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Iodine/Visible Light Photocatalysis for Activation of Alkynes for Electrophilic Cyclization Reactions

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Abstract: Photocatalytic organic synthesis needs photocatalysts to initiate the reactions and to control the reaction paths. Available photocatalytic systems rely on electron transfer or energy transfer between the photo-excited catalysts and the substrates. We explore a concept based on the photo-promoted catalyst coupling to the substrate and the photo-triggered catalyst regeneration by elimination from the catalytic cycle. A catalytic amount of elementary I_2 is applied as both a visible light photocatalyst and a π-Lewis acid, enabling the direct activation of alkyne C≡C bonds for electrophilic cyclization reactions, one of the most important reactions of alkyne. Visible light is crucial for both the iodocyclization of the propargyl amide and the deiodination of the intermediate. Singlet oxygen is found to play a key role in the regeneration of I_2. This system shows good functional group compatibility for the generation of substituted oxazole aldehydes and indole aldehydes. Hence this study provides a readily accessible alternative catalytic system for the construction of heterocycle aldehyde derivatives by sunlight photocatalysis.

Keywords: visible light; photoredox; photocatalysis; alkyne; iodine

1. INTRODUCTION

Recently, visible light photocatalysis has been vastly explored as a conceptually related valuable method for organic synthesis.[1] This mild, efficient, economic and environmentally-friendly method has the potential to succeed in numerous organic transformations that need very complex procedures or very harsh conditions (e.g., high temperature, noble metal complexes, strong acids or bases, multistep, etc), or even were inaccessible, by the traditional synthetic protocols.[1a, b, 2] The key of these photocatalysis is a redox-active compound as the photocatalyst, such as coordination complexes like $Ru(bpy)_3^{2+}$, conjugated organics[3] like acridines,[4] PDI[5] and eosin Y,[6] and inorganic semiconductors[7] like CdS and TiO_2. The photocatalyst is excited by incident photons to generate a charge-separation state, and the subsequent single electron transfer (SET) makes the substrate 1e-oxidized or 1e-reduced which undergoes reaction cascades to give the desired product (Figure 1A, paths I and II), while the photocatalyst is regenerated by another SET with the intermediates or the co-catalyst.[1a, b, 2] Besides, energy transfer from the photo-excited catalyst to the substrate has also been applied in photosynthesis (path III).[8]

Comparing with photocatalysis, the transition-metal catalysis has long been applied in laboratory and in industrial applications for organic synthesis.[9] Due to the ability of the transition metal complexes of complexing with the substrates through oxidative addition, the reaction pathways can be readily fine-tuned.

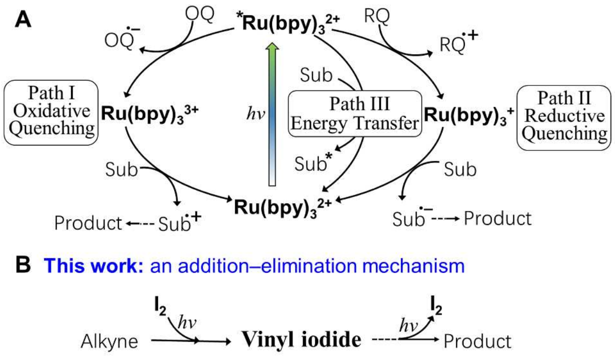


Figure 1. The three typical paths of $Ru(bpy)_3^{2+}$ photocatalysis and the new photocatalytic model of this work. In the new addition–elimination model, the photocatalyst (i.e., I_2) at its excited state and the substrate react to form an intermediate (iodination), and at the final stage of the cascade reactions the photo-deiodination reaction gives the desired product and the regenerated photocatalyst. The abbreviations are: Sub = substrate, RQ = reductive quencher, OQ = oxidative quencher.

We anticipate if a photocatalyst possesses a second function of complexing with the substrate to control the reaction pathways – a combination of the advantages of both photocatalysis and transition metal catalysis (Figure 1B), the scope of photocatalysis will be greatly expanded. Herein, we report elementary iodine is such a dual-functional, efficient visible-light photocatalyst. Excited by visible light of the solar spectrum, iodine can directly couple with the C≡C triple bond, and at the final step of the reaction cascade, the photo-deiodination gives the desired product and regenerates I_2. The syntheses of oxazole aldehydes and indole aldehydes from propargyl amides are chosen as the model reaction.

Since alkynes are a class of fundamental chemicals in synthesis, the direct activation of C≡C for addition reactions is very important and is one of the most important applications of C≡C moieties. For this, the π-Lewis acidic transition-metal complexes such as Au-, Pd- and Cu-complexes, are widely employed in activation of alkynes by forming π-complexes intermediates.[9b, 10] Considering activation of C≡C bonds by photocatalysis, it might be challenging to adopt the SET paths (Figure 1A) to directly activate C≡C bonds for synthetic purposes, presumably due to their relatively high redox potentials which can lead to highly unstable intermediates by SET. For example, in a recent study, degradation of the C≡C moiety rather than useful synthesis occurred in the $Ru(bpy)_3^{2+}$ photocatalysis.[11] While rare examples proposed 1e-reduction activation of the C≡C bonds (the radical anion pathways;[1b] Figure 1A, path II) for coupling reactions,[6] in most studies only the counterparts of the alkynes were activated.[2] For successful application of sunlight in activation of alkynes, transition-metal catalysis has been coupled with photocatalysis, such as dual Au/photoredox [12], dual Cu/photoredox[13], in order to take the advantage of the π-Lewis acidity of the transition metals.

