PAPER

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Photoinduced successive oxidative ring-opening and borylation of indolizines with NHC–boranes†

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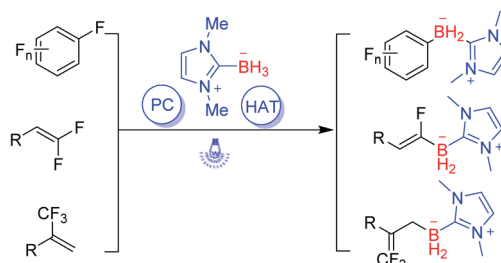and Xiang Liu [iD] *

A facile photoinduced successive oxidative ring-opening and borylation of indolizines with NHC–boranes *via* a one-pot method has been unveiled. This photo-promoted strategy enables the formation of unsaturated NHC–boryl carboxylates under transition metal-free and radical initiator-free conditions. A wide array of pyridine-containing NHC–boryl carboxylates were directly prepared in moderate to good yields. This work contributes to a better understanding of the reactivity and photo-behavior of both indolizines and NHC–boranes.

Organoboron compounds are of vital significance in modern organic synthesis, and they also show great promise in luminescent materials, covalent organic frameworks, and pharmaceutical industries.[1–3] *N*-Heterocyclic carbene (NHC)–boranes have recently gathered a lot of attention in building various C–B bonds.[4] In fact, as an increasingly popular and reliable boron source, NHC–boranes have the typical characteristics of being: (1) weaker B–H bonds compared to other LB·BH$_3$; (2) stable solids under ambient conditions; (3) easily prepared on the gram scale. Owing to these advantages, many borylation methods *via* NHC–boryl radicals have been extensively exploited.[5] Among them, photochemical borylations with high efficiency have become a powerful, practical, and economic strategy.[6] For example, Xie and Zhu reported a photoinduced inverse hydroboration of imines and alkenes with NHC–boranes.[7] Visible-light-induced selective defluoroborylation of fluorinated alkenes have been well established by Wu, Wang, Yang, and co-workers (Scheme 1a).[8] Recently, Curran reported an Ir-catalyzed 1,4-hydroboration of electron-deficient arenes with NHC–BH$_3$ under CFL irradiation (Scheme 1b).[9] Very recently, Wang, Liang, and Zhu disclosed a photoinduced regio- and stereoselective fluorocarboborylation of alkenes.[10] However, direct C–H borylation of *N*-heterocycles especially for indolizines utilizing NHC–boranes have not been successfully developed.
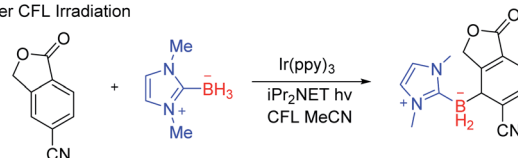
Indolizines, which contain 10 π-electrons, are isoelectronic with indole. So, they represent an important class of *N*-heterocycles and are widely applied in the field of material science.[11] We have long been committed to developing green and

sustainable new methods for C–H bond functionalization of indolizines to synthesize indolizines derivatives.[12] In 2019, we disclosed visible-light-induced intermolecular [3 + 2] alkenylation–cyclization of indolizines to obtain pyrrolo[2,1,5-*cd*]indolizines.[13] Very recently, we successfully constructed pyrrolo
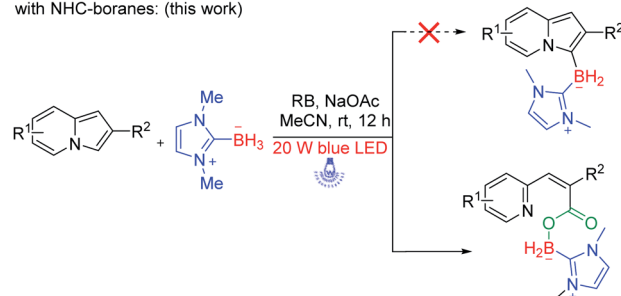
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Scheme 1 Visible light-induced borylation with NHC–BH$_3$.

