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Recyclable Cu/g-C_3N_4 nanometric semiconductor catalyzed *N*-formylation of amines *via* photocatalytic aerobic oxidative C–C bond cleavage of aldehydes under visible-light irradiation

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ABSTRACT

Due to its difficulty and complexity, the cleavage and subsequent functionalization of the C(sp^3)-C(sp^3) single bond has received less attention than the C–C bond formation reactions that have been extensively studied. Herein, by utilizing Cu/g-C_3N_4 nanometric semiconductor as a recyclable photocatalyst, an aerobic oxidative C–C bond cleavage of aldehydes was developed with the promotion of amines under visible light irradiation. Based on the reaction, phenylacetaldehyde was selected as a highly efficient formylation reagent for amines. Under blue light irradiation, good to excellent yields of formamides were achieved for various amines in 1 atm oxygen atmosphere at room temperature. This methodology offers a practical, neutral and gentle alternative to the preparation of formamides.

Utilizing sunlight to drive organic transformations is the most promising choice to meet our needs for green synthesis, in which the reactions promoted by visible light may provide a more efficient and greener method [1–3]. Generally, in most of organic reactions driven by visible light, photocatalysts are indispensable [4,5]. However, most of reported photocatalysts involve transition metal complexes and organic dyes, which usually suffered from high cost, poor stability & recyclability [6–8]. Thus, heterogeneous photocatalysts are becoming more attractive due to their ease of separation, high thermo-chemical stability, and possible application on a large scale [9–11].

C(sp^3)-C(sp^3) single bonds are the fundamental building blocks to make up organic compounds [12]. There is no doubt that the selective cleavage and functionalization of the C–C bond is of great significance in organic synthesis and biomass utilization, and has attracted much attention in recent years [13–17]. Among the various methodologies reported, some great progresses have been achieved recently for the C–C bond cleavage of amines as well as in aldehydes, in which formamide could be generated as the final product. The methodology might provide a convenient alternative for the synthesis of formamides. In 2012, Jiao's groups reported an excellent example of the cleavage of C–C bond in aldehydes in the presence of Mn(III) catalyst with the promotion of amines, and the reaction provided an efficient approach for *N*-formylation of amines by using hexanal as formylation reagent (Scheme 1a) [18]. Similarly, soon after, Xia's group and Wang's group described a photocatalytic C–C bond cleavage of aldehydes *via* the enamines intermediate by $Ru(bpy)_3Cl_2{\cdot}6H_2O$, respectively (Scheme 1b) [19–21]. Subsequently, Wang *et al.* also developed the cleavage of C–C bond of tributylamine at interfacial CuO-Cu_2O sites, in which *N,N*-dibutylformamide was collected as the product at high temperature (Scheme 1c) [22]. In 2018, Sarpong *et al.* reported a silver-salt mediated cleavage of C–C bonds in unstrained cyclic amines and fluorinated formamide was achieved (Scheme 1d) [23]. Moreover, a Cu(I/II)-pyridine catalyst was also reported by Beller and his coworkers for the C–C bonds scission of amines, and formamide was given as product (Scheme 1e) [24]. Obviously, in most of the above examples, it is often necessary to use, for example, complex & non-recoverable catalysts, high temperatures or stoichiometric oxidants to facilitate the reaction.

Very recently, a novel high nitrogen content mesoporous carbon nitride material, PCN (polymerised carbon nitride) nanorods, was synthesized in our group for loading copper nanoparticles. The Cu/PCN nanocomposite can be used as a highly efficient photocatalyst for the oxidative cleavage of C(sp^3)-C(sp^3) bond of amines under blue light irradiation in an oxygen atmosphere at 1–20 bar (Scheme 1f) [25].

