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# N-substituted-3(10H)-acridones as visible-light photosensitizers for organic photoredox catalysis

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ABSTRACT

N-Substituted-3(10H)-acridones have been established as visible-light organic photocatalyst. These photosensitizers are efficient for oxidative coupling reaction of N-aryl tetrahydroisoquinolines with various nucleophiles. Notably, N-methyl-3(10H)-acridone (**Ia**) is stable and can be effectively prepared. It is a water-soluble and atom-economic catalyst, and thus holds promise for green chemical applications. Mechanistic studies confirm a single electron transfer (SET)-induced radical process and a rate-limiting step. Analysis of the photocatalytic reactivity–structure relationship reveals that the acridones are robust and tunable photosensitizers for photoredox catalysis.

## 1. Introduction

Visible light constitutes the major part of sunlight, which provides clean and renewable energy for the nature. Application of solar photocatalysts on an industrial scale has been an aspiration since a century ago.[1] Photocatalysts mainly include transition metal chromophores and organic chromophores. $[Ru(bpy)_3]Cl_2$ and iridium polypyridyl complexes are among the best organometallic photoredox catalysts with well demonstrated versatility in organic synthesis.[2] On the other hand, “metal-free” organic chromophores have long been recognized for their ability to initiate photoredox catalysis.[3] Despite the significant advances in the field of photoredox catalysis, development of robust, versatile and eco-friendly organic photocatalysts is still highly desirable. In this study, N-substituted-3(10H)-acridones **Ia~f** (Fig. 1) are prepared as visible-light photosensitizers for organic photoredox catalysis.

As part of our program to develop inhibitors of epigenetic enzymes, we became interested in 3-hydroxy-N-methylacridinium ion (Ac$^+$OH) and its derivatives.[4] This compound could be synthesized according to the literature procedures. Interestingly, N-methyl-3(10H)-acridone (**Ia**)[5] was obtained as an orange red solid whose structure was confirmed by X-ray crystallography (see Supporting Information (SI): Fig. S6). Given its unique chromophore structure and photophysical properties (see SI: Figs. S2~5, Tables S1~2), we reasoned that **Ia** might find its utility as a visible-light organic photocatalyst. To the best of our knowledge, there are no any reports concerning its applications in organic photoredox catalysis.[6]

## 2. Result and discussion

To test this hypothesis, photocatalytic oxidative coupling reaction of N-phenyl tetrahydroisoquinoline (**1a**) with nitromethane was chosen as the model reaction (Table 1). Firstly, different types of light sources were examined (entries 1–5, Table 1). To our delight, the desired product **3a** was obtained in 77% yield after 7 h of irradiation with blue LED at room temperature (entry 2, Table 1). It was found that the reaction was significantly affected by the volume of nitromethane (entries 8, 11, Table 1). A screening of solvents revealed that MeOH was the best solvent allowing for production of **3a** in 82% yield (see in the supporting information). The catalyst loading also had a significant impact on the reaction. While 1–5 mol % catalyst loading afforded good product yields and appropriate reaction speed (entries 8, 12, 13, Table 1),

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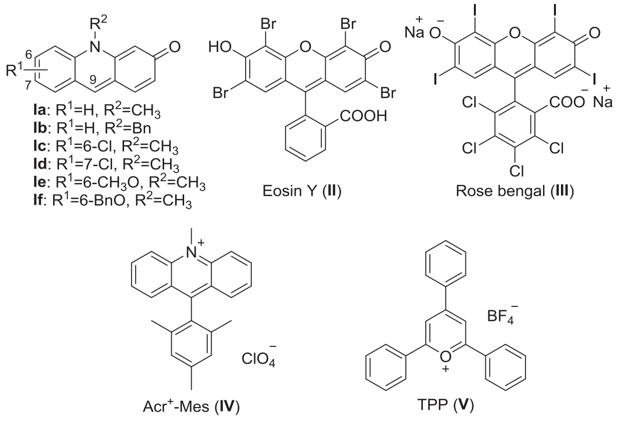
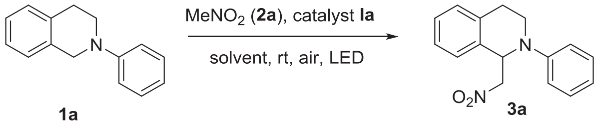


**Fig. 1.** Visible-light photosensitizers for organic photoredox catalysis.

0.01–0.001 mol % catalyst loading resulted in decreased reaction speed and conversion rate (entries 15, 16, Table 1). Surprisingly, TON (turnover number) and TOF (turn over frequency) of **Ia** could reach approximately 79000 and 3950 $h^{-1}$, respectively (entry 16, Table 1). The reaction proceeded very poorly in the absence of air (entry 18, Table 1), indicating the critical role of oxygen. When the reaction was run under an oxygen atmosphere, the reaction proceeded very fast at the early stage, however, the overall conversion rate was not as good as with using air (entries 8, 19, Table 1). Notably, the reaction did not take place at all in the dark (entry 20, Table 1). The photocatalyst was also required for efficient conversion (entry 17, Table 1). To investigate the photocatalytic reactivity–structure relationship of acridones, a series of acridones **Ia~f** (Fig. 1) were synthesized following the literature procedures[4,12] (see SI: Scheme S1 and experimental section). To compare the photocatalytic efficiency of **Ia~f**, the CDC reaction of **1a** with nitromethane was carried out (Table 1). Notably, all the acridones tested were efficient photocatalysts for this CDC reaction, leading to a complete conversion within 7.5 h. Acridone **Ia** exhibited almost the same reactivity with **Ib** (entries 8 and 22, Table 1), indicating the negligible effect caused by different N-substituted groups. Acridones **Ic** and **Id** with 6-Cl or 7-Cl substitution showed obviously decreased reaction rate (entries 23 and 24, Table 1), implying that electron-withdrawing groups might have negative effect on the photocatalytic activity. On the other hand, the introduction of a methoxy or benzyloxy group at the 6 position of **Ie** or **If** resulted in an increase in photocatalytic efficiency (entries 25 and 26, Table 1), indicating that electron-donating substituents on the benzene ring may be favorable for the photocatalytic activity. Together, various acridones represent a new class of robust and tunable organic photoredox catalysts. Finally, acridone **Ia** was found to be a novel and highly efficient organic photoredox catalyst.

**Table 1**
Photocatalytic Reaction of N-phenyl Tetrahydroisoquinoline with Nitromethane.[a]

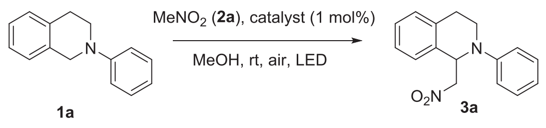


| Entry | **Ia** (mol%) | LED Color | **2a** (mL) | Time (h) | Conv. (%)[b] | Yield (%)[c] |
|---|---|---|---|---|---|---|
| 1 | 1 | white | 0.5 | 7 | 96 | 70 |
| 2 | 1 | blue | 0.5 | 7 | 99 | 77 |
| 3 | 1 | green | 0.5 | 7 | 82 | 56 |
| 4 | 1 | red | 0.5 | 7 | <10 | 8 |
| 5 | 1 | yellow | 0.5 | 7 | <10 | 6 |
| 6 | 1 | blue | 0.1 | 6 | 91 | 61 |
| 7 | 1 | blue | 0.5 | 6 | 94 | 72 |
| 8 | 1 | blue | 1 | 6 | 100 | 82 |
| 9 | 1 | blue | 1.5 | 6 | 96 | 68 |
| 10 | 1 | blue | 2 | 6 | 97 | 66 |
| 11 | 1 | blue | 2.4 | 6 | 88 | 58 |
| 12 | 5 | blue | 1 | 4.5 | 100 | 79 |
| 13 | 2 | blue | 1 | 5 | 100 | 74 |
| 14 | 0.1 | blue | 1 | 11 | 100 | – |
| 15 | 0.01 | blue | 1 | 20 | 94 | – |
| 16 | 0.001 | blue | 1 | 20 | 79 | – |
| 17 | 0 | blue | 1 | 20 | 56 | – |
| 18[d] | 1 | blue | 1 | 6 | 31 | – |
| 19[e] | 1 | blue | 1 | 6 | 93 | – |
| 20[f] | 1 | – | 1 | 6 | 0 | – |
| 21[g] | 1 | blue | 1 | 6 | 24 | – |
| 22 | **Ib (1)** | blue | 1 | 6 | 100 | 80 |
| 23 | **Ic (1)** | blue | 1 | 7 | 100 | 82 |
| 24 | **Id (1)** | blue | 1 | 7.5 | 100 | 77 |
| 25 | **Ie (1)** | blue | 1 | 5 | 100 | 78 |
| 26 | **If (1)** | blue | 1 | 5 | 100 | 85 |