Due to the π-Lewis acidity, I_2 has been widely explored in catalysis especially in the iodocyclization of alkynes via a I^+ mechanism for the synthesis of heterocyclic compounds.[14] The photophysical and photochemical processes of I_2 have also long been studied. As early as in 1972, Olmsted III and Karal[15] reported that photoexcited I_2 could sensitize the formation of singlet oxygen under visible light irradiation. However, while there have been few reports on using I_2 in photocatalytic reactions, they were limited to UV-photocatalysis for selective formation of aldehydes by oxidation of styrenes,[16] benzyl alcohols[17] and amines,[18] as well as for the degradation of organic pollutants,[19] and therein the photo-generated I· radicals were proposed to be the active species and I_2 was regenerated by the oxidation of I^- or I_3^- by ground state O_2.

In this work, we demonstrate that under visible light or sunlight irradiation, a catalytic amount of I_2 can realize the highly efficient activation of alkyne amides for electrophilic cyclization reactions. The mechanism involves a light-promoted iodocyclization reaction of the propargyl amide and a light-triggered deiodination of the iodide intermediate, by which I_2 is incorporated in the catalytic cycling. Singlet oxygen is found to play a key role in the regeneration of iodine. Hence this study not only provides a low-cost, highly efficient, mild, eco-friendly and additive-free catalytic system for construction of oxazole aldehyde derivatives and indole aldehyde derivatives, but also provides a dual-functional visible light photocatalytic system in which I_2 can serve as both a sensitizer/catalyst and a π-Lewis acid.

2. RESULTS AND DISCUSSION

2.1 Outcome of the I_2/visible light photocatalysis in propargyl amide cyclization. Inspired by the general interests of oxazoles in synthetic chemistry and the propargylic amides [9a, 11, 14, 20] being versatile building precursors to prepare them via an electrophilic 5-*exo-dig* cyclization approach,[9b, 11, 14, 21] we began our research by choosing N-(prop-2-yn-1-yl)benzamide (**1**; Figure 2) as the model compound, to examine the outcome of yielding 2-(2-phenyloxazol-5-yl)acetaldehyde (**1b**) using the I_2/visible light catalytic system.

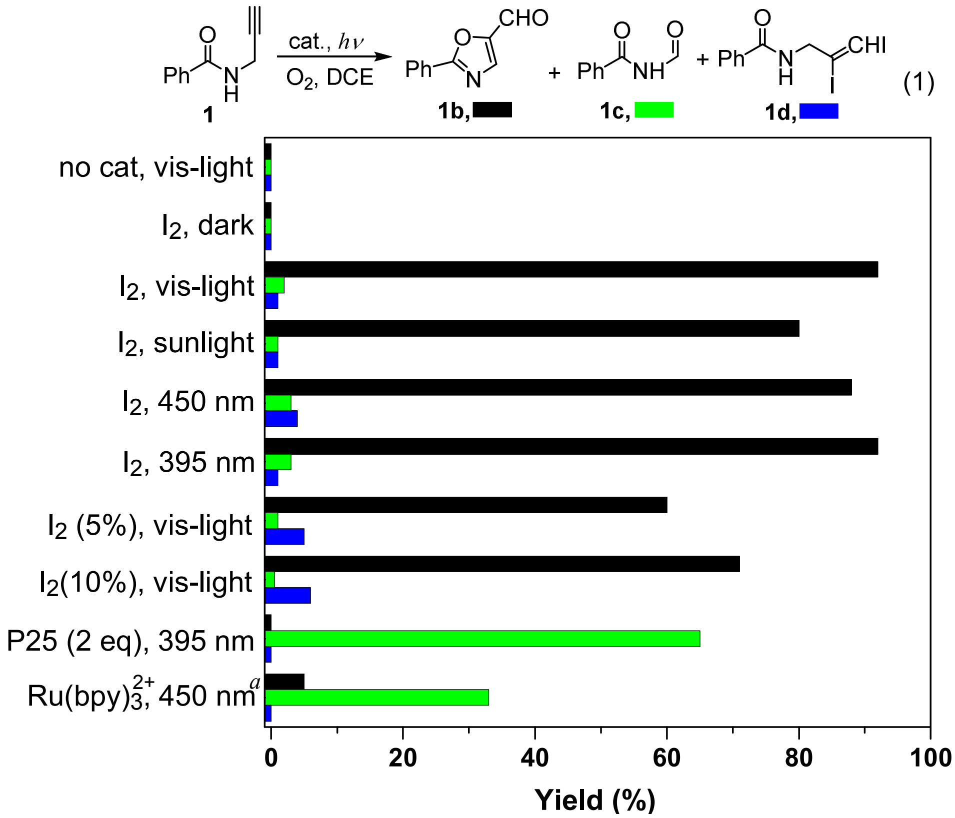


Figure 2. The products of **1** under various conditions. The other unspecified conditions: 20 mol% catalyst, 0.15 mmol **1**, 2.0 mL of DCE, 1 atm O_2, ambient temperature (16 °C), 3-8 h. The yields were obtained by high-performance liquid chromatography (HPLC). [a] Data adapted from ref. 11.