[2,1,5-*cd*]indolizine rings *via* visible-light-induced intermolecular [3 + 2] cycloaddition of indolizines and alkynes.[14] Considering the great value of organoboron compounds, we expected that direct C–H borylation of indolizines with NHC–boranes would be realized *via* a clean photoredox system (Scheme 1c). However, the desired borylated indolizines were not observed *via* photoinduced C(sp^2)–H borylation of indolizines and NHC–boranes. It turned out that sequence photooxygenation–borylation of indolizines occurred, delivering the deconstructive NHC–boryl carboxylates, and this type of borane compound is rarely reported.[15] Herein, we disclose our unexpected findings that successive oxidative ring-opening and borylation of indolizines with NHC–boranes was accomplished under the irradiation of visible light. A variety of NHC–boryl carboxylates could be afforded through this manner (Scheme 1c).

To optimize the conditions, we employed 2-phenylindolizine **1a** and NHC–borane **2a** as the model substrates for reaction development (Table 1). Initially, rose bengal (RB) was used as the photosensitizer in MeCN. The unexpected product **3a** was obtained in 36% yield after reaction proceeded at room temperature for 12 h with a 20 W blue LED (455 nm) (Table 1, entry 1). After this, we tried to optimize the reaction using other photosensitizers. Eosin Y, rhodamine 6G, fluorescein, and Ir(ppy)$_3$ were investigated, and the results indicated that none

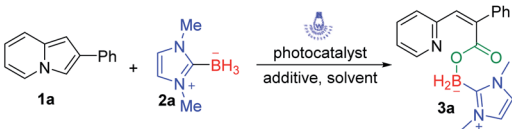of them promoted this reaction better than RB under blue LED irradiation (Table 1, entries 2–5).

Then, we turned our attention to examining the effect of different additives, such as Cs$_2$CO$_3$, K$_2$CO$_3$, DBU, DABCO, and NaOAc (Table 1, entries 6–10). Among them, NaOAc gave the best result, providing the target NHC–boryl carboxylate **3a** in 72% yield (Table 1, entry 10). Encouraged by this result, we next tried to test the reaction using various solvents (Table 1, entries 10–14). It was found that only MeCN gives the target product **3a** in good yield (entry 10), and other solvents led to lower yield. In addition, we verified that the product was not obtained without photosensitizer and light (Table 1, entries 15 and 16). We then examined the effect of the atmosphere on this ring-opening and borylation reaction. After filling the reaction with N$_2$ and O$_2$, respectively, the results show that reactions performed at O$_2$ atmosphere produce product **3a** normally but those filled with N$_2$ do not (Table 1, entries 17 and 18). We can hardly observe the product in the presence of Cu(I) or Cu(II) salts (Table 1, entries 19 and 20). Thus, the optimal reaction conditions were achieved by adding 5 mol% RB and 2 equiv. of NaOAc in MeCN at room temperature for 12 h under 20 W blue LED.

With a set of optimized reaction conditions in hand, we next examined the substrate scope with respect to various indolizine derivatives (Scheme 2). The reaction proceeded well under the standard reaction conditions and afforded the corresponding NHC–boryl carboxylates **3a–3aa** in 56–75% yields. For example, alkyl substituents (–Me or –Et) and electron-donating substituents (–OMe), electron-withdrawing substituents (–Br) substituted on the indolizine ring did not affect the reactivity, and they were effective to afford NHC–boryl carboxylates under the optimized conditions (**3b–3g**). A series of various functional groups substituted on the ortho, para and meta position of benzene ring were compatible too (**3h–3r**). We next tested the reactivity of the substrates that are dichlorosubstituted on benzene rings, and the desired products **3s** and **3t** were obtained in 70% and 72% yields. Furthermore, when the model substrate **1a** was replaced by 2-(4-fluorophenyl)-8-methylindolizine **1u**, 2-(4-chlorophenyl)-8-methylindolizine **1v**, and their analogues(**1w–1z**), respectively, the corresponding products (**3u–3z**) were obtained in good yields as well. The molecular structure of the product **3w** was determined by X-ray crystallography (CCDC number: 2116778) (Scheme 3). In addition, the reaction of 2-(naphthalen-2-yl) indolizine **1aa** with **2a** was also performed to give the desired NHC–boryl carboxylate **3aa** in 70% yield.

Next, we further turned our attention to exploring the NHC–borane of this photoinduced successive oxidative ring-opening and borylation reaction. We employed (1-isopropyl-3-methyl-1*H*-imidazol-3-ium-2-yl) trihydroborate **2b** instead of **2a** to participate in photoinduced transformation (Scheme 4). It was pleased to find that the desired NHC–boryl carboxylate **4a** was obtained in 71% yield under the standard reaction conditions.

After the substrate scope exploration of this transformation, the scale-up experiment was studied. We enlarged the model substrate **1a** to 1.0 mmol with **2a** (2 mmol) under the irradiation with a 20 W blue LED for 12 h, and we found that boryl carboxylate product **3a** was still produced though the yield has a small decrease (49%) (Scheme 5).

**Table 1** Optimization of the reaction conditions^a

Entry	Photocatalyst	Additive	Solvent	Yield^b (%)
1	Rose bengal	—	CH$_3$CN	36
2	Eosin Y	—	CH$_3$CN	18
3	Rhodamine 6G	—	CH$_3$CN	n. d.
4	Fluorescein	—	CH$_3$CN	n. d.
5	Ir(ppy)$_3$	—	CH$_3$CN	23
6	Rose bengal	Cs$_2$CO$_3$	CH$_3$CN	51
7	Rose bengal	K$_2$CO$_3$	CH$_3$CN	38
8	Rose bengal	DBU	CH$_3$CN	21
9	Rose bengal	DABCO	CH$_3$CN	14
10	**Rose bengal**	**NaOAc**	**CH$_3$CN**	**72**
11	Rose bengal	NaOAc	THF	68
12	Rose bengal	NaOAc	DCE	60
13	Rose bengal	NaOAc	Toluene	45
14	Rose bengal	NaOAc	DMSO	51
15	—	NaOAc	CH$_3$CN	n. d.
16^c	Rose bengal	NaOAc	CH$_3$CN	n. d.
17^d	Rose bengal	NaOAc	CH$_3$CN	70
18^e	Rose bengal	NaOAc	CH$_3$CN	n. d.
19^f	Rose bengal	NaOAc	CH$_3$CN	n. d.
20^g	Rose bengal	NaOAc	CH$_3$CN	n. d.

^{a} Standard conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), photocatalyst (5 mol%), additive (0.4 mmol), solvent (2 mL), and irradiation with a 20 W blue LED for 12 h, air, n. d. = not detected. ^{b} Isolated yields. ^{c} Without light. ^{d} Under O$_2$. ^{e} Under N$_2$. ^{f} CuI (5 mol%). ^{g} Cu(OAc)$_2$ (5 mol%).
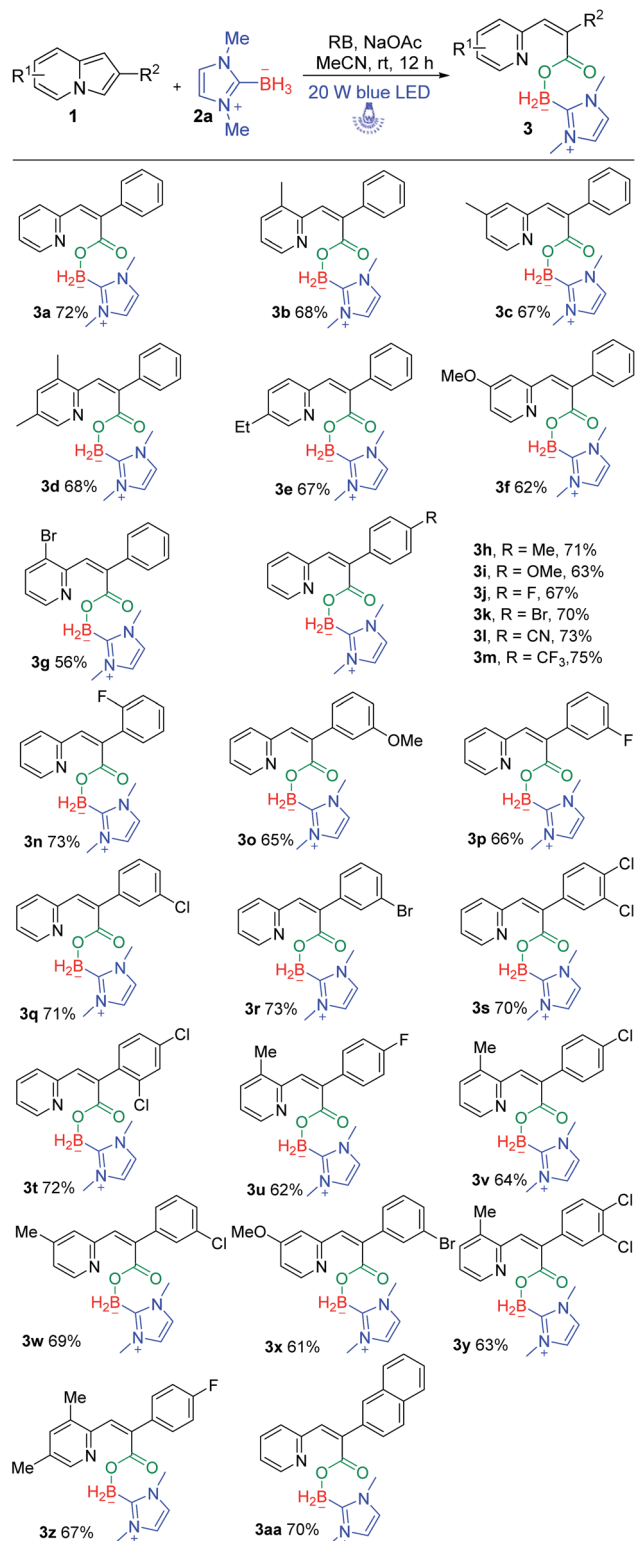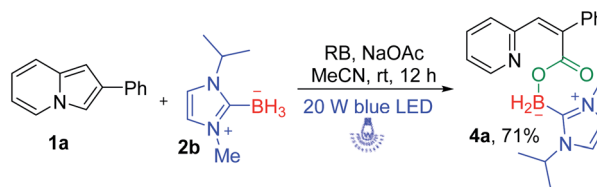
Scheme 2 Substrate scope of 2-phenylindolizine[a]. [a]Reaction conditions: **1** (0.2 mmol), **2a** (0.4 mmol), RB (5 mol%), NaOAc (0.4 mmol), MeCN = 2 mL, irradiation with a 20 W blue LED for 12 h, air, isolated yield.

To gain some insight into the mechanism of this transformation, several controlled experiments were designed and carried out (Scheme 6). The yield of **3a** dropped sharply when
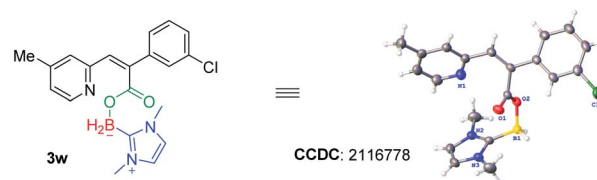
**Scheme 3** Crystal structure of compound **3w**.

Scheme 4 Substrate scope of NHC–borane[a]. [a]Reaction conditions: **1a** (0.2 mmol), **2b** (0.4 mmol), RB (5 mol%), NaOAc (0.4 mmol), MeCN (2 mL), and irradiation with a 20 W blue LED for 12 h. Isolated yield.

the reaction of **1a** with **2a** was conducted in the presence of a radical scavenger 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) or 2,6-di-*tert*-butyl-4-methylphenol (BHT).

