Organic Letters

Photoinduced C(sp^2)−H/C(sp^2)−H Cross-Coupling of Alkenes: Direct Synthesis of 1,3-Dienes

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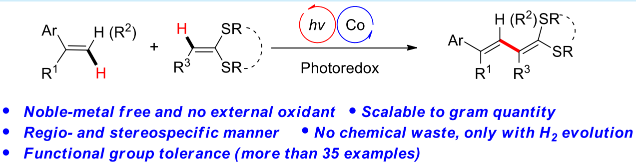
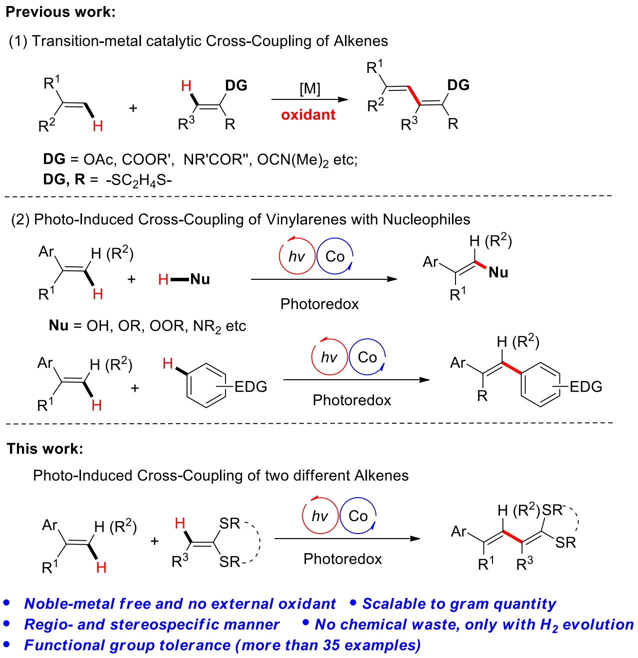


ABSTRACT: A highly concise route to substituted 1,3-dienes from vinylarenes and ketene dithioacetals under photoinduced cross-coupling reaction is described. The reaction proceeded in a highly regio- and stereoselective manner and showed broad functional group tolerance. More than 35 substituted 1,3-dienes were synthesized with good to excellent yields through the construction of the Csp^2−Csp^2 bond without using noble metal and external oxidants, and natural sunlight could also induce the reaction to afford gram-scale synthesis under ambient conditions.

The 1,3-diene scaffold, frequently found in natural products[1] and biologically active molecules,[2] is important and also acts as a versatile precursor for diverse molecules.[3,4] Although numerous methods for the synthesis of 1,3-dienes,[5−8] especially the step- and atom-efficient direct cross-coupling approach of two different alkenes catalyzed by transition metals (Scheme 1, eq 1),[6−8] the use of expensive metal catalysts, harsh oxidative conditions, multiple prefunctionalization steps of substrates, and the poor selectivity for highly substituted alkene substrates limit their applicability. Therefore, the development of mild catalytic methodologies for direct C(sp^2)−H/C(sp^2)−H cross-coupling between alkenes remains a formidable challenge.

Scheme 1. Cross-Coupling reactions of alkenes



Visible-light photoredox catalysis has emerged recently as an attractive research area in green synthetic chemistry and offered an opportunity to overcome the shortcomings of using transition-metal catalysts in C−H functionalization.[9−11] Taking advantage of the visible light, various organic transformations were realized; for instance, a photoredox/cobaloxime dual catalytic system[12] was applied to the bond-forming reactions of vinylarenes[13−17] with selected nucleophiles such as H_2O,[14] alcohols,[15] and aliphatic acids[16] without the use of external oxidants (Scheme 1, eq 2-1). More recently, the dehydrogenative Csp^2−Csp^2 bond formation reaction between arenes and alkenes was reported by Lei and co-workers (Scheme 1, eq 2-2).[17,18] However, the visible-light photoredox catalyzed direct C(sp^2)−H/C(sp^2)−H cross-coupling between two alkenes under external oxidant-free conditions has not been established.

Herein, we report the first example of photoinduced C(sp^2)−H/C(sp^2)−H crossing-coupling between two alkenes without the use of external oxidants, and the readily available ketene dithioacetals[8a,19−21] were selected as the internal alkenes due to their high reactivity toward electrophiles (Scheme 1).