The reaction was carried out simply by combining the substrate (0.15 mmol of **1**) and a catalytic amount of iodine (e.g., 20 mol%) in a solvent (e.g., 1,2-dichloroethane, DCE) under 1 atm O_2 at ambient temperature (ca. 16 °C), and visible light drives the reaction in a high efficiency, e.g., yield of **1b** > 90% after 2-hour irradiation (Figure 2). The light source is a 300 W Xenon lamp equipped with a 400-nm longpass filter (light intensity = 174 mW cm^{-2}) to simulate the visible region of the solar irradiation. Defining the quantum efficiency as reacted **1** divided by amount of photons reaching the reaction cross section, herein the quantum efficiency of visible light reaches 0.55%. Motivated by the advantages of solar photocatalysis,[1a] we also checked the outcome of reaction 1 irradiated by outdoor sunlight and, to our delight the solar synthesis was of high efficiency. The yield of **1b** reached 80% after the 8-hour reaction and the quantum efficiency of sunlight is as high as 2.4%. If the same reaction was carried out using a 450 ± 10 nm blue LED, the yield of **1b** was also as high as 88% with a quantum efficiency of 0.5%. This outcome approaches that using 395 ± 10 nm LED. However, without light irradiation, for the same reaction (with 20 mol% I_2) the conversion of **1** was as low as 10%, while no **1b** was yielded; instead, ca. 10% of 5-(iodomethylene)-2-phenyl-4,5-dihydrooxazole (**1a**) was formed. Control experiments also showed that, without I_2, **1** remained intact upon light irradiation. This is consistent with the electronic absorption spectra (Figure 3) which show both **1** and **1a** have negligible absorbance at $\lambda > 350$ nm, and I_2 is the only visible-light absorber in this catalytic system. Also, because O_2 is the only source of carbonyl-O of **1b**, activation of O_2 must be involved in the photocatalytic reaction. Therefore, I_2 is an efficient visible-light photocatalyst and it effectively activates O_2 for oxygenation reactions; a highly efficient solar photocatalytic system has been established for activation of the alkyne for electrophilic additions.

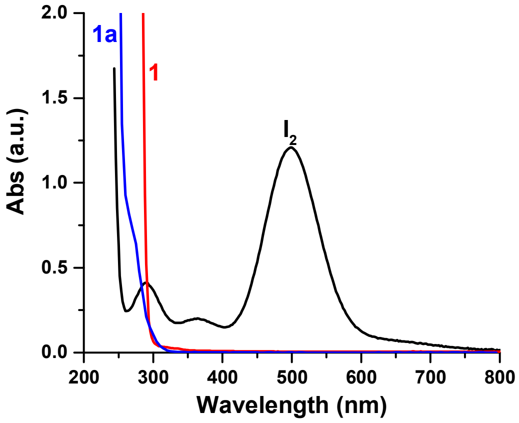


Figure 3. The UV-vis spectra of the DCE solutions of I_2 (7.6 mM), **1** (0.28 M) and **1a** (1.16 M).

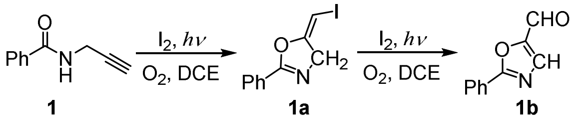
Products of **1** by photocatalysis using TiO_2/UV and $Ru(bpy)_3^{2+}$/visible light, the most popular heterogeneous and homogeneous photocatalytic systems, respectively, are compared with the current I_2/visible light system.

TiO_2 and $Ru(bpy)_3^{2+}$ are known to activate the substrates by electron transfer processes (Figure 1). However, under 395 nm LED irradiation for TiO_2, or under 450 nm irradiation for $Ru(bpy)_3Cl_2$, **1** was mainly degraded to an aldehyde (**1c**), instead of yielding any cyclization product (Figure 2). This might suggest that ET processes be relatively challenging for activation of C≡C bonds for synthetic purposes. Wang et al. recently used eosin Y/visible light for activation of alkynes for S-nucleophiles addition for the synthesis of α-vinyl sulfones.[6] The authors proposed that the reaction was initiated by 1e-reduction of the C≡C bond by the photo-excited dye.[6] To our knowledge, despite the great dependency on the additives in such catalysis, this is one of the very rare examples of using the ET mechanism to activate the C≡C bonds in solar synthesis.

Due to its importance, reaction 1 has been studied time and again using Au(I) catalysis,[22] the $PPh_3AuNTf_2/Fe(acac)_2$/peroxide system,[11] the $Pd(II)/Cu(II)/O_2$ system,[23] the Hg(II) system,[24] the $Hg(II)/Ce^{4+}$ system,[24] and the hypervalent iodine (NIS)/O_2 system,[25] respectively, under relative harsh conditions. Comparing to these catalytic systems, while the current yield is comparable or even better, the advantage of the I_2/visible light photocatalysis is obvious, for example, it adopts a cheap, readily available and eco-friendly photocatalyst, it works under very mild reaction conditions, it uses costless sunlight and dioxygen as the reagents, and moreover any additive is not necessary.

