the desired product **3j** in 36% yield. We were also able to synthesize the phthalide of 2-naphthoic acid in decent yield (**3l**). Electron-withdrawing halogen containing benzoic acids were viable substrates (**3m**–**o**), where sensitive bromo and iodo functionalities remained untouched under the catalytic conditions. Delightfully, catalytic conditions proved efficient in the presence of coordinating free-hydroxy functionality in *ortho*- as well as *para*-positions and the corresponding phthalides **3p** and **3q** were obtained in good yields, albeit an increase of temperature to 50 °C was necessary. Acetamido functionality, a well-known directing group in C–H bond activation reactions, was also compatible to dispense 56% yield of **3r**.

To this end, we attempted to delve into the consonance of other coupling partners under the current conditions. Delightfully, ethyl acrylate was also well-suited under the catalytic conditions, furnishing **3s**–**u** in good yields (Scheme 2).[12a] The protocol was also competent to perform an oxidative annulation between benzoic acid and alkyne at room temperature to produce isocoumarin **5** in 76% yield (Scheme 3).[12b]



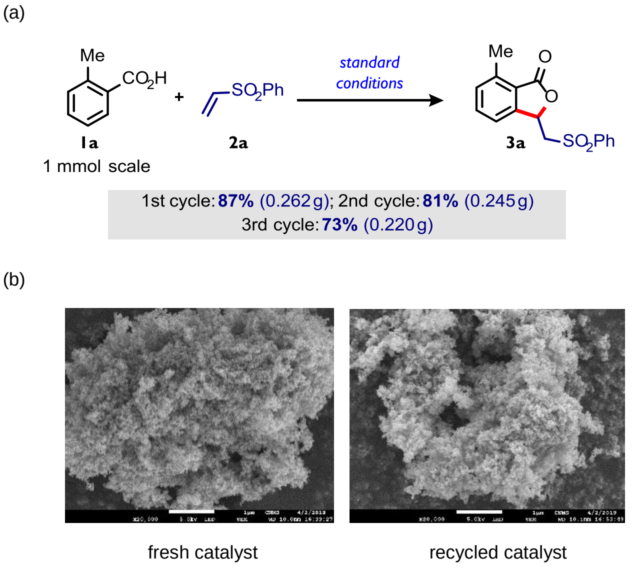
Scheme 3. Ruthenium/photo-redox catalyzed oxidative annulation of 2-toluic acid and alkyne.

To understand the mode of action of the catalytic system, we next performed a set of control experiments. Deuterium exchange experiment disclosed that a reversible metalation process is involved in this case (Scheme 4a). Kinetic isotope effect (KIE) studies indicated that the metalation step is kinetically relevant with k_H/k_D = 2.7 (Scheme 4b). Addition of superstoichiometric amounts of radical scavengers such as BHT and 1,1-diphenylethylene significantly inhibited the reactivity, suggesting the involvement of a single electron transfer process (Scheme 4c). Intriguingly, in the case of 1,1-diphenylethylene, we also observed the formation of benzophenone, which clearly signified the superoxide radical formation during the process (Scheme 4d). Further, light on-off experiment showed that the product formation enhances significantly in the presence of light, while small changes in reaction yields in the absence of light account for the slow background reaction (Scheme 4e).



Scheme 4. Mechanistic studies.

One prime advantage of heterogeneous photocatalyst over homogeneous photocatalyst is its reusability. To establish the reusable nature of the current photocatalyst, we first recovered the TiO_2 nanoparticles after the reaction and then employed for successive annulation reactions under standard conditions. Gratifyingly, we observed almost similar outcome with the recycled catalyst (Figure 1a, see SI for details). We have also compared the morphology of the fresh catalyst with the recycled catalyst. Analysis of FESEM pattern of both the catalysts implied that the morphology of the catalyst was intact after the reaction (Figure 1b, see SI for details).[13]



fresh catalyst recycled catalyst

Figure 1. Reusability of the photocatalyst: (a) reaction with recovered catalyst; (b) FESEM image of the catalyst before and after reaction.

In conclusion, we have demonstrated ErB modified-TiO$_2$ nanoparticles as a potent photocatalyst for Ru(II)-catalyzed C–H bond activation reactions through a model oxidative olefination/annulation strategy between arene carboxylic acid and olefins. The reaction is operationally simple and delivers diverse sulfonated phthalides in good yields. The photocatalyst is recoverable and reusable. Study of the recovered photocatalyst indicated an identical morphology as with the initial catalyst. Further use of such heterogenous photocatalysts for visible-light mediated organic transformations are ongoing in our laboratory.

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Keywords: Heterogeneous Photocatalysis • Ru(II)-Catalysis • Cooperative Catalysis • C-H Activation • Weak Coordination

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[13] Details of FESEM studies have been provided in Supporting Information (pages S8-10).

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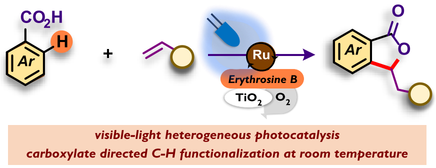
Entry for the Table of Contents



A merger of visible-light heterogeneous photocatalysis with ruthenium catalysis is reported for C–H olefination/annulation of benzoic acids and activated olefins at room temperature to forge functionalized phthalides.

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