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Communication

Consecutive visible-light photoredox decarboxylative couplings of adipic acid active esters with alkynyl sulfones leading to cyclic compounds

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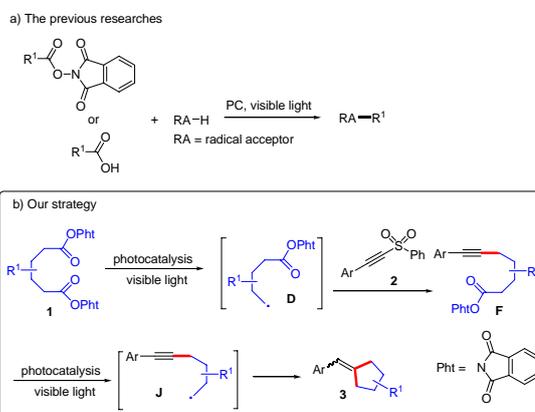
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Novel and efficient consecutive photoredox decarboxylative couplings of adipic acid active esters (bis(1,3-dioxoisindolin-2-yl)-substituted hexanedioates) with substituted 1-(2-arylethynylsulfonyl)benzenes have been developed under visible-light photocatalysis. The successive photoredox decarboxylative C-C bond formation at room temperature afforded the corresponding cyclic compounds in good yields with tolerance of some functional groups.

Formation of carbon-carbon bonds is a fundamental and important chemical transformation in organic synthesis. However, it is a great challenge to develop consecutive formation of two C-C bonds using readily available starting materials under mild conditions. Carboxylic acids and their derivatives widely occur in organic molecules and natural products, and their chemical transformations provide diverse compounds.¹ For example, the decarboxylative strategy of carboxylic acids and their derivatives has provided some valuable reactions in organic synthesis,² such as Heck-type reactions,³ allylations,⁴ redox-neutral cross-coupling reactions,⁵ and oxidative arylations.⁶ Recently, visible-light photoredox catalysis has attracted much attention, and it has emerged as a powerful activation protocol in new chemical transformations.⁷ Correspondingly, some achievements have been gained on photoredox decarboxylative couplings of carboxylic acids and their derivatives were used as the radical precursors.⁸ DiRocco and coworkers have developed the use of stable organic acid peroxides activated by visible-light photoredox catalysis in the presence of Ir(III) catalysts, and the reactions effectively achieved the direct methyl-, ethyl-, and cyclopropylation of a variety of biologically active heterocycles.⁹ Tunge and coworkers have reported the decarboxylative allylation of amino alkanolic acids and their esters via the dual catalysis of Ir(ppy)₂(bpy)[BF₄] and Pd(PPh₃)₄.¹⁰ Organic carboxylic acid active esters¹¹ and free carboxylic acids¹² as the radical precursors have been used in the visible-light photoredox couplings in the presence of photocatalysts (PC) and radical acceptors (RA) (see Scheme 1a). More importantly, MacMillan and co-workers have developed a pioneering photoredox decarboxylative couplings of *N*-protected α -amino acids.¹³ To the best of our knowledge, there is no report on photoredox decarboxylative coupling of dicarboxylic acids and their derivatives thus far. Herein, we report consecutive visible-light photoredox couplings of substituted adipic acid active esters (Scheme 1b). Our strategy is

as follows: Treatment of bis(1,3-dioxoisindolin-2-yl)-substituted hexanedioate (**1**) under visible-light photocatalysis produces radical **D**, and intermolecular coupling (the first coupling) of **D** with alkynyl sulfone (**2**) provides **F**. Subsequently, photocatalysis of **F** forms radical **J**, and intramolecular coupling (the second coupling) of **J** affords the target product (**3**).