2.2 The photocatalytic tandem reaction. We noticed that when the amount of I_2 was less than 20 mol%, the yield of **1b** increased with the catalyst loading (Figure 2), and meanwhile the purple color of the I_2/DCE solution diminished quickly in the beginning of the photocatalytic reaction. With more than 20 mol% I_2, the solution color changed from purple to red but recovered at the reaction late stage. The UV-vis spectrum of the discoloring solution (i.e., early stages of the reaction) indicates I_3^- was formed (see Figure S2).

Using HPLC, we found the photocatalytic reaction 1 involves only one intermediate, i.e., an iodide complex **1a**. No other stable intermediate was identified by GC-MS analyses, either. When **1a** was subjected to the same reaction conditions, it resulted solely in **1b** in over 95% yield. UV-vis spectroscopic study ruled out formation of I_3^- in this step (Figure S3). Hence, reaction 1 involves the tandem iodocyclization of **1** followed by the deiodination of **1a** (eq 2).



(2)

Detailed kinetic profile of the tandem reaction (eq 2) was then obtained (Figure 4A). It was found out that as the photocatalytic reaction proceeded, the key intermediate **1a** was accumulated within the first 25 min and during this period **1b** was hardly formed. The highest yield of **1a** reached nearly 30%, which is 1.5 times of the amount of initially added I_2. Afterwards, **1a** was gradually consumed with the production of **1b**. For comparison, the kinetics of the dark reaction was also studied (Figure 4B). The color of the mixture reduced greatly after 20 min, indicating the consumption of I_2 and formation of I_3^- which was confirmed by UV-vis spectra. The dark reaction gave **1a** as the major product rather than any amount of the oxazole aldehyde **1b**. The yield of **1a** reached a plateau of ca. 17%, which is ca. half of the catalyst loading (note that 30 mol% of I_2 was used in this case).

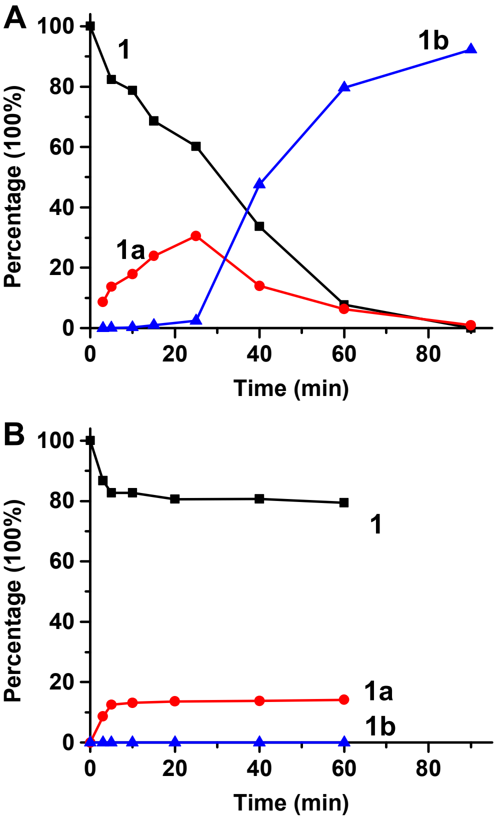
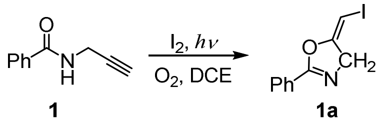


Figure 4. Reaction kinetic profiles of (**A**) the photocatalytic and (**B**) the dark reactions. Conditions: 20 mol% I_2 for **A** and 30 mol% I_2 for **B**, O_2, DCE, 395 nm LED, 16 °C.

2.3 The photo-promoted iodocyclization reaction of the propargyl amide. As mentioned above, in the early stage of the photocatalytic reaction (e.g., within the first 6 min), accumulation of the intermediate **1a** dominated the reaction (eq 3), no **1b** was formed, and meanwhile I_2 was converted to **1a** and I_3^-. This is also true for the same reaction carried out in the dark (Figure 4). Hence, the absorbance change of I_2 can be used as a quick solution to track the reaction, and thereby the effect of visible light in the 5-*exo*-dig iodocyclization of **1a** (eq 3) can be quantitatively evaluated. For this, a DCE solution containing the substrate was carefully agitated by O_2 bubbles (to ensure mixing and to maintain 1 atm O_2), and to this solution was quickly added the 20 mol% of I_2 (in DCE) to initiate the photocatalytic reaction or the dark reaction. The kinetics was then monitored by UV-vis spectroscopy at 500 nm at which I_2 is the only light absorber of the reaction mixture. As shown in Figure 5, I_2 was quickly converted during both the photocatalytic reaction and the dark reaction. However, the data shows that the photocatalytic reaction is faster than the dark reaction, indicating that visible light promotes the iodocyclization reaction of **1**. In addition, if the photocatalytic reaction was carried out under Ar atmosphere, then the conversion of I_2 is faster than that under O_2. This phenomenon is consistent with the role of O_2 in regeneration of I_2 and will be discussed later.



