Visible-Light Photoredox-Catalyzed α-Allylation of α-Bromocarbonyl Compounds Using Allyltrimethylsilane

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The development of a greener allylation reagent for α-allylation of carbonyl compounds is of great necessity. Here we present allyltrimethylsilane as a novel allylation reagent in the photoredox-catalyzed α-allylation of carbonyl compounds such as ketones, esters, and amides. The reaction process shows good functional group tolerance and generates a good yield of the product. The reaction mechanism is a radical-mediated reaction by photo-induced single electron transfer.

Keywords: Allylation, α-Bromocarbonyl compounds, Visible-light, Photoredox catalysis, SET

Carbonyl and allylic groups are among the most important functional groups in organic synthesis because they can easily be converted to other functional groups and applied in carbon–carbon bond-forming reactions.[1] Thus, the α-allylation of carbonyl compounds has been intensely researched in organic chemistry.[2] A common example of classical allylation reactions is the allylation of enolates with electrophilic allyl halides. As a matter of fact, enolate chemistry is moisture sensitive and has scale-up limitations due to the use of a strong base in generating enolate. Furthermore, Pd-catalyzed allylation of nucleophiles with allylic halides, acetates, and carbonates (Tsuji–Trost reaction) has proved to be a mild method for α-allylation of carbonyl compounds (Scheme 1(a)).[2a, 3] This method is widely used due to its mild reaction conditions, wide substrate range, and stereochemical control. However, this reaction uses stabilized enolate such as an anion of malonate, but enolates from ketones, esters, and amides are rarely used.

An alternative strategy for α-allylation of carbonyl compounds is a radical-mediated reaction. With respect to anion chemistry, a radical-mediated reaction is less sensitive to moisture, acidic proton, and electrophilic functional groups but environmentally unsafe when toxic reagents such as organotin or selenium are used. Recently, visible light photoredox catalysis is an emerging research area in organic chemistry because of its environmental sustainability.[4] Visible photocatalysts can generate radical intermediates used in carbon–carbon or carbon–heteroatom bond formation reactions via electron transfer mechanisms. The radical in the α-position of the carbonyl group is electrophilic[5] and is highly reactive with electron-rich alkenes. The generation of radical intermediates from α-halocarbonyl compounds using a visible light photocatalyst and addition reactions of the α-carbonyl radicals with various alkenes have been well studied.[4b, 6]

This study investigates the visible light photoredox-catalyzed α-allylation of carbonyl compounds using α-halocarbonyl compounds as α-carbonyl radical precursors. Allyltributyltin is a commonly used reagent for allylation in classical radical reactions[7] and UV-mediated photochemistry (Scheme 1(b)).[8] Recently, Reiser and coworkers investigated the potential use of allyltributyltin in visible light photocatalytic reactions.[9] Despite reports on several reagents from previous studies, the development of a novel allylation reagent is still required due to toxicity. Recently, Yasuda and coworkers developed allyltrifluoroborate as a new-type allylation reagent for α-allylation of carbonyl compounds using eosin Y as photocatalyst (Scheme 1 (b)).[10] Our research group is interested in using organosilicon groups in photoredox catalysis and recently, we developed organosilicon groups as radical precursors in photocatalytic reactions.[11] Also, we investigated the potential use of allyltrimethylsilane as a novel allylation reagent for α-allylation of carbonyl compounds because of its neutral, stable, and nontoxic nature. Reiser and coworkers reported allyltrimethylsilane as an allylation reagent in photoredox-catalyzed α-allylation of carbonyl compounds.[12] However, their study only investigates three samples using diethyl bromomalonate as α-carbonyl radical's precursor. Here we report the visible light photoredox-catalyzed α-allylation of various carbonyl compounds using allyltrimethylsilane (Scheme 1(c)).

In the initial study, we conducted α-allylation of 2-bromoacetophenone **1a** and allyltrimethylsilane **2a** using *fac*-Ir(ppy)$_3$ as a photoredox catalyst in various solvents under blue light emitting diodes (LEDs) irradiation. This reaction produced a coupled ketone **3a** with the best yield in MeCN among several solvents (Table 1 entries 1, 5–7). In the catalyst screening, we observed that other

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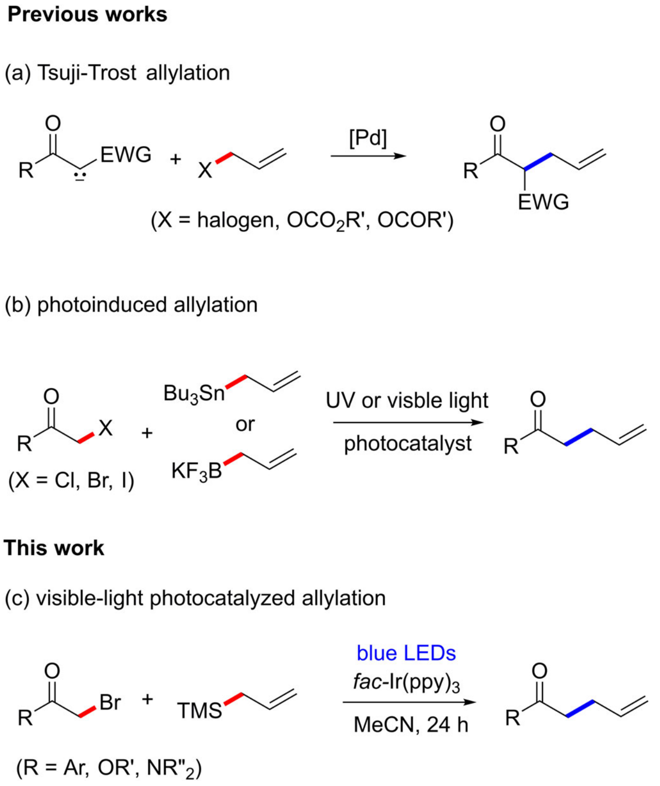
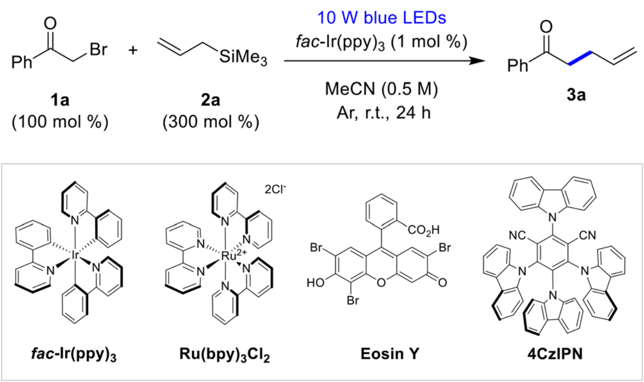
[†] These authors contributed equally to this work.



Scheme 1. α-Allylation of carbonyl compounds.

Table 1. Optimization of reaction conditions.[a]



entry	deviation from standard conditions	yield (%)[b]
1	none	80[c]
2	using eosin Y (1 mol %)	nd
3	using 4CzIPN (1 mol %)	nd
4	using Ru(bpy)$_3$Cl$_2$ (1 mol %)	nd
5	EtOAc instead of MeCN	13
6	DCM instead of MeCN	13
7	DMF instead of MeCN	17
8	MeCN (0.2 M)	53
9	MeCN (0.1 M)	20
10	without PC	nd
11	in the dark	nd

nd, not detected.

[a] Reaction conditions: **1 a**, **2 a**, catalyst, solvent with 10 W blue LEDs (452 nm) irradiated at room temperature for 24 h under argon atmosphere in a pressure tube.

[b] Yield determined by ^{1}H NMR (internal standard: methyl benzoate).

[c] Isolated yield by flash column chromatography.

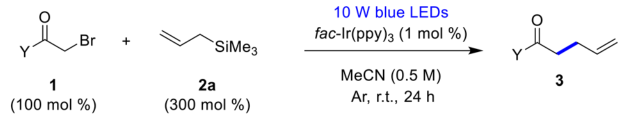
photocatalysts did not produce the desired product **3a** (Table 1 entries 1–4). Furthermore, the results show that a high concentration of acetonitrile provided better yields than low concentrations (Table 1 entries 1, 8–9). Finally, we observed that the optimization conditions of the reaction of 2-bromoacetophenone **1a** with three equivalents of allyltrimethylsilane **2a** in the presence of 1.0 mol% of *fac*-Ir(ppy)$_3$ in 0.5 M of acetonitrile at room temperature irradiated at 10 W blue LEDs under an argon atmosphere produced the desired products **3a** with 80% yield (Table 1, entry 1). The control experiments revealed the essential role of the visible light photoredox catalyst in the reaction (Table 1, entries 10–11).

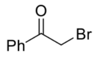
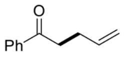
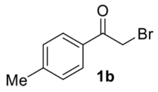
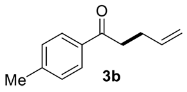
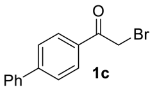
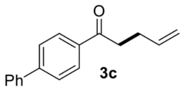
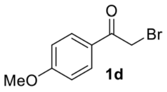
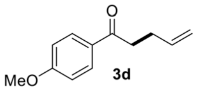
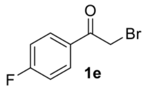
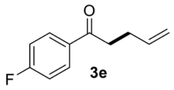
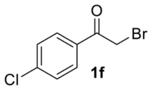
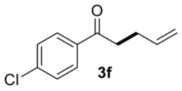
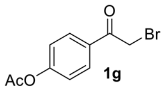
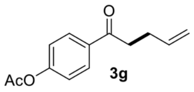
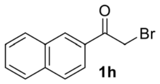
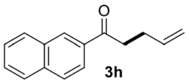
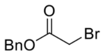
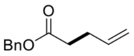
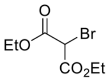
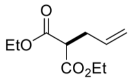
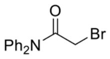
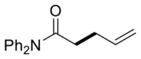
Using the optimized reaction conditions, we explored the scope of α-allylation of carbonyl compounds employing different α-halocarbonyl compounds (Table 2). Generally, the reaction exhibited a broad substrate scope and good functional group tolerance. Also, a series of aryl ketones produced the corresponding allylation products in good yields (**3a-h**). Functional groups such as alkyl (**3b**), aryl (**3c, h**), alkoxy (**3d**), halogen (**3e, f**), and ester (**3g**) were well-tolerated. Furthermore, the results showed no particular relationship between the electronic environment of the ketone and the yield of the product. Also, the naphthene-substituted ketone (**3h**) generates the corresponding product in good yield. Additionally, the substrate scope was successfully extended to α-bromoesters (1i, j) and α-bromoamide (1k), in which the esters and amides showed similar reactivity to ketones. Substrate investigations showed that α-allylation of ketones, esters, and amides were efficient in photoredox catalysis.

The reaction mechanism was also investigated. We predicted the mechanism that governed the reduction of 2-bromoacetophenone 1a, and the α-carbonyl radical was generated by an excited photocatalyst. In literature, the reduction potential of 2-bromoacetophenone **1a** is −0.49 V vs. SCE in MeCN,[13] which implies that the excited photocatalyst [*fac*-Ir(ppy)$_3$*] can be reduced **1a.**[14] Moreover, Stern–Volmer fluorescence quenching experiments were conducted with 2-bromoacetophenone **1a** and allyltrimethylsilane **2a**. The results showed that only **1a** quenched the excited photocatalyst, whereas **2a** did not (Figure 1). Additionally, a radical trapping experiment was conducted using 2,2,6,6-tetramethyl-1-piperidyloxy (TEMPO) as a radical trapping reagent. No product was observed in the presence of TEMPO except a radical-coupled product **4a**, thus indicating a radical-based pathway (Scheme 2(a)).

Based on our control experiments and literature[6c, 9, 12], we proposed the reaction mechanism depicted in Scheme 2 (b). The *fac*-Ir(ppy)$_3$ was excited by irradiating with blue LEDs and the excited photocatalyst reduces 2-

Table 2. Substrate scope of various α-Bromocarbonyl compounds.[a]



entry	α-bromocarbonyl compouns **1**	product **3**	yield (%)
1	 **1a**	 **3a**	80
2	 **1b**	 **3b**	63
3	 **1c**	 **3c**	55
4	 **1d**	 **3d**	48
5	 **1e**	 **3e**	61
6	 **1f**	 **3f**	55
7	 **1g**	 **3g**	60
8	 **1h**	 **3h**	73
9	 **1i**	 **3i**	67
10	 **1j**	 **3j**	70
11	 **1k**	 **3k**	58

[a] Reaction conditions as given in Table 1, entry 1; reported yields are for isolated material. See Supporting information for details.

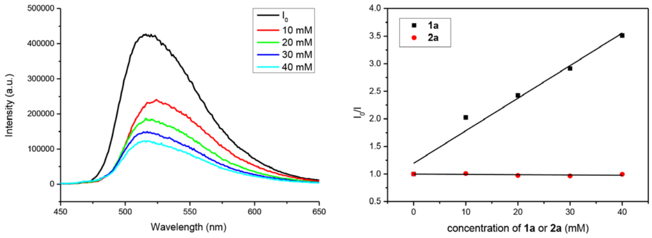
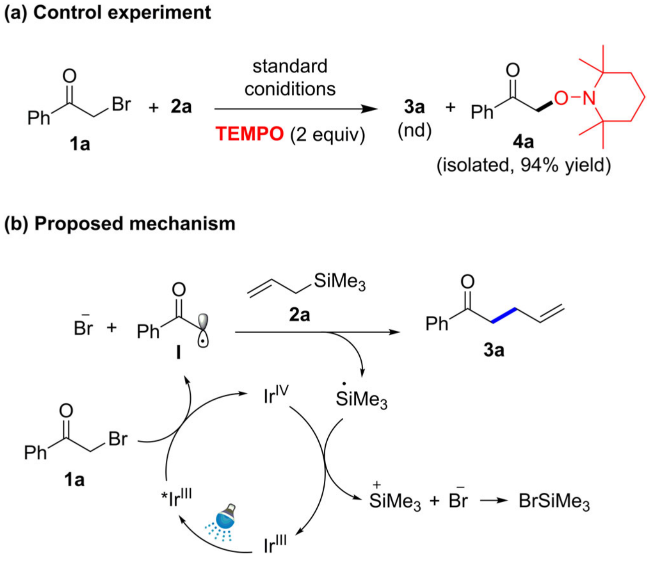


Figure 1. Luminescence quenching of *fac*-Ir(ppy)$_3$ by **1a** (left). Stern–Volmer plot (right).



Scheme 2. Control experiment and proposed reaction.

bromoacetophenone **1a**. Subsequently, Br$^-$ was released from the reduced **1a**, thereby forming a α-carbonyl radical intermediate **I**. The radical addition of an electrophilic α-carbonyl radical **I** and an electron-rich alkene **2a** produces **3a** via the elimination of trimethylsilyl radical. The catalyst cycle was completed via the oxidation of trimethylsilyl radical by the oxidized photocatalyst (Ir^{IV}).

In conclusion, we developed allyltrimethylsilane as a novel allyl reagent in the photoredox catalytic α-allylation of carbonyl compounds such as ketones, esters, and amides. The developed allylation reaction generates products with good tolerance and yields for different functional groups. The reaction mechanism consists of the generation of α-carbonyl radicals and radical addition reaction by photocatalyzed single electron transfer mechanism. This study demonstrates the development of a new strategy for the allylation of α-carbonyl compounds using allylsilanes.

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Supporting Information. Additional supporting information may be found online in the Supporting Information section at the end of the article.

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