We commenced the reaction of styrene **1a** with α-acetyl dithioacetal **2a** as a probe to try the reaction and optimize the reaction conditions in the presence of a photoredox catalyst with a cobaloxime catalyst under blue LED irradiation (Table 1). Several selected acridinium photosensitizers and cobalox-

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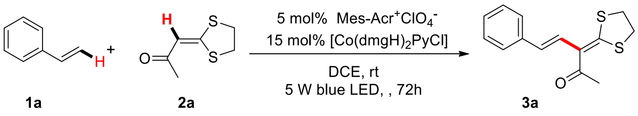
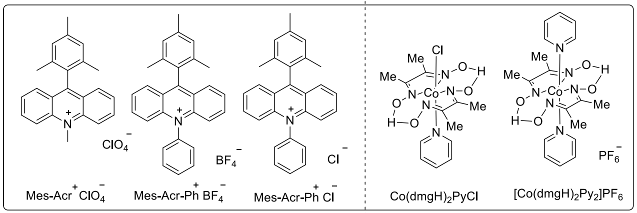
Table 1. Optimization of the Reaction Conditions[a]



entry	variation from the standard conditions	yield (%)[b]
1	none	87
2	Mes-Acr-Ph$^+$BF$_4^-$ instead of Mes-Acr$^+$ClO$_4^-$	68
3	Mes-Acr-Ph+Cl$^-$ instead of Mes-Acr$^+$ClO$_4^-$	67
4	Ir(ppy)$_2$(dtb-bpy)PF$_6$ instead of Mes-Acr$^+$ClO$_4^-$	nr
5	[Co(dmgH)$_2$Py$_2$]PF$_6$ instead of Co(dmgH)$_2$PyCl	61
6	Cu(OAc)$_2$ instead of Co(dmgH)$_2$PyCl	nr
7	PhSSPh instead of Co(dmgH)$_2$PyCl	nr
8	MeCN as solvent	64
9	3 mol% Mes-Acr$^+$ClO$_4^-$ and 8 mol% Co(dmgH)$_2$PyCl as catalyst	80
10	**1a: 2a** = 2: 1	82
11	without Mes-Acr$^+$ClO$_4^-$	nr
12	without Co(dmgH)$_2$PyCl	nr
13	without light	nr

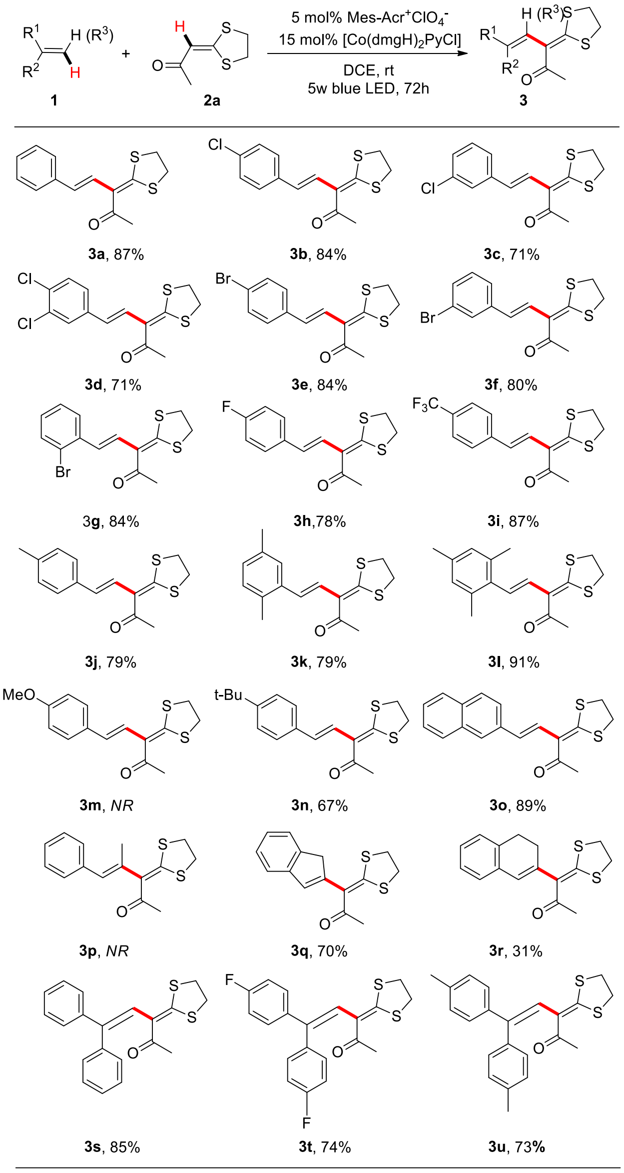


[a] Styrene **1a** (1.5 mmol), α-acetyl dithioacetal **2a** (0.5 mmol), Mes-Acr$^+$ClO$_4^-$ (5 mol %), Co(dmgH)$_2$PyCl (15 mol %), and DCE (2 mL) were stirred in a tube irradiated using 5 W blue LEDs at rt for 72 h. [b] Isolated yields.