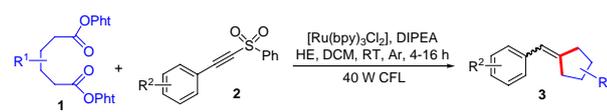


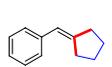
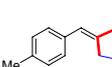
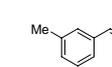
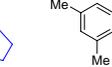
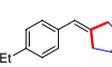
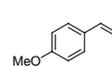
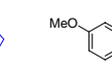
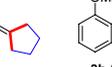
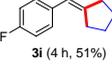
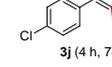
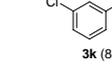
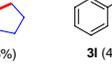
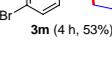
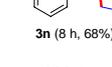
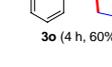
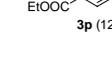
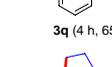
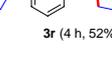
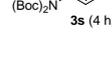
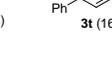
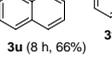
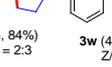
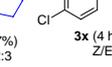
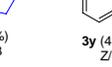
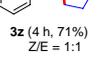
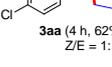
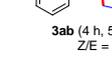
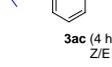
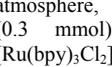
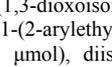
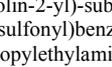
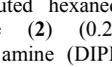
Scheme 1 (a) The previous photoredox decarboxylative couplings of carboxylic acid active esters or free carboxylic acids. (b) Our strategy on consecutive photoredox decarboxylative couplings of adipic acid active esters (**1**) with alkyne sulfones (**2**).

Consecutive photoredox decarboxylative couplings of bis(1,3-dioxoisindolin-2-yl)hexanedioate (**1a**) with 1-(2-phenylethynylsulfonyl)benzene (**2a**) was selected as the model reaction to optimize conditions including photocatalysts, solvents, atmosphere and time (see Table S1 in Supporting Information). The results showed that the optimal photoredox conditions are as follows: 1.0 mol% [Ru(bpy)₃]Cl₂ as the photocatalyst, 4.4 equiv of diisopropylethylamine (DIPEA) and 3.0 equiv of Hantzsch ester (HE) (relative to amount of **2a**) as the radical initiators and reductants in dichloromethane (DCM) at room temperature under argon atmosphere. After obtaining the optimized photoredox conditions, we investigated the substrate scope on consecutive decarboxylative couplings of various bis(1,3-dioxoisindolin-2-yl)-substituted hexanedioates (**1**) with 1-(2-arylethynylsulfonyl)benzenes (**2**) (Table 1). We first attempted various substituted 1-(2-arylethynylsulfonyl)benzenes (**2**) using bis(1,3-dioxoisindolin-2-yl)hexanedioate (**1a**) as the partner. Different substituted 1-(2-arylethynylsulfonyl)benzenes (**2**) displayed obviously different reactivity, and substrates **2** containing electron-donating groups gave higher yields than those containing electron-withdrawing groups. For example, alkyne

sulfones with methyl, ethyl, methoxyl on aryl rings (see **3b-h**) provided higher yields than those with ester groups (see **3p-r**). Alkyne sulfones containing biphenyl and naphthalene (see **3t** and **3u**) also donated the corresponding products in 52% and 66% yields, respectively. Other bis(1,3-dioxoisindolin-2-yl)-substituted hexanedioates (**1**) were investigated, and *cis*- and *trans*-form products were obtained in good yields (Note: *Z/E* ratios were determined by ^1H NMR) (see **3v-ac**). The consecutive visible-light photoredox decarboxylative couplings showed tolerance of some functional groups including ether (see **3f-h**, **3w** and **3ac**), C-F bond (see **3i**), C-Cl bond (see **3j-l**, **3x** and **3aa**), C-Br bond (see **3m-o**), esters (see **3p-r** and **3y**) and amide (see **3s**).

Table 1 Consecutive photoredox decarboxylative couplings of bis(1,3-dioxoisindolin-2-yl)-substituted hexanedioates (**1**) with alkynyl sulfones (**2**)^a