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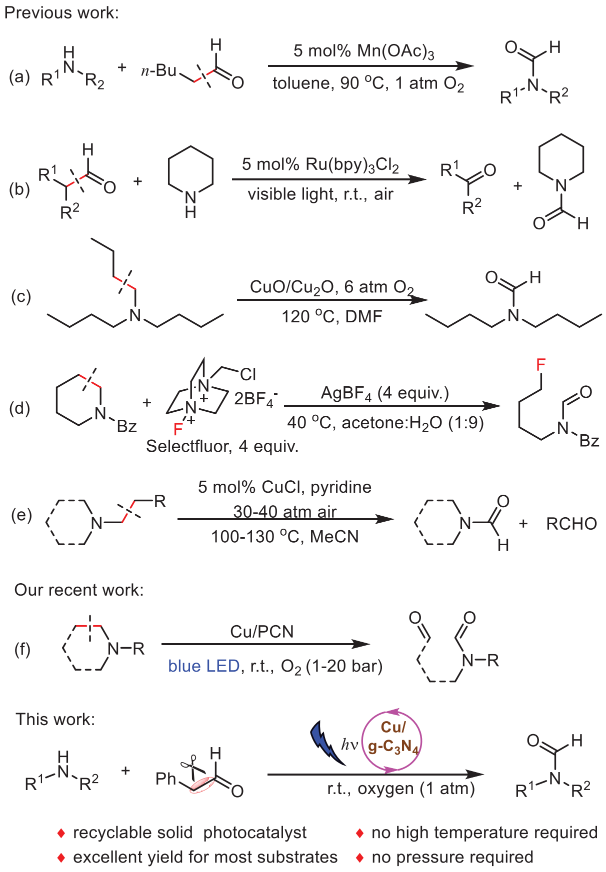
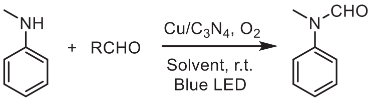


Scheme 1. C–C bond cleavage to construct formamides.

As one of the most popular CN materials, graphitic carbon nitride (g-C_3N_4) has been widely reported as an important photocatalyst recently in many fields. However, pure g-C_3N_4 usually suffers relatively low photochemical efficiency because of its low electronic conductivity, low specific surface area, and fast recombination of photogenerated electron-hole pairs [26,27]. To improve photocatalytic performance of the material, the combination of g-C_3N_4 and coinage metal nanoparticals, provides an effective strategy, owning to the latter's strong interactions with resonant incident photons through excitation of the localized surface plasmon resonance (LSPR) [28]. Also, the introduction of Cu, Ag or gold NPs facilitates the separation of charge [hole (h^+) and electron (e^-)] as well as inhibits the recombination of h^+/e^- effectively in g-C_3N_4. Based on this strategy, Ag/g-C_3N_4 nanocomposite has been utilized as a highly efficient photocatalyst in our recent works, in which a single electron oxidation (SEO) process of heteroatoms (oxygen or nitrogen) occurred on the surface of the photocatalyst effectively under visible light irradiation [29,30].

Herein, with Cu/g-C_3N_4 nanometric semiconductor as photocatalyst, a photocatalytic aerobic oxidative C–C bond cleavage of aldehydes was achieved with the promotion of amines under visible light irradiation. Based on the reaction, phenylacetaldehyde was selected as a highly efficient formylation reagent for amines. Under blue LED, various formamides were achieved with good to excellent yields in 1 atm oxygen at room temperature. It is worthy of noting that the nanometric semiconductor photocatalyst can be recovered & reused conveniently for several times with satisfying yields. The reaction is exemplary to synthesize formamides *via* the C–C bond cleavage of aldehydes on heterogeneous photocatalyst, and might provide a convenient alternative for the synthesis of formamides.

Table 1
Optimization of reaction conditions.[a]