ime catalysts were investigated in 1,2-dichloroethane (DCE). To our delight, the use of 5 mol % of Mes-Acr$^+$ClO$_4^-$ and 15 mol % of Co(dmgH)$_2$PyCl resulted in the formation desired 1,3-dienes **3a** in 87% (entry 1). Replacing Mes-Acr$^+$ClO$_4^-$ with other photocatalysts, such as acridinium photosensitizers Mes-Acr-Ph$^+$BF$_4^-$ or Mes-Acr-Ph$^+$Cl$^-$, caused clear decline of the yields of **3a** (entries 2 and 3). No **3a** was detected with Ir(ppy)$_2$(dtb-bpy)PF$_6$ as the sensitizer (entry 4). The yield of **3a** was decreased to 61% when [Co(dmgH)$_2$Py$_2$]PF$_6$ was used as a proton-reduction catalyst (entry 5). No **3a** was detected when Cu(OAc)$_2$ or PhSSPh was applied to replace Co(dmgH)$_2$PyCl (entries 6 and 7). A decreased yield of **3a** was formed with MeCN as the solvent (entry 8). A slightly lower yield was obtained when reducing either the amount of catalyst (3 mol % Mes-Acr$^+$ClO$_4^-$ and 8 mol % Co(dmgH)$_2$PyCl (entry 9) or substrate **1a** (entry 10). In addition, it was proved that no **3a** was produced in the absence of Mes-Acr$^+$ClO$_4^-$, Co(dmgH)$_2$Cl$_2$ or light (entries 11−13), respectively, indicating these components were essential for the photo-induced C(sp^2)−H/C(sp^2)−H cross-coupling reaction described above.

With the optimized reaction conditions (Table 1, entry 1), the scope of the visible-light-induced C(sp^2)−H/C(sp^2)−H cross-coupling reaction was investigated in detail. At first, α-acetyl dithioacetal **2a** was selected as the model reactant to react with vinylarenes **1**, and the results are shown in Scheme 2. A range of styrenes having electron-deficient group on the aryl ring, such as halogens (**1b−1h**) or trifluoromethyl (**1i**), provided the desired 1,3-dienes (**3b−3i**) in good to excellent yields. On the other hand, styrenes bearing electron-donating groups on the aryl ring, such as methyl (**1j−1l**) and *tert*-butyl (**1n**), also gave the desired products (**3j−3l** and **3n**) in good yields. In addition, 2-vinylnaphthalene (**1o**) was a suitable vinylarene component for the desired 1,3-diene **3o**. However, it is surprising that 4-MeO-styrene (**1m**) failed to give the desired cross-coupling product (for details, see the mechanism studies). Obviously, *ortho*-, *meta*-, *para*-, and multisubstituted vinylarenes **1** did not show a significant difference in reactivity (**1b−1g** and **1j−1l**). Gratifyingly, in the case of indene **1q** and 1,2-dihydronaphthalene **1r** as the cyclic internal alkenes, the

Scheme 2. Scope of Vinylarenes 1 in the C(sp^2)−H/C(sp^2)−H Cross-Coupling Reaction[a,b]

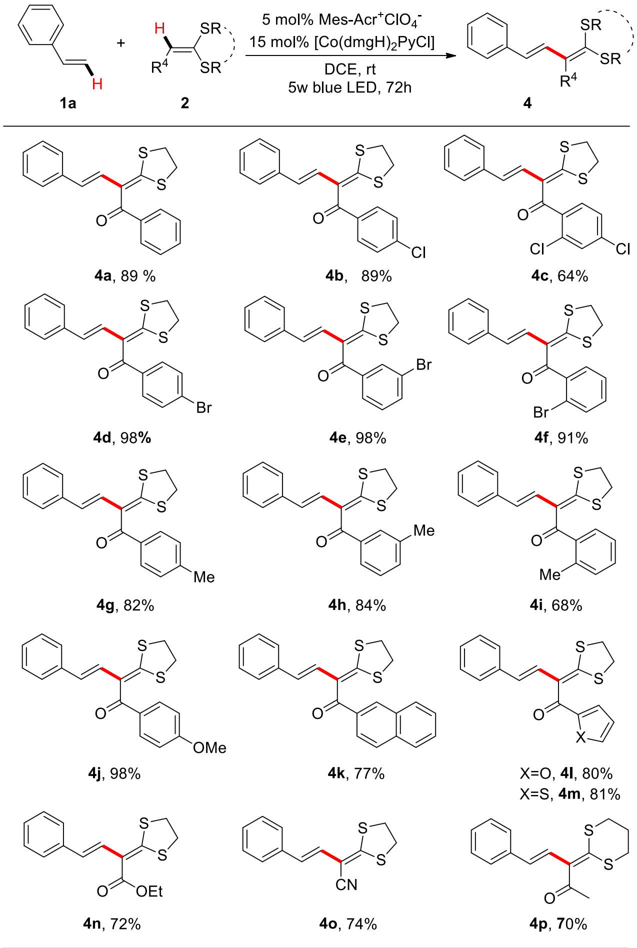


[a] Vinylarene **1** (1.5 mmol), α-acetyl dithioacetal **2a** (0.5 mmol), Mes-Acr$^+$ClