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Metal-free, visible-light-mediated transformation of aryl diazonium salts and (hetero)arenes: an efficient route to aryl ketones†

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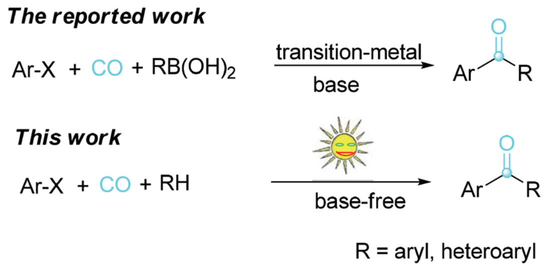
A visible-light-catalyzed synthesis of aryl ketones from aryldiazonium salts, CO and (hetero)arenes at room temperature is discovered. This transformation represents an efficient and attractive synthetic utilization of aryl diazonium salts.

Aryl ketones are common structural motifs in natural products and are versatile building blocks in the synthesis of more complex natural products, pharmaceuticals, agricultural chemicals, dyes, and other commercially important materials.[1] Owing to their structural diversity and remarkable biological functions, the synthesis and transformation of aryl ketones has been and continues to be a topic of research interest for synthetic organic chemists.[2] One approach towards efficient aryl ketone synthesis is carbonylation of aromatic C–H bonds with CO and aromatic boronic acids.[3] This method has provided a straightforward route to versatile unsymmetric diaryl ketones. The approach relies on the development of a wide range of robust metal catalysts which elegantly combine many central transition metals (*i.e.*, Ru, Pd, Co, *etc.*) and diverse organic ligands. The use of transition-metal catalysts is often expensive and is required to be completely removed from products, especially in the synthesis of pharmaceutical compounds. To overcome the drawbacks of the above-mentioned transformation methods, photocatalysis may provide a valuable alternative that avoids the use of transition metals, ligands, bases, or elevated temperatures.[4]

Visible light photoredox catalyst initiated organic transformations are emerging as uniquely powerful tools for constructing new chemical bonds in organic synthesis due to their more environmentally benign sustainability and mild operating conditions. Many visible-light photoredox catalysts such as metal or non-metal complexes have been used to solve the problem of visible light absorption efficiency.[5] By using these methods, readily available, reactive aryl diazonium salts have been widely utilized as a convenient aryl radical source.[6] As a result, many unusual transformations of these reagents have been carried out by photocatalysis. It has been reported that in the presence of a certain amount of CO aryl radicals can be easily and efficiently converted into acyl radicals which will be further oxidized to benzylidyneoxoniums by the oxidized dye radical cation. Recently, the group of Xiao reported an intramolecular carboxylation reaction for the formation of 9*H*-fluoren-9-one.[6c] However, the intermolecular carboxylation reactions for the synthesis of aryl ketones from aryl diazonium salts, CO and (hetero)arenes using visible-light-induced photoredox catalysis have not been reported. Inspired by the pioneering work from the groups of Xiao and Wangelin, we envisioned that (hetero)arenes might serve as a platform to trap benzylidyneoxoniums. In connection with our broader interest in visible-light-induced photocatalysis,[7] herein we disclose our preliminary results on visible-light promoted transformation of aryldiazonium salts and (hetero)arenes for the synthesis of aryl ketones under base-free and transition-metal-free conditions under a carbon monoxide atmosphere.[8] The method involves a redox reaction driven by visible light and catalyzed by Eosin Y (Scheme 1).



Scheme 1 Synthesis of aryl ketones *via* redox carbonylation.

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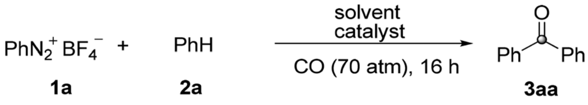
The effort was initiated by using phenyl diazonium tetrafluoroborate **1a** with benzene **2a** as a model reaction in the presence of Eosin Y (1 mol%) under irradiation with 5 W white LED light and a CO pressure of 70 atm in MeCN at room temperature. The desired benzophenone **3aa** was formed in 74% yield after 16 h (Table 1, entry 1). Interestingly, the yield of **3aa** dramatically enhanced to 82% when the reaction was performed with 5 W green LED light (Table 1, entry 2). Extensive screening of solvents revealed that MeCN provided the best results (Table 1, entries 2–5). In addition to Eosin Y, other organic dyes such as Fluorescein, Rhodamine B and Rose Bengal (RB) were less active in this acylation process (Table 1, entries 6–8). Lower pressures of CO resulted in low conversion (Table 1, entry 9). However, the reaction did not take place in the absence of either the visible-light photoredox catalysts (Table 1, entry 10) or additional visible light (Table 1, entry 11).

With the optimal reaction conditions established, we applied the above visible-light photocatalysis protocol to a range of both aryl diazonium salts **1** and (hetero)arenes **2** to investigate the scope. The scope of aryldiazonium salts **1** was initially explored in the presence of benzene **2a**, Eosin Y (1 mol%) under irradiation with 5 W green LED light and a CO pressure of 70 atm in MeCN at room temperature. As summarized in Table 2, this visible-light-induced acylation process displayed high functional-group tolerance and proved to be a general method for the preparation of aryl ketones. Aryl diazonium salts bearing electron-donating groups at the *para* position of the phenyl ring, such as methyl and methoxyl, proceeded smoothly in the reaction to give the corresponding aryl ketones **3ab–3ac** in good yields (Table 2, entries 1 and 2). However, a substituent at the *ortho* position of the phenyl ring gave the corresponding product **3ad** with a decreasing yield (Table 2, entry 3). These results indicated that the steric effects affected the efficiency of the reactions. When using the *meta*-substituted aryl diazonium salts as the substrate, the corresponding aryl ketone **3ae** was formed in 70% yield (Table 2, entry 4). Electron-withdrawing-group-substituted aryl diazonium salts, such as **1f–1i**, were also well tolerated in the reaction to afford the corresponding aryl ketones **3af–3ai** in 59–77% yields (Table 2, entries 5–8). These results indicate that the electronic nature of the aryl diazonium salts has little influence on the acylation process. Aryl diazonium salt with a naphthyl group (**1j**) also participated in this visible-light-induced acylation process, affording the desired product in 62% yield (Table 2, entry 9).

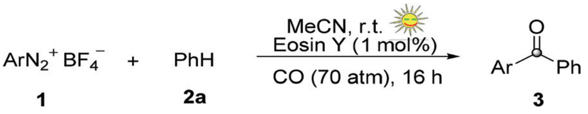
Table 1 Optimization of the reaction conditions[a]

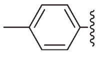
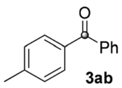
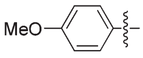
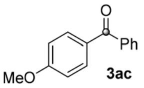
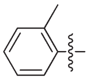
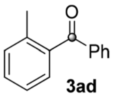
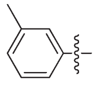
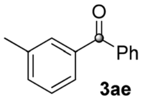
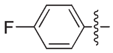
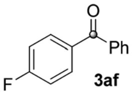
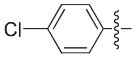
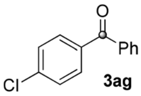
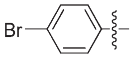
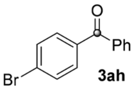
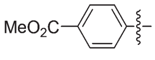
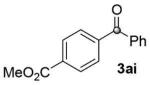
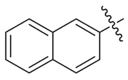
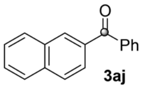


Entry	Catalyst	Solvent	Yield[b](%)
1	Eosin Y	CH_3CN	74
2[c]	Eosin Y	CH_3CN	82
3	Eosin Y	DMSO	63
4	Eosin Y	THF	21
5	Eosin Y	EtOAc	16
6	Fluorescein	CH_3CN	56
7	Rhodamine B	CH_3CN	31
8	RB	CH_3CN	22
9[d]	Eosin Y	CH_3CN	73
10	None	CH_3CN	0
11[e]	Eosin Y	CH_3CN	0

[a] Reaction conditions: **1a** (0.3 mmol), **2a** (0.3 mmol), catalyst (1 mol%), solvent (2.0 mL), room temperature, CO (70 atm), 5 W white LED light for 16 h. [b] Isolated yield. [c] 5 W green LED light. [d] CO (60 atm). [e] In the dark.

Table 2 Scope of aryldiazonium salts **1**[a]

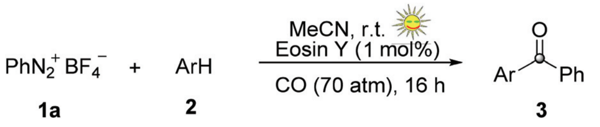


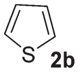
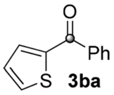
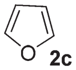
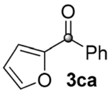
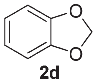
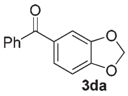
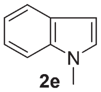
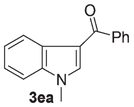
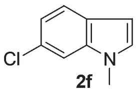
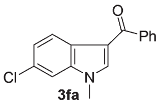
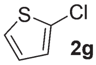
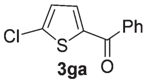
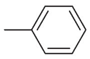
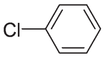
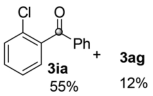
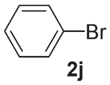
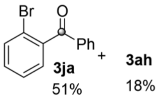
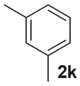
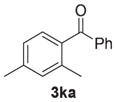
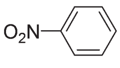
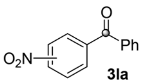
Entry	Aryldiazonium salts **1**	Aryl ketone **3**	Yield[b] (%)
1	 **1b**	 **3ab**	71
2	 **1c**	 **3ac**	68
3	 **1d**	 **3ad**	56
4	 **1e**	 **3ae**	70
5	 **1f**	 **3af**	77
6	 **1g**	 **3ag**	64
7	 **1h**	 **3ah**	75
8	 **1i**	 **3ai**	59
9	 **1j**	 **3aj**	62

[a] Reaction conditions: **1** (0.3 mmol), **2a** (0.3 mmol), Eosin Y (1 mol%), MeCN (2.0 mL), room temperature, CO (70 atm), 5 W green LED light for 16 h. [b] Isolated yield.

The visible-light-induced acylation was also tested on several other (hetero)arenes. The reaction was particularly effective with electron-rich aromatic rings. Heteroaromatic substrates **2b**–**2e** underwent this reaction to furnish the corresponding products in 63%–84% yields (Table 3, entries 1–4). To highlight the utility of this transformation, the electron-deficient heteroarenes **2f**–**2g** were subjected to the standard reaction conditions. The desired products were obtained in moderate yields (Table 3, entries 5 and 6). When toluene **2h** was employed, the reaction afforded the two regioisomers **3ab** and **3ad** in 61% and 14% yield, respectively (Table 3, entry 7).

Table 3 Scope of (hetero)arenes **2**[a]



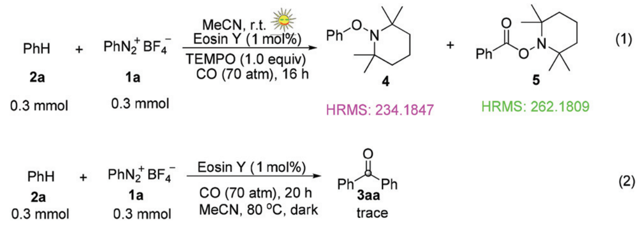
Entry	(Hetero)arenes 2	Aryl ketone 3	Yield[b] (%)
1	 **2b**	 **3ba**	84
2	 **2c**	 **3ca**	77
3	 **2d**	 **3da**	63
4	 **2e**	 **3ea**	82
5	 **2f**	 **3fa**	66
6	 **2g**	 **3ga**	54
7[c]	 **2h**	**3ab** + **3ad** 61% 14%	75
8[c]	 **2i**	 **3ia** 55% + **3ag** 12%	67
9[c]	 **2j**	 **3ja** 51% + **3ah** 18%	69
10	 **2k**	 **3ka**	51
11	 **2l**	 **3la**	0