(3)

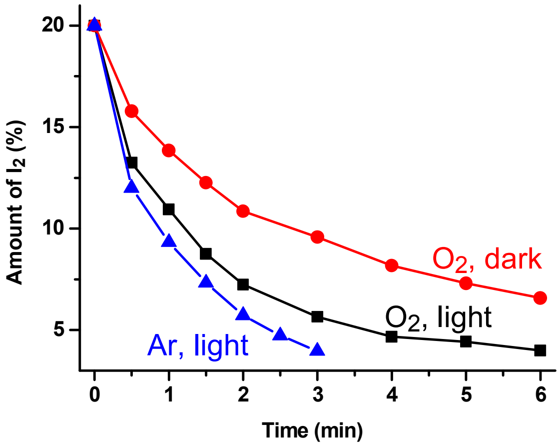
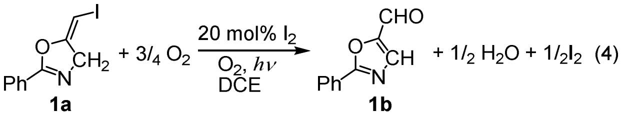


Figure 5. Conversion of I_2 under O_2 (■) or under Ar (▲) atmosphere during irradiation, or under O_2 atmosphere in the dark (●). Conditions: 20 mol% I_2, DCE, 395 nm LED, 16 °C.

2.4 The photocatalytic deiodination of the vinyl iodide. We now show the oxidative deiodination of the vinyl iodide is a photocatalytic reaction with I_2 as the photocatalyst (eq 4).



First, to verify the function of I_2, we quantified the reaction kinetics under light irradiation with or without added 20 mol% I_2. Release of I_2 from **1a** was eyed as the solution turned purple. The UV-vis absorbance change of the solution at 500 nm (Figure 6) shows that with or without added I_2, **1a** could be nearly quantitatively converted to **1b** and 0.5 eq of I_2. However, without added I_2, an obvious induction period existed, during which the reaction solution gradually turned purple (accumulation of I_2), showing this is an autocatalytic reaction. With added 20 mol% I_2, the induction period disappeared, and hence the photoexcited I_2 must serve as the catalyst in this reaction (eq 4).

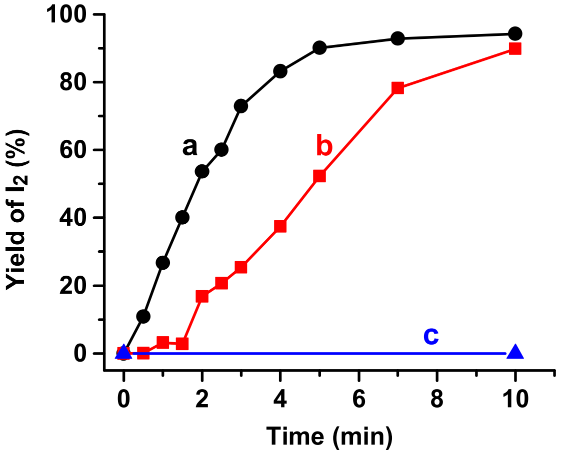


Figure 6. Formation of I_2 during the reaction of **1a**: (**a**) 20 mol% I_2, light; (**b**) no I_2, light; (c) no I_2, dark. Other conditions: O_2, DCE, 395 nm LED, 16 °C.

Besides, to verify the role of light as a reagent in the reaction, the **1a**/DCE solution was settled under 1 atm O_2 at ambient or elevated (80 °C) temperatures, and by ambient light irradiation or kept in the dark. It was found out that conversion of **1a** was nearly 0 in the dark reaction at ambient temperature. Hu et al.[25] recently reported that the oxidative deiodination of **1a** to give **1b** can be achieved at 80 °C. Flynn et al.[21c, d] also reported that the deiodination of an analogous vinyl iodide can be accomplished at elevated temperature. Consistent with their reports, at 80 °C under ambient light irradiation, **1a** was nearly quantitatively converted to **1b** (95% HPLC yield) after 24 h reaction. However, when the same reaction was performed in the dark, the conversion was low and less than 15% **1b** was yielded. We further examined the dark reaction of eq 1 in which a stoichiometric amount of I_2 was present. For this, **1** and 110 mol% I_2 was reacted at ambient temperature for 1 h, and then the mixture was maintained 80 °C for 10 h. The substrate conversion reached completion, however, this dark, thermal reaction yielded mainly the aldehyde **1c** (55% yield; the degradation product) and a little amount of the desired cyclization product **1b** (6% yield). In all, the above control experiments clearly indicate the essential role of light in the formation of **1b**.

For the photocatalytic reaction with 20 mol% added I_2, the absorbance of I_2 is thousands of times larger than the concomitant species, i.e., **1a** and **1b**. Hence the autocatalytic reaction of **1a** should be minor when I_2 is present. Therefore, in both the tandem reaction (eq 1) and the deiodination reaction (eq 4) with added I_2, I_2 is the actual light absorber and the photocatalyst.

