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Visible-light-induced photoxidation-Povarov cascade reaction: synthesis of 2-arylquinoline through alcohol and N-benzylanilines under mild conditions *via* Ag/g-C_3N_4 nanometric semiconductor catalyst

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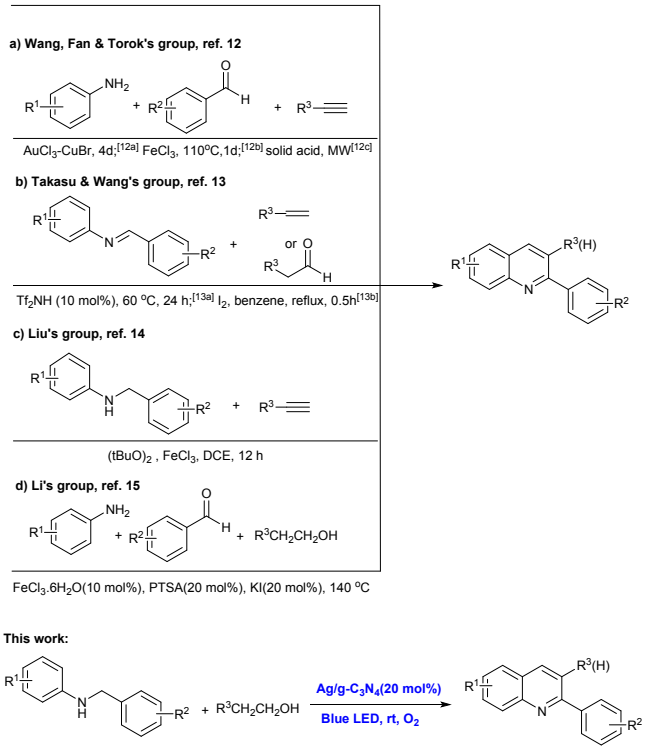
With Ag/g-C_3N_4 nanometric semiconductor as photocatalyst, 2-arylquinolines were synthesized through a photoxidation-Povarov cascade reaction of N-benzylanilines and alcohols under visible light irradiation. Under the blue light of a 3W LED, good yields were achieved for various substrates in oxygen at room temperature. This methodology provides a green and mild alternative for the formation of 2-arylquinoline derivatives. Remarkably, the Ag/g-C_3N_4 nanocomposite can be conveniently recovered and reused for several times with satisfied yields.

The utilization of solar radiant energy to drive organic reactions stands out as the most promising choice to meet our demand for green synthesis due to its abundance, absence of cost, and eco-friendly nature.[1] Recently, many photocatalytic synthetic reactions have been reported.[2] However, most of the examples are involved in metal complexes or dyes as catalyst. There are limited examples with solid nanometric semiconductor as photocatalyst,[3] in which, to the best of our knowledge, few of examples for a cascade reaction.[4]

Due to the strong localized surface plasmon resonance (LSPR) effect, coinage metal nanoparticles were recognized as a new form of medium that is particularly efficient in harvesting light energy for chemical processes over a wide range of the visible and UV regions of the solar spectrum.[5] On the other hand, graphitic carbon nitride (g-C_3N_4) is a novel aggregate type semiconductor material and works as an important catalyst for building a new photocatalytic system.[6] The combination of Ag NPs and g-C_3N_4, provides a novel strategy to enhance the photocatalytic performance of g-C_3N_4.[7] In our recent research, Ag/g-C_3N_4 nanocomposite has exhibited highly photocatalytic activities toward aerobic oxidative amidation of aromatic aldehydes under visible light irradiation.[8]



Scheme 1. Selected recent Povarov reactions for the synthesis of 2-arylquinolines.

Quinolines and their derivatives represent a wild variety of biological activities and are valuable synthetic intermediates for many synthetic compounds with pharmacological properties,[9] in which 2-arylquinoline backbones are important structure for biologically active molecules.[10] Moreover, these compounds are also crucial intermediates for the preparation of dyes, polymers and materials with unique electronic and optical properties. [11]

Recently, a few elegant examples to construct quinolines have been disclosed. Among these examples (Scheme 1), Wang's, Fan's and Török's groups demonstrated a Povarov reaction of aniline, benzaldehyde and phenylacetylene (Scheme 1, a), respectively.[12] Takasu's group reported a

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cyclization-dehydroaromatization of N-arylaldimine and alkene. Also, with aldehyde instead, a synthetic methodology for substituted quinolines was developed by Wang's group (Scheme 1, b).[13] With DTBP as oxidant, Liu and his co-workers described an iron-catalysed annulation of N-alkyl aniline and alkyne to construct quinoline skeleton (Scheme 1, c).[14] Moreover, in Li's group reported example, with $FeCl_3$-PTSA-KI as catalyst combination, ethanol, instead of alkene or alkyne, participated in reacting with aromatic aldehydes and anilines to give quinoline at high temperature (Scheme 1, d). [15]