Based on our experimental results and literature reports,[13,16] the possible mechanisms for this reaction of the ring-opening and borylation of indolizines have been depicted in Scheme 7. Under visible-light irradiation, the ground state of RB is converted to the excited RB* *via* the energy transfer, which interacts with $^3O_2$ to give the $^1O_2$ and RB to realize the photoredox cycle. In the presence of singlet oxygen, **1a** readily forms the perepoxide exciplex **A** which is easily transferred to peroxidic zwitterion intermediate **B**. Subsequently, the intermediate **B** produced the intermediate **C** by intramolecular electron transfer. Then the trace amount of water in the solvent attack at C3 of intermediate **C** and cleavage the C–N bond to give the intermediate **D**, which would get rid of a molecule of water to generate acrylic acid intermediate **E**. Finally, the intermolecular reaction of acrylic acid intermediate **E** to NHC–borane **2a** furnishes the target product **3a**.
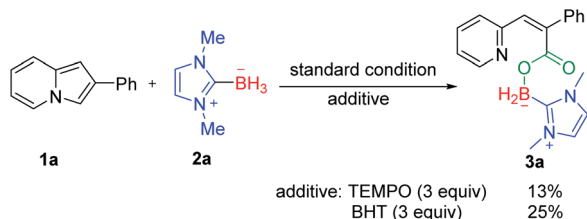
Conclusions

In summary, we have developed an environmentally benign visible-light-induced ring-opening and borylation of indolizines strategy, which is benign using visible light as energy source
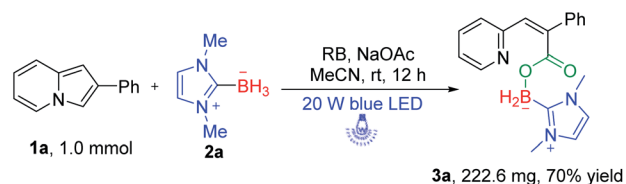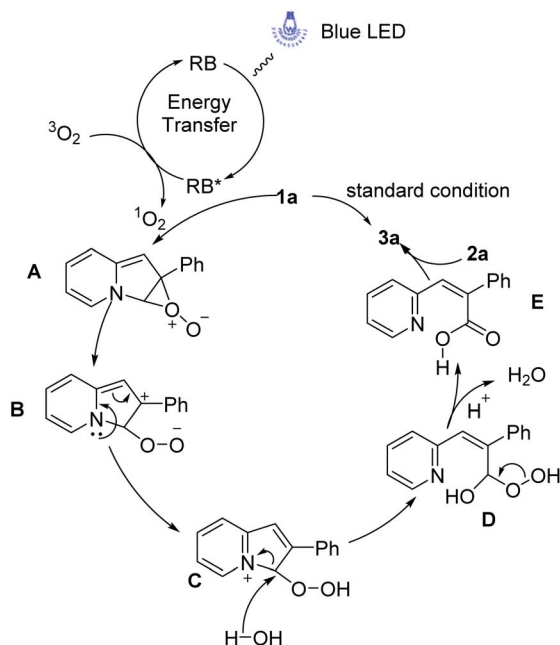
Scheme 5 Scale-up experiment[a]. [a]Reaction conditions: **1a** (1.0 mmol), **2a** (2.0 mmol), RB (5 mol%), NaOAC (2 mmol), MeCN (10 mL), and irradiation with a 20 W blue LED for 12 h.

Scheme 6   Control experiment.

Scheme 7   Plausible mechanistic pathway.

and air as oxidant. A broad range of ring-opening and borylation of indolizines derivatives were conveniently synthesized in moderate to good yields with good functional group tolerance. Furthermore, other ring-opening reactions of indolizines are ongoing and will be reported in the near future.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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