2.5 The engagement of singlet oxygen in the iodocyclization and the deiodination reactions. It has been established that visible light (390 – 700 nm) is sufficient to excite an I_2 molecule to its excited triplet state ($^3I_2^*$; eq 5),[26] which can sensitize the ground-state dioxygen to produce singlet oxygen (eq 6),[15, 26] and can also split into 2 equivalents of I· radicals (eq 7).[26]

$$^1I_2 + h\nu \rightarrow {}^3I_2^* \qquad (5)$$

$$^3I_2^* + {}^3O_2 \rightarrow {}^1I_2 + {}^1O_2 \quad (6)$$

$$^3I_2^* \rightarrow I\cdot + I\cdot \quad (7)$$

Formation of singlet oxygen in the I_2/visible light photocatalytic synthesis of **1b** was investigated by the peroxidation of α-terpinene.[27] For this, reaction 1 and reaction 4 were independently carried out with added α-terpinene (1 equiv). The expected peroxidation product of α-terpinene by $^1O_2$, namely, ascaridole, was indeed identified using GC-MS (Figure S4).[27a]

To determine whether singlet oxygen plays a key role in the photocatalytic reaction outcome and in the regeneration of I_2, a set of control experiments were carried out (Table 1). Under the standard conditions, with only 20 mol% I_2, both the conversion of **1** and the yield of **1b** are near to 100%, while the highest accumulated yield of **1a** could reach 1.5 times of the amount of the initially added I_2. However, without O_2, the light-driven reaction was greatly suppressed and became a stoichiometric reaction (entries 2–3); therein light perhaps can only affect the reaction rate, instead of contributing to the reaction outcome. In both cases, I_3^- was detected. Hence, to enable iodine as a catalyst in the light-driven reaction, oxygen is essential in the regeneration of I_2.

Table 1. Modification of experimental parameters [abcd]

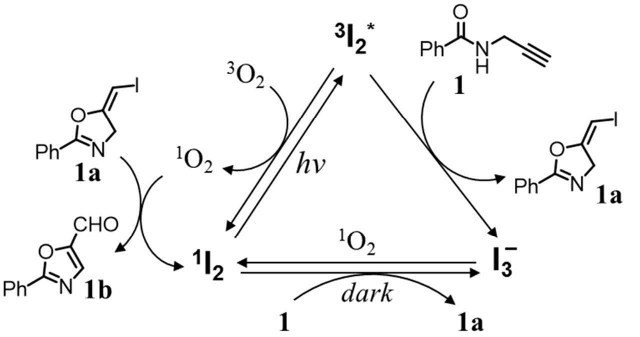
entry	change of conditions	$1 \rightarrow 1a + 1b$, 2h	$1a \rightarrow 1b$, 0.5 h
		conv / **1a** /**1b**, %	conv / **1b**, %
1	no change	100 / 0 / 92	100 / 95
2	dark	15 / 8 / 0	*n.r.*
3	Ar	10 / 9 / 0	*n.r.*
4	carotene, light	13 / 8 / 0	*n.r.*
5	carotene, dark	8 / 7 / 0	*n.r.*
6	TEMPO, light	30 / 11 / 0	*n.r.*
7	TEMPO, dark	25 /10 / 0	*n.r.*
8	TMP, light	15 / 8 / 0	*n.r.*
9	TMP, dark	17 / 6 / 0	*n.r.*
10	SOD, light	100 / 0 / 87	100 / 90

[a] Other unspecified conditions: 0.15 mmol substrate, 20 mol% I_2, 2 mL DCE, 1 atm O_2, 16 °C, 395 nm LED. [b] Two equivalents of the scavengers were added. [c] HPLC yields. [d] *n.r.* is short for "no reaction".

The effects of various scavengers were then investigated, including three $^1O_2$ scavengers like carotene, 2,2,6,6-tetramethyl-1-piperidinooxy (TEMPO), 2,2,6,6-tetramethyl-4-piperidone (TMP) and an $O_2^{\bullet-}$ quencher, superoxide dismutase (SOD). It was found out that with each of the three $^1O_2$ scavengers added (entries 4-9), conversion of **1** to **1a** under light irradiation was greatly suppressed, and meanwhile the deiodination of **1a** was completely quenched. Hence, contribution of photocatalysis was indeed quenched. Therefore, singlet oxygen must be an important active oxygen species in the photocatalytic reaction. Further, it serves to oxidize I_3^- to regenerate I_2 in the iodocyclization reaction (eq 3) and to initiate the deiodination of **1a** (eq 4). Consistent with this, when SOD was adopted to selectively quench $O_2^{\bullet-}$, the photocatalytic reactions were hardly affected (entry 10), and hence the involvement of $O_2^{\bullet-}$ can be ruled out.

We consider that $^3O_2$ is not directly responsible for the oxidative regeneration of I_2 from I_3^-. Otherwise, in the dark reaction of Figure 4B, more iodide complex **1a** should have been produced; however, therein the low atomic efficiency of I_2 actually indicates the inability of the dark reaction in regeneration of I_2 from I_3^-, due to the lack of an oxidizing reagent like $^1O_2$. Further, the $^1O_2$ scavengers (entries 4-9) should not be able to quench $^3O_2$-involved reactions. Importantly, comparing the redox potentials, because $E°(I_2/I^-) = +0.536$ V is more positive than that of the $^3O_2/^3O_2^-$ pair (-0.16 V), direct oxidation of I^- to I_2 by ground state $^3O_2$ is thermodynamically unfavorable by an abiotic, thermal, one-electron transfer process.[28] By contrast, the $^1O_2/^1O_2^-$ pair has a positive enough potential of +0.83 V for the oxidative regeneration of I_2.

2.6 Mechanism for the photocatalytic reaction. With the above evidences and discussions, a mechanism for the I_2/visible light photocatalysis is proposed (Scheme 1). In this mechanism, I_2 serves as the photo-absorber, the singlet oxygen sensitizer and one of the reactants of the iodocyclization reaction. The π-Lewis acidity of the photo-excited iodine makes it readily activate the C≡C bonds of **1** for the nucleophilic addition by the amide moiety. Singlet oxygen plays the key role in the regeneration of I_2 by the oxidation of I_3^- and by the oxidative deiodination of **1a**.



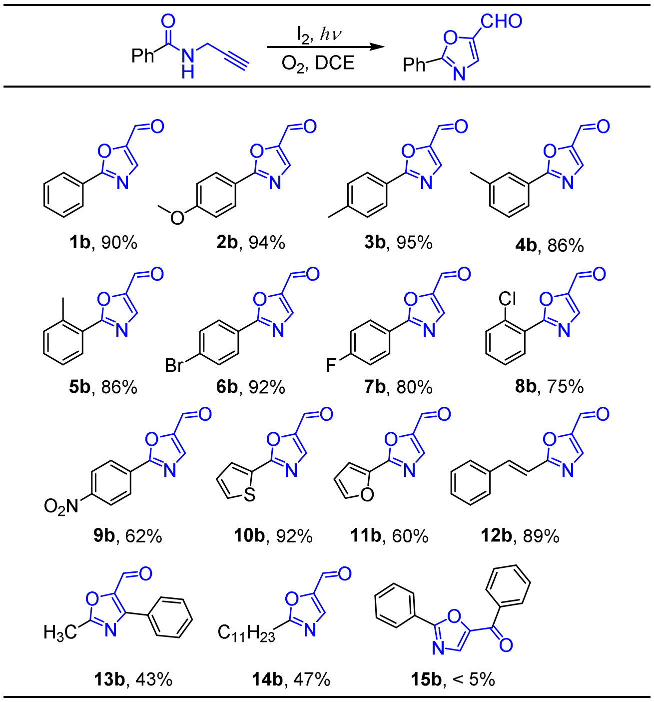
Scheme 1. The proposed mechanism

The above mechanism explains why the highest accumulated yield of **1a** in the photocatalyzed reaction (of Figure 4A) exceeds the amount of initially added I_2. This is due to the oxidation of I_3^- by singlet oxygen, which enhances the atomic-efficiency of I_2 in the iodocyclization reaction (the first step of the cascade reaction). Contribution of dark reaction (by $^1I_2$) in the formation of **1a** is not excluded, but regeneration of I_2 by oxygen can be triggered only by light irradiation.

2.7 Scope of the I_2/visible light photocatalysis in the electrophilic cyclization of alkyne amides. With the success in highly efficient synthesis of **1b** using the I_2/visible light photocatalysis and the mechanism revealed, a variety of substituted propargyl amides were then investigated in this new photocatalytic system to examine the substrate compatibility (Table 2). The substrates with

EWGs and EDGs at the benzene ring of **1** all furnished the corresponding oxazole aldehydes in good to excellent yields (**1b-9b**). Heteroaromatic substrates (**10b**, **11b**) and vinyl substituted propargyl amides (**12b**) also worked well. The aliphatic substituted propargyl amides gave acceptable yields (**13b**, **14b**). For internal alkynes, the desired product was poor (**15b**), making this simple strategy impractical.

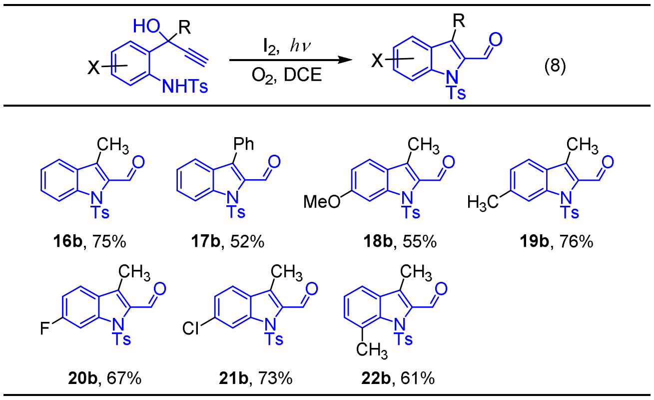
Table 2. Reaction scope for syntheses of oxazole aldehydes [abc]



[a] Conditions: 0.15 mmol substrate, 20 mol% I_2, 2 mL DCE, 1 atm O_2, 16 °C, visible light. [b] Isolated yields. [c] 4 h.

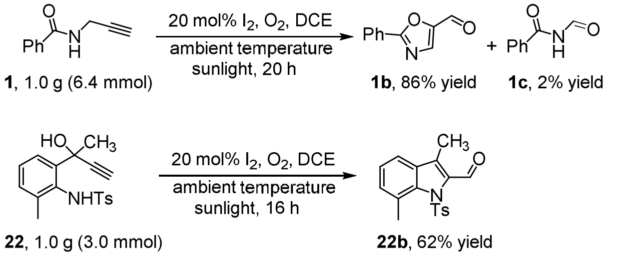
In order to test the potential of the I_2/visible light system in more challenging reactions, the 5-*exo*-dig cyclization of 2-tosylaminophenylprop-1-yn-3-ols for the preparation of substituted indole aldehyde was then investigated (eq 8).[29] Previous reports have demonstrated that such transformation is very challenging for Au catalysis for which transition-metal co-catalysts, Lewis acids, oxidants and elevated temperature are usually essential for the success.[11, 29b] For example, efficient syntheses of substituted indoles catalyzed by AuCl was performed in the presence of AgOTf, hexamethylphosphoramide and $CaSO_4$ under reflux conditions.[29b] Efficient syntheses of substituted indole aldehydes were realized by using the dit-BuXphosAu(CH_3CN)SbF_6/$FeCl_2$ dual catalytic system.[11] However, to our delight, the I_2/visible light photocatalytic system, which is carried out without any additive and under very mild conditions, proves to be a practical protocol for this transformation (Table 3).