In most of examples above, complicated & non-recyclable catalysts, high temperature or stoichiometric oxidants have to be used frequently to promote the reaction. Thus, to develop an environmental friendly and green methodology is still under investigation. Herein, with Ag/g-C_3N_4 nanometric semiconductor as photocatalyst, we hope to report a green and mild alternative for the synthesis of 2-arylquinoline derivatives *via* a photoxidation-Povarov cascade reaction of N-benzylanilines and alcohols under visible light irradiation. Under the blue light of a 3W LED, good yields were achieved for various substrates at room temperature in oxygen. Remarkably, the Ag/g-C_3N_4 nanocomposite can be conveniently recovered and reused for several times with satisfied yields.

The g-C_3N_4 was prepared through the solvothermal process by using melamine and cyanuric chloride as precursors in acetonitrile at 180 °C.[8,16] With the porous g-C_3N_4 as support, Ag/g-C_3N_4 hybrid material was then prepared by a facile reduction method in ethanol solution with $AgNO_3$ and trisodium citrate as starting materials (the detailed preparation and characterization were provided in ESI).

For the optimization of conditions, the reaction of N-(4-meoxy)benzyl aniline (**1a**) and ethanol was selected as the porotype. Under the blue light of a 3W LED, the desired product, 2-(4-methoxyphenyl) quinoline (**2a**), was isolated with 62% of yield at room temperature under oxygen atmosphere (entry 1, Table 1).

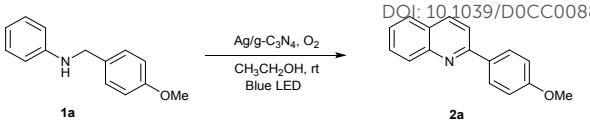
g-C_3N_4 and Ag NPs were then utilized alone as the photocatalyst, respectively. As seen from entries 2&3 in Table 1, the absence of either Ag NPs or g-C_3N_4 went against this reaction. The combination of g-C_3N_4 and metal nanoparticals seems to be essential in the reaction.

Subsequently, under blue light irradiation, a blank reaction was carried out in the absent of photocatalyst and no reaction occurred (entry 4, Table 1). As another controlled experiment, a reaction in dark was also examined (entry 5, Table 1). From both of the results above, obviously, either the visible light irradiation or photocatalyst is indispensable in the reaction.

On the other hand, bulk-C_3N_4[17] was utilized instead of g-C_3N_4, which proved to be less effective in the reaction (entry 6, Table 1). Moreover, copper, instead of silver, was supported by g-C_3N_4 and used to catalyse the reaction under the same conditions, but only 38% of **2a** was isolated (entry 7, Table 1).

Different loadings of the photocatalyst were also screened in entries 8 & 9, 20 mol% of Ag/g-C_3N_4 is the best of choices, and up to 78% of **2a** was achieved. Furthermore, some additives, such as PTSA and aniline, were then added in the reaction, respectively. The desired product declined to only 12% and 9% yield, respectively (entries 10 & 11，Table 1). [18]

Table 1. Optimization of reaction conditions. [a]



1a 2a

Entry	Catalyst (mol%)	Additive	Yield [%] [b]
1	Ag/g-C_3N_4 (10)	none	62
2[c]	g-C_3N_4	none	36
3	Ag NPs (10)	none	27
4	none	none	n.r.
5[d]	Ag/g-C_3N_4 (10)	none	n.r
6	Ag/bulk-C_3N_4 (10)	none	49
7	Cu/g-C_3N_4 (10)	none	38
8	Ag/g-C_3N_4 (5)	none	53
9	Ag/g-C_3N_4 (20)	none	78
10	Ag/g-C_3N_4 (20)	PTSA (20 mol%)	12
11	Ag/g-C_3N_4 (20)	Aniline (20 mol%)	9
12[e]	Ag/g-C_3N_4 (20)	none	43
13[f]	Ag/g-C_3N_4 (20)	none	23
14[g]	Ag/g-C_3N_4 (20)	none	23

[a] Reaction conditions, unless otherwise noted: N-benzylaniline (**1a,** 0.10 mmol), ethanol (2.0 mL), photocatalyst, and 3W blue LED at ambient temperature in oxygen for 48 h. [b] Isolated Yield. [c] g-C_3N_4 (20 mg). [d] Reaction in dark. [e] 15W blue LED. [f] Reaction time: 24h. [g] Reaction in air.

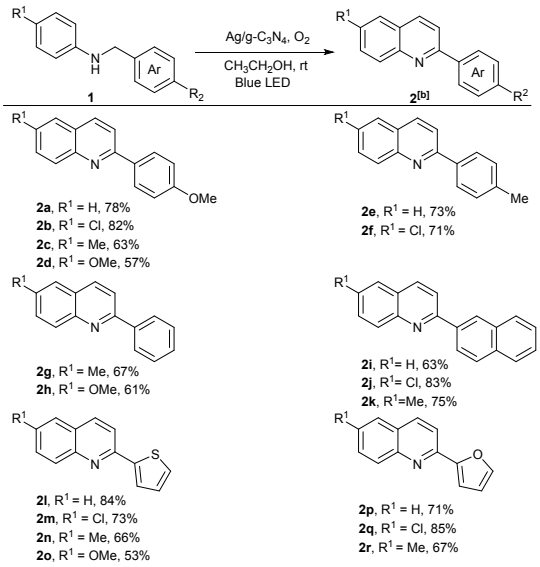
When the intensity of light was enhanced to 15W, however, the yield of **2a** was decreased to 43% (entry 12, Table 1). We also tried to short the reaction time to 24h, but significantly lower yield was observed (entry 13, Table 1). Moreover, if the reaction was conducted in air, only 23% yield was obtained (Table 1, entry 14).

With the optimal conditions in hand (entry 9, Table 1), we scanned the scope of the synthetic methodology for quinoline derivatives. In the Ag/g-C_3N_4-catalyzed, visible-light-induced Povarov tandem reaction, various N-benzylanilines were examined under the standard reaction with ethanol as substrate & solvent, and the results are summarized in Table 2.

As shown in Table 2, moderate to good yields were achieved for various substrates. It seems that the substitutes on anilines show marked effect on the reaction. As seen from **2a-2d**, the *para*-substituted electron-donating groups, such as methyl and methoxyl, were disfavoured to the reaction, and a similar trend was also observed from the other series. Most of substrates derived from 4-cholo-aniline gave the yields around 80% (**2b, 2f, 2j, 2m** and **2q**); on the contrary, only 50-60% of yields were obtained from 4-methoxy-aniline derivatives (**2d,**

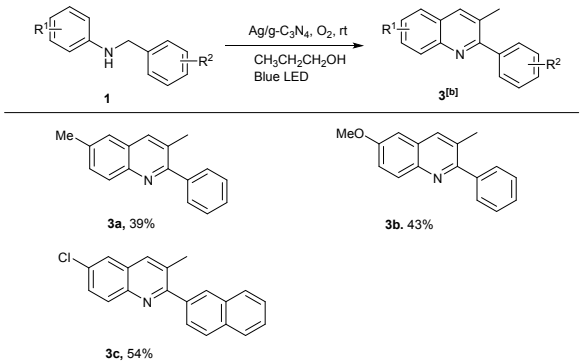
2h and **2o**). Moreover, 2-heteroaryl-substitued quinolines were also synthesised via the current method, and up to 85% of yield was achieved (**2l**-**2o** & **2p**-**2r**).

Table 2. Scope of the photoxidation-Povarov tandem reaction.[a]



[a] The reaction was carried out by using N-benzylanilines (**1,** 0.10 mmol), ethanol (2.0 mL), photocatalyst (20 mol%), oxygen atmosphere, and 3W blue LED irradiation at ambient temperature for 48 h. [b] Isolated yield.

Table 3. The synthesis of substituted 2-aryl-3-methyquinolines with n-propanol[a].



[a] the reaction was carried out by using N-benzylanilines (**1**, 0.10 mmol), n-propanol (2.0 mL), photocatalyst (20 mol%), oxygen atmosphere, and 3W blue LED irradiation at ambient temperature for 48 h. [b] Isolated yield.

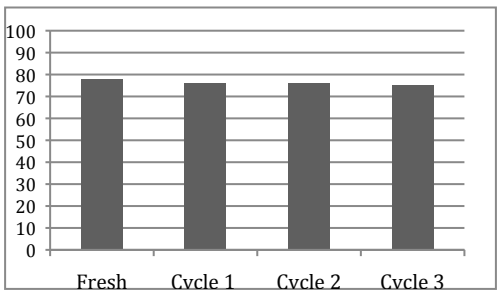
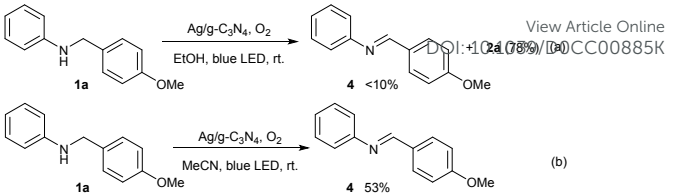
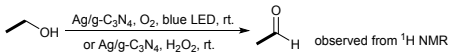


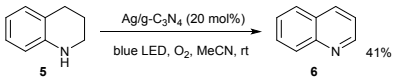
Figure 1. The recyclability of Ag/g-C_3N_4 photocatalyst in the reaction of **1a** & ethanol.



Scheme 2. The formation of imine **4** on Ag/g-C_3N_4



Scheme 3. Ag/g-C_3N_4 catalysed oxidation of EtOH under blue light or with H_2O_2.



Scheme 4. Ag/g-C_3N_4 catalysed dehydroaromatization of tetrahydroquinoline.

To widen the applicability of the procedure, n-propanol, instead of ethanol, was then tested as the substrate as well as the solvent. As shown in Table 3, the tandem reaction proceeded smoothly with n-propanol, giving **3a**-**3c** with reasonable to moderate yields.

As a kind of heterogeneous photocatalyst, the Ag/g-C_3N_4 nanocomposite can be easily separated from the reaction mixture by centrifugation and reused for new reaction. Thus, the recyclability of the nanocomposite catalyst in the reaction of **1a** & ethanol was investigated (Figure 1). As shown in Figure 1, the Ag/g-C_3N_4 catalyst could be recovered and reused for 3 times at least without appreciable loss in yields.

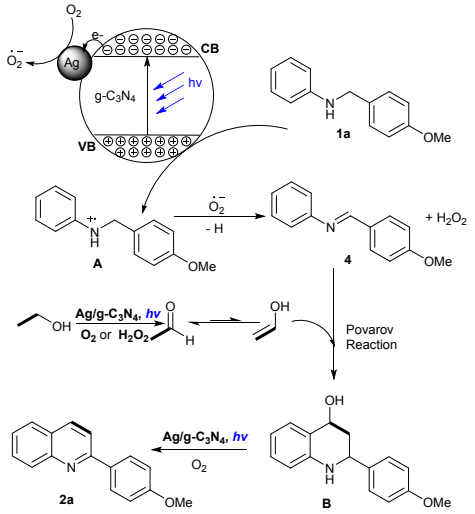
From the reaction mixture of **1a** & ethanol, an imine compound (**4**), was isolated as by-product (Scheme 2, a). In our previous research on the mechanism of the Ag/g-C_3N_4 catalysed oxidative amidation of aldehydes under visible light, the single-electron oxidation of THF occurred on the catalyst's surface has proven to be the initial step for the reaction.[8] We proposed that the imine **4** might be formed following a similar approach. Thus, as a controlled experiment, **1a** was then treated in MeCN solution alone with Ag/g-C_3N_4 under blue light irradiation in oxygen at room temperature, and 53% of **4** were isolated.

On the other hand, two blank reactions without **1a** were also carried out under oxygen or with H_2O_2, respectively. From crude NMR, the formation of acetaldehyde was observed in both of the reactions (Scheme 3). Furthermore, as a model-reaction, tetrahydroquinoline (**5**) was also treated by Ag/g-C_3N_4 & blue light in MeCN under oxygen atmosphere, and 41% of quinoline (**6**) was isolated after 24 h (Scheme 4). It suggested that Ag/g-C_3N_4 might also be an effective catalyst for the dehydroaromatization of tetrahydroquinoline derivatives under visible light irradiation.

Based on these results above and relative literature reports,[7, 8, 13b] a plausible reaction mechanism was proposed in Scheme 5. Initially, under visible light irradiation, g-C_3N_4 can be excited to generate conduction band electrons (e^-) and valence band holes (h^+), and then, amine **1a** released one electron on the valence band holes to give N-radical cation intermediate (**A**). On the other hand, the photogenerated electrons excited to conduction band were entrapped by Ag NPs, and could reduce

the electron acceptor O_2 to superoxide radical anion. [3, 8, 19] Furthermore, with the promotion of superoxide radical anion, the N-arylaldimine (**4**) was then formed.[20]

Subsequently, the *in situ* formed N-arylaldimine (**4**) reacted with acetaldehyde, which is from the *in situ* photo-oxidation of ethanol with Ag/g-C_3N_4 as catalyst, to generate the intermediate **B** underwent a Povarov process.[13b] Finally, **B** went through oxidative dehydroaromatization to give the final product **2a**.



Scheme 5. Proposed reaction mechanism.

Conclusions

In summary, a solid nanometric semiconductor, Ag/g-C_3N_4, was utilized successfully as a recyclable photocatalyst for a photoxidation-Povarov tandem reaction of N-benzylanilines and ethanol under visible light irradiation in oxygen. The transformation provided an environment-friendly alternative for the synthesis of 2-arylquinoline derivatives. Further studies to gain more mechanistic details of this reaction and apply this strategy to other organic transformations are ongoing in our laboratory.

Acknowledgments

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Conflicts of interest

There are no conflicts to declare.

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Ag/g-C_3N_4 nanometric semiconductor catalyzed cascade reaction for the synthesis of 2-arylquinoline through alcohol and N-benzylanilines under visible light irradiation