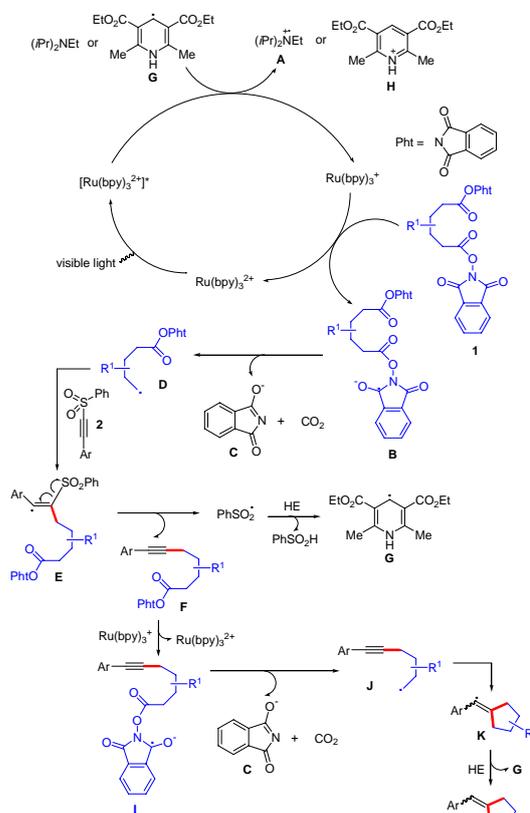


3 (Time, Yield ^b)			
			
3a (4 h, 90%)	3b (4 h, 73%)	3c (4 h, 76%)	3d (4 h, 71%)
			
3e (8 h, 67%)	3f (4 h, 97%)	3g (4 h, 66%)	3h (4 h, 80%)
			
3i (4 h, 51%)	3j (4 h, 74%)	3k (8 h, 56%)	3l (4 h, 65%)
			
3m (4 h, 53%)	3n (8 h, 68%)	3o (4 h, 60%)	3p (12 h, 45%)
			
3q (4 h, 65%)	3r (4 h, 52%)	3s (4 h, 44%)	3t (16 h, 52%)
			
3u (8 h, 66%)	3v (4 h, 84%) <i>Z/E</i> = 2:3	3w (4 h, 67%) <i>Z/E</i> = 2:3	3x (4 h, 56%) <i>Z/E</i> = 2:3
			
3y (4 h, 66%) <i>Z/E</i> = 2:3	3z (4 h, 71%) <i>Z/E</i> = 1:1	3aa (4 h, 62%) <i>Z/E</i> = 1:1	3ab (4 h, 56%) <i>Z/E</i> = 1:1
			
3ac (4 h, 66%) <i>Z/E</i> = 1:1			

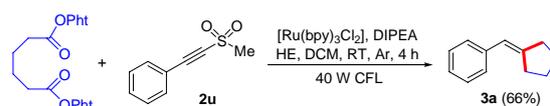
^a Reaction conditions: under irradiation of visible light and argon atmosphere, bis(1,3-dioxoisindolin-2-yl)-substituted hexanedioate (**1**) (0.3 mmol), 1-(2-arylethynylsulfonyl)benzene (**2**) (0.2 mmol), $[\text{Ru}(\text{bpy})_3\text{Cl}_2]$ (2 μmol), diisopropylethylamine amine (DIPEA) (0.88 mmol), Hantzsch ester (HE) (0.6 mmol), dichloromethane (DCM) (1.5 mL), temperature (rt, $\sim 25^\circ\text{C}$), time (4-16 h) in a sealed Schlenk tube. ^b Isolated yield. Boc = *tert*-butyloxycarbonyl.

In order to explore the visible-light photoredox decarboxylative mechanism, reaction of bis(1,3-dioxoisindolin-2-yl) hexanedioate (**1a**) with 1-(2-phenylethynylsulfonyl)benzene (**2a**) was performed in the presence of three equiv of 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) as the radical-trapping agent under the standard conditions, and the reaction did not work, which implied that the reaction underwent a free-radical intermediate process. In addition, PhSO_2H as by-product was

isolated from coupling **1a** and **2a** under the standard conditions, and its structure was confirmed by ^1H and ^{13}C NMR. Therefore, a plausible mechanism on the consecutive visible-light photoredox decarboxylative couplings is proposed in Scheme 2 according to the results above and the previous references.⁷⁻¹⁴ Irradiation of $[\text{Ru}(\text{bpy})_3]^{2+}$ with visible light leads to the oxidizing excited-state $[\text{Ru}(\text{bpy})_3]^{2+*}$ ($E_{1/2}^{*\text{III/I}} = +0.77\text{ V}$ vs SCE in MeCN ^{7a}), and the photoexcited catalyst accepts an electron from DIPEA ($E_{1/2}^{\text{red}} = +0.65\text{ V}$ vs SCE in MeCN ¹⁴) to provide $[\text{Ru}(\text{bpy})_3]^+$, in which DIPEA transforms into **A**. One electron in $[\text{Ru}(\text{bpy})_3]^+$ transfers to phthalimide in **1** produces radical **B** regenerating catalyst $[\text{Ru}(\text{bpy})_3]^{2+}$, and subsequent leaving of phthalimide anion (**C**) and carbon dioxide from **B** gives radical **D**. Addition of **D** to alkyne sulfone (**2**) leads to radical **E**, and homolytic cleavage C-S bond in **E** donates **F** releasing radical PhSO_2^\cdot . Reaction of PhSO_2^\cdot with Hantzsch ester (HE) provides PhSO_2H and radical **G**,^{7a} and treatment of the photoexcited catalyst with **G** gives $[\text{Ru}(\text{bpy})_3]^+$ and **H**. Similarly, treatment of **F** with $[\text{Ru}(\text{bpy})_3]^+$ produces radical **I** regenerating catalyst $[\text{Ru}(\text{bpy})_3]^{2+}$, and elimination of **C** and carbon dioxide from **I** affords radical **J**. Intramolecular cyclization of **J** forms radical **K**. Finally, treatment of **K** with HE generates the desired target product (**3**) liberating **G**.



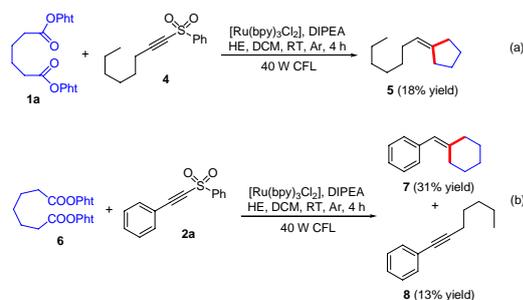
Scheme 2 A plausible mechanism on the consecutive visible-light photoredox decarboxylative couplings.



Scheme 3 Reaction of ((methylsulfonyl)ethynyl)benzene (**2u**) with **1a** under the standard conditions.

Reaction of ((methylsulfonyl)ethynyl)benzene (**2u**) with **1a** was attempted under the standard conditions, and the target product (**3a**) was obtained in 66% yield (Scheme 3).

We attempted 1-(oct-1-ynylsulfonyl)benzene (**4**) as the radical accepter under the standard conditions. Unfortunately, visible-light photoredox decarboxylative coupling of **1a** with **4** gave poor yield (Scheme 4a), so 1-(2-alkylethynylsulfonyl)benzenes are not good substrates. Further, visible-light photoredox decarboxylative coupling of pimelic acid active ester (**6**) with **2a** was performed, and six-membered cycle **7** and internal alkyne **8** were obtained in 31% and 13% yields, respectively (Scheme 4b).



Scheme 4 (a) Visible-light photoredox decarboxylative coupling of **1a** with 1-(oct-1-ynylsulfonyl)benzene (**4**). (b) Visible-light photoredox decarboxylative coupling of pimelic acid active ester (**6**) with **2a**.

In summary, we have developed novel and efficient consecutive visible-light photoredox decarboxylative couplings of substituted adipic acid active esters (bis(1,3-dioxoisindolin-2-yl)-substituted hexanedioates) with 1-(2-arylethynylsulfonyl)benzenes under the assistant of the photocatalyst [Ru(bpy)₃]Cl₂ and visible-light, in which the starting materials are readily available. Importantly, the reactions were performed at room temperature, and the successive photoredox decarboxylative couplings led to formation of two C-C bonds. The present discovery should provide a novel and practical strategy for synthesis of cyclic molecules, and we believe that it will find wide applications in various fields.

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Notes and references

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† Electronic supplementary information (ESI) available: General procedure for visible-light photoredox synthesis of internal alkynes, characterization data for compounds **3a-ac**, references, and ¹H and ¹³C NMR spectra of compounds **3a-ac**. See <http://dx.doi.org/10.1039/b000000x/>

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