1a 2 3a

Entry	Photocat. (mol%)	**2** (equiv.)	R	Solvent	Yield (%)[b]
1	Cu/g-C_3N_4 (10)	**2a** (3)	*n*-Pr	MeCN	85
2	Cu NPs (10)	**2a** (3)	*n*-Pr	MeCN	n.r.
3[c]	g-C_3N_4 (10)	**2a** (3)	*n*-Pr	MeCN	35
4	Cu/g-C_3N_4 (15)	**2a** (3)	*n*-Pr	MeCN	82
5	Cu/g-C_3N_4 (7.5)	**2a** (3)	*n*-Pr	MeCN	85
6	Cu/g-C_3N_4 (5)	**2a** (3)	*n*-Pr	MeCN	85
7	Cu/g-C_3N_4 (2.5)	**2a** (3)	*n*-Pr	MeCN	76
8	Cu/g-C_3N_4 (5)	**2a** (3)	*n*-Pr	H_2O	43
9	Cu/g-C_3N_4 (5)	**2a** (3)	*n*-Pr	ethanol	62
10	Cu/g-C_3N_4 (5)	**2a** (3)	*n*-Pr	acetone	90
11	Cu/g-C_3N_4 (5)	**2b** (3)	Me	acetone	35
12	Cu/g-C_3N_4 (5)	**2c** (3)	Et	acetone	65
13	Cu/g-C_3N_4 (5)	**2d** (3)	Bn	acetone	95
14	Cu/g-C_3N_4 (5)	**2d** (2.5)	Bn	acetone	97
15	Cu/g-C_3N_4 (5)	**2d** (2)	Bn	acetone	99
16	Cu/g-C_3N_4 (5)	**2d** (1.5)	Bn	acetone	90
17[d]	Cu/g-C_3N_4 (5)	**2d** (2)	Bn	acetone	85
18[e]	Cu/g-C_3N_4 (5)	**2d** (2)	Bn	acetone	n.r.
19	–	**2d** (2)	Bn	acetone	n.r.

[a] Reaction conditions, unless otherwise noted: *N*-methylaniline **1a** (0.20 mmol), solvent (2.0 mL), photocatalyst, 23 W blue LED, at ambient temperature in oxygen for 24 h.
[b] Yield of isolated product.
[c] g-C_3N_4 (11.2 mg).
[d] 23 W white LED.
[e] In the dark.

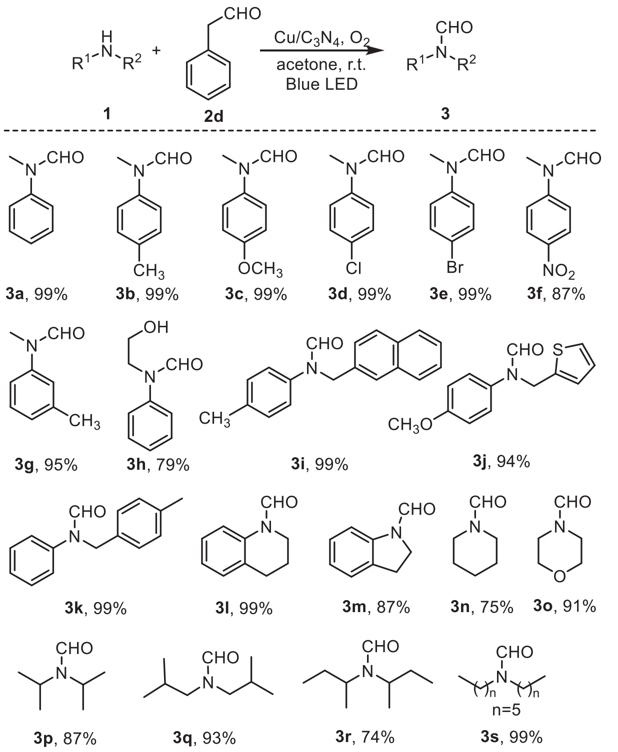
Through a solvothermal process in acetonitrile at 180 °C followed by roasting at 500 °C, the g-C_3N_4 was prepared with melamine and cyanuric chloride as starting materials [28,31]. Cu NPs was then loaded on the g-C_3N_4 by reducing $Cu(OAc)_2$ with $NaBH_4$ in ethanol solution, and the Cu/g-C_3N_4 hybrid material was obtained, which was then characterized by TEM, XRD, XPS, UV–vis and PL (The detailed characterization and discussion are provided as Figs. S1-S5 in Supporting information).

With the Cu/g-C_3N_4 nanocomposite as catalyst, the formylation of *N*-methylaniline (**1a**) was selected as the prototype to start our investigation for the optimized reaction conditions, and the data were summarized in Table 1.

Under the blue light of a 23 W household LED bulb, *n*-butyraldehyde (**2a**) was firstly examined at room temperature in 1 atm oxygen atmosphere, and the desired product, *N*-methyl-*N*-phenylformamide (**3a**), was isolated with 85% yield (Table 1, entry 1). Cu NPs or g-C_3N_4 were then utilized alone to catalyze the reaction, respectively. It can be seen from entries 2 and 3 in Table 1 that the absence of either Cu NPs or g-C_3N_4 was not beneficial to the reaction. Obviously, the introduction of Cu NPs enhanced the photocatalytic efficiency of g-C_3N_4 and promoted the photocatalytic cleavage of C–C bonds leading to corresponding formamides. Meanwhile, some other heterogeneous photocatalysts, such as Ag/g-C_3N_4 and TiO_2, were also evaluated, but no highly photocatalytic activity was observed (Table S1 in Supporting information).

Subsequently, different catalyst dosages were screened (Table 1, entries 4–7). 5 mol% of Cu/g-C_3N_4 is the best of the choices, and up to 85% of **3a** was observed. It can be seen from Table 1 that H_2O and ethanol were not suitable for the reaction, while a higher yield of 90% was achieved in acetone (Table 1, entries 6, 8–10).

Besides butyraldehyde, acetaldehyde (**2b**), propionaldehyde (**2c**) and phenylacetaldehyde (**2d**) were also utilized in the reaction as the formylation reagent, respectively (Table 1, entries 11–13). No-



Scheme 2. Scope of the reaction in terms of amines. The reaction was carried out by using **1a** (0.2 mmol), **2d** (0.4 mmol), acetone (2.0 mL), Cu/g-C_3N_4 (5 mol%), 23 W blue LED, at ambient temperature in oxygen for 20 h. Yield of isolated product.

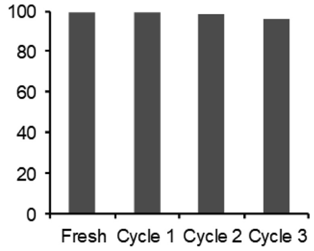
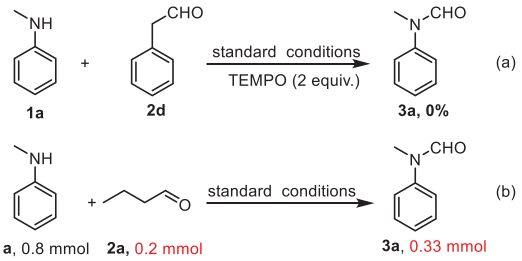


Fig. 1. The recyclability of Cu/g-C_3N_4 photocatalyst.



Scheme 3. Control experiments.

tably, since enamine has been confirmed as the key intermediate in the reaction [19–21], phenylacetaldehyde (**2d**), which could react with **1a** to generate a stable enamine intermediate due to the conjugation effect of aromatic ring, gave **3a** with 95% yield as the best result (Table 1, entry 13). Furthermore, when 2 equiv. of **2d** was used, up to 99% of **3a** was achieved (Table 1, entry 15 *vs.* entries 13, 14 and 16).

When the same power of white LED was utilized instead of the blue LED, the yield of **3a** decreased to 85% (Table 1, entry 17). Moreover, the reaction did not occur in the absence of visible light (Table 1, entry 18) or photocatalyst (Table 1, entry 19).

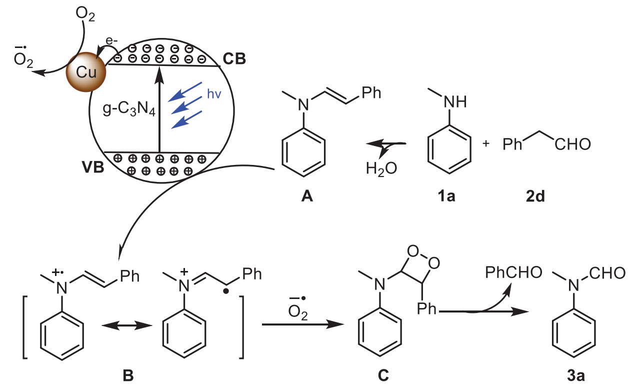
Obviously, the current photocatalytic methodology has great potential to be an alternative to synthesize formamides. Thus, having identified our optimized reaction conditions (Table 1, entry 15), the Cu/g-C_3N_4 catalyzed *N*-formylation of amines *via* a photocatalytic aerobic oxidative C–C bond cleavage of aldehydes under visible-light irradiation was extended to various amine substrates.