[a] Reaction conditions: **1a** (0.3 mmol), **2** (0.3 mmol), Eosin Y (1 mol%), MeCN (2.0 mL), room temperature, CO (70 atm), 5 W green LED light for 16 h. [b] Isolated yield. [c] GC yield.

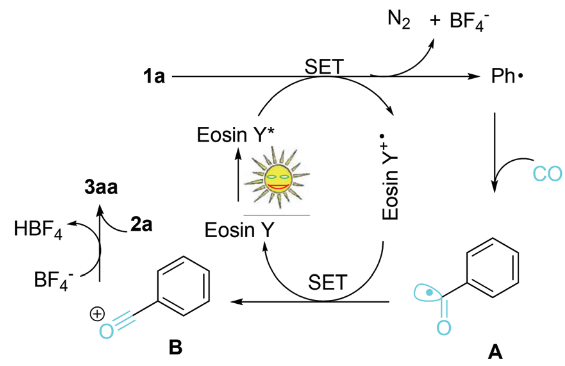
This visible-light-induced acylation protocol could also be applied to substrates **2i**–**2j** (Table 3, entries 8 and 9). Importantly, the polysubstituted benzene derivative **2k** gave the desired product **3ka** in good yield (Table 3, entry 10). Unfortunately, nitrobenzene did not deliver the corresponding ketone under the same reaction conditions (Table 3, entry 11).

To gain an insight into the course of the reaction, we conducted a series of control experiments.[6b,6c] When a radical-trapping reagent, 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) (1.0 equiv.), was added to the model reaction, no aryl ketone was obtained (Scheme 2, eqn (1)). These results suggest that the photoreaction proceeds *via* a radical pathway. Furthermore, the product yields severely dropped when no photocatalyst was present in the reaction and/or under dark conditions. Reactions in the dark and at increased temperatures (up to 80 °C) gave no desired product (Scheme 2, eqn (2)), which excludes homolytic bond cleavage of the starting material to an aryl radical under these conditions.

On the basis of these preliminary results, and those of previous studies,[6,9–11] we propose the mechanism shown in Scheme 3. Initially, photoexcitation of Eosin Y by visible light generates excited [Eosin Y*]. Then the electron-deficient phenyl diazonium tetrafluoroborate **1a** accepts one electron from the excited [Eosin Y*]. This single-electron transfer (SET) results in the generation of a phenyl radical ($Ph^•$) and the oxidized dye radical cation [Eosin $Y^{+•}$]. The resulting phenyl radical ($Ph^•$) is rapidly trapped by CO to give a benzoyl radical **A**. Further oxidation of **A** by [Eosin $Y^{+•}$] results in the benzylidyneoxonium **B**. Finally, electronic trapping of **B** by benzene gives the desired aryl ketone **3aa**.



Scheme 2 Control experiment.



Scheme 3 Plausible mechanism.

In summary, we have developed a metal-free and base-free carbonylation reaction by photoredox catalysis with green light. Mechanistic studies support the sequential operation of SET reduction, carbonylation, and back electron transfer to give acylium cations. Aryl ketones can be prepared from arene diazonium salts, CO, and (hetero)arenes at room temperature under irradiation with visible light. Most importantly, simple and readily available Eosin Y emerges as an efficient catalyst, rather than a metal catalyst, which is often expensive and is required to be completely removed from products, especially in the synthesis of pharmaceutical compounds. Further investigations of the mechanism of the reaction and its application are ongoing in our laboratory.

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Notes and references

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