[a] Conditions: **1a** (0.25 mmol), **2a**, catalyst **Ia**, solvent (total solution volume 2.5 mL), air, r.t., blue LED irradiation (6W, λ = 450 ± 10 nm).
[b] Conversion rate was determined by $^1$H NMR, 1,1,2,2-tetrachloroethane as internal standard.
[c] Isolated yields after column chromatography.
[d] Reaction was run under nitrogen atmosphere.
[e] Reaction was run under oxygen atmosphere.
[f] Reaction was run in the dark.
[g] One equivalent of TEMPO was added.

Next, we wanted to compare acridone **Ia** with the common photoredox catalysts, including Eosin Y (**II**),[7a] Rose Bengal (**III**),[7b] $Acr^+$-Mes (**IV**),[7c] TPP (**V**),[7d] and $[Ru(bpy)_3]Cl_2$.[2a,8] As shown in Table 2, photocatalytic reaction of N-phenyl tetrahydroisoquinoline with nitromethane was run in the presence of various photocatalysts. LED with different color was used to match the maximum absorption wavelength of each catalyst. To our delight, under the same reaction condition, **Ia** (1 mol%) showed the best photocatalytic capability, enabling an almost complete conversion after 6 h (entry 1, Table 2), while $Acr^+$-Mes (**IV**) induced only 81% conversion (entry 4, Table 2). Eosin Y (**II**) and Rose Bengal (**III**) showed moderate activity for photocatalysis (entries 2 and 3, Table 2). TPP (**V**) was a weak catalyst for this reaction with only 46% conversion (entry 5, Table 2). Notably, **Ia** had a slightly higher conversion rate than $[Ru(bpy)_3]Cl_2$ (entry 6, Table 2). Together, in this context, acridone **Ia** was more efficient than the common photocatalyst such as $[Ru(bpy)_3]Cl_2$ and $Acr^+$-Mes (**IV**). It is worth noting that **Ia** has a very good water-solubility, thus allowing for green chemical applications with using water as a solvent.

**Table 2**
Comparison of Acridone Ia with Common Photocatalysts.[a]



| Entry | Catalyst | LED color | Time (h) | Conversion (%)[b] | Yield (%)[b] |
|---|---|---|---|---|---|
| 1 | **Ia** | blue | 6 | 99 | 97 |
| 2 | **II** | green | 6 | 56 | 54 |
| 3 | **III** | green | 6 | 58 | 56 |
| 4 | **IV** | blue | 6 | 81 | 74 |
| 5 | **V** | blue | 6 | 46 | 41 |
| 6 | $[Ru(bpy)_3]Cl_2$ | blue | 6 | 95 | 95 |

[a] Conditions: **1a** (0.25 mmol), **2a** (1 mL), catalyst (1 mol%), MeOH (1.5 mL), air, r.t., LED irradiation.
[b] Conversion rate and yields were determined by $^1$H NMR, 1,1,2,2-tetrachloroethane as internal standard.