As shown in Scheme 2, good to excellent yields were achieved for various substrates. It was discovered that substituted *N*-methylaniline bearing Me, OMe, Cl, Br and NO_2 groups at *para*- or *meta*-positions afforded the products **3b-3g** in 87%–99% yields, respectively. The results indicated that strong electron-withdrawing group (-NO_2, **3f**) was disfavored to the reaction, which might be due to the low electron density inhibiting the formation of enamines *in situ*. Furthermore, the *N*-substituted anilines, such as *N*-ethanol, *N*-naphthylmethyl, *N*-thienylmethyl and *N*-benzyl could be transformed efficiently into the desired products, respectively (**3h-3k**). In addition, 1,2,3,4-tetrahydro-quinoline and indoline could also be converted into the corresponding products in excellent yields (**3l-3m**). Also, a series of aliphatic amines could react smoothly to give corresponding formamides. Aliphatic cyclic amines, such as piperidine and morpholine, afforded the amides with 75% and 91% of yield, respectively **(3n-3o)**. Usually, the formylation of high stereo-hindered amines is a challenging task due to the weak nucleophilicity of the nitrogen atom [32]. To our delight, when several stereo-hindered amines were applied, 74%–93% isolated yields were achieved (**3p-3r**). It is noteworthy that long-chain aliphatic amine also afforded up to 99% yield for the corresponding formamide (**3s**).

One of advantages of heterogeneous catalysts is that they are easy to be recovered and reused. By centrifugation, the Cu/g-C_3N_4 nanometric semiconductor photocatalyst could be easily isolated from the reaction mixture, and reused directly for a new reaction. Thus, with the reaction of **1a** & **2d** as prototype, the recyclability of the solid photocatalyst was investigated (Fig. 1). It can be seen that the Cu/g-C_3N_4 catalyst was recovered and reused effectively. There was no appreciable loss in yields observed even after 3 cycles (99% yield in fresh reaction *vs.* 96% in the third recycle).

To realize the possible reaction mechanism, the following control experiments were carried out under the standard conditions. As shown in Scheme 3, firstly, when the radical scavenger TEMPO was added, the reaction was obviously inhibited and no desired product **2d** was obtained (Scheme 3a). It suggested that the reaction involved a radical process. Furthermore, to verify that the additional aldehydes produced by C–C bond cleavage could be formed in this transformation [18], 4 equiv. of **1a** was added in the reaction with **2a**. As a result, the desired product **3a** was obtained in 0.33 mmol (1.65 equiv. relative to **2a**). The higher yield of **3a** confirmed that the propionaldehyde might be one of the byproducts of the reaction (Scheme 3b).

Accordingly, based on the results above and relevant literature reports [18–21,25,33], a plausible reaction mechanism was proposed in Scheme 4. Initially, the enamine (**A**) was formed *in situ* from *N*-methylaniline (**1a**) and 2-phenylacetaldehyde (**2d**). On the other hand, the photocatalyst could be excited under the visible light irradiation and generate conduction band electrons (e^-) and valence band holes (h^+). Next, enamine (**A**) undergoes a single electron oxidation (SEO) process on the valence band holes and *N*-radical cation radical (**B**) was generated, meanwhile the electron acceptor O_2 could be reduced to a superoxide radical anion ($O_2^{\cdot -}$) by the photogenerated electrons which were excited to the conduction band and entrapped by Cu NPs [29,30,34–36]. Then, the intermediate **C** is formed *via* the cycloaddition of **B** and $O_2^{\cdot -}$. Finally, the fragmentation of **C** would lead to yield the desired product formamide (**3a**) and benzaldehyde.



Scheme 4. Proposed reaction mechanism.

In summary, a recyclable solid photocatalyst, Cu/g-C_3N_4 nanometric semiconductor, was utilized successfully to catalyze an aerobic oxidative C–C bond cleavage of aldehydes with the promotion of amines in oxygen at 1 atm under visible light irradiation. The transformation provided a convenient and mild alternative for the synthesis of formamides derivatives. With phenylacetaldehyde as the formylation reagent of amines, good to excellent yields of formamides were achieved for various amines under blue light irradiation. Further research is being carried out in our laboratory to obtain more details of the mechanism and to extend this strategy to other organic transformations.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.cclet.2022.108001.

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