Table 3. Syntheses of indole aldehydes [abc]



[a] Conditions: 0.15 mmol substrate, 20 mol% I_2, 2 mL DCE, 1 atm O_2, 16 °C, 395 nm LED. [b] Isolated yields. [c] 4 h.

2.8 Gram scale reaction. To highlight the efficiency of the I_2/visible light system for practical application in the activation of alkynes for the 5-*exo*-dig cyclization reactions, we conducted the cyclization of **1** and **22** on gram scale on a laboratory windowsill using sunlight as the only source of irradiation. Interestingly, the outcome is even better (Scheme 2) than the smaller scale reaction. With 1.0 g (6.4 mmol) of **1** the reaction achieved completion after only ca. 20 h sunlight irradiation, providing an 86% yield of **1b**. The yield of **22b** reached 62%, almost the same as the smaller scale reaction using 395 nm LED irradiation (Table 3).



Scheme 2. Gram-scale synthesis of **1b** and **22b** using I_2/sunlight photocatalysis

3. CONCLUSION

In conclusion, linked by I_2/visible light activation of C≡C triple bond followed by nucleophilic addition by electron-donating amide groups, we have exhibited I_2 is an efficient visible light photocatalyst for synthesis of oxazole aldehyde and indole aldehyde derivatives. Light is crucial for triggering these catalytic transformations under mild conditions, using a catalytic amount of I_2 and without any additives. Elementary I_2 serves as both a visible light photocatalyst and a π-Lewis acid during the photocatalysis. Singlet oxygen plays a pivotal role in I_2 regeneration.

We anticipate that the novel photocatalytic path (Figure 1B) and the dual functions of I_2 in visible light photocatalysis, will enable the simple, economic and eco-friendly approach of a variety of syntheses which are challenging for other catalytic systems, especially those relevant to C≡C activations which are currently being performed mainly with transition metals under relatively harsh conditions.

ASSOCIATED CONTENT

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Notes

The authors declare no competing financial interest.

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/xxxxxxxxxxx.

Detailed experimental procedures, supplementary data, and characterization data of all the compounds (PDF)

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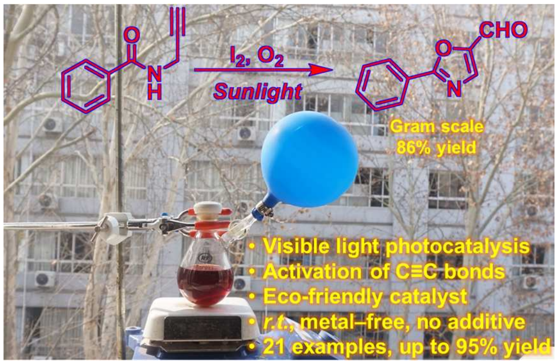
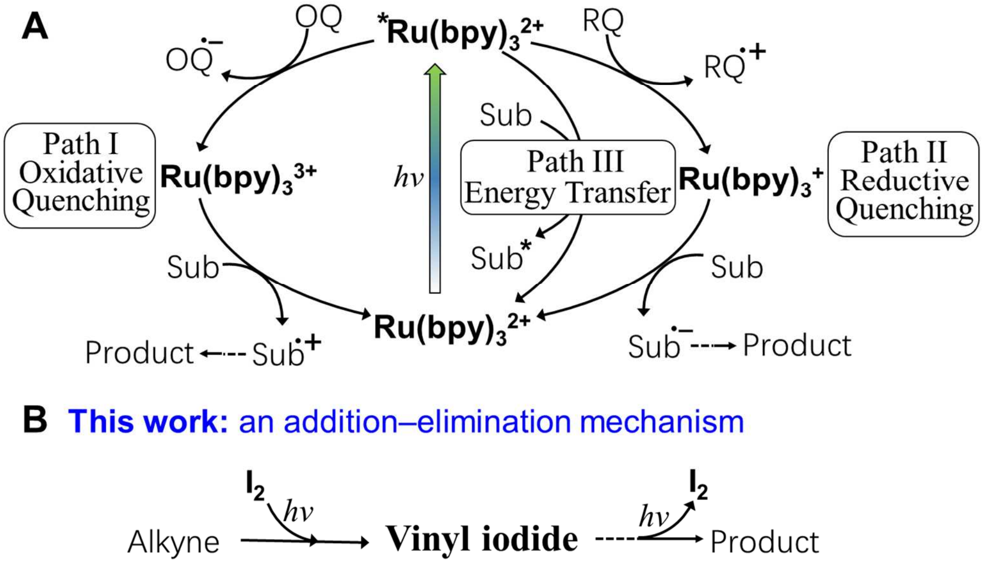
Table of Contents Artwork





the high resolution version of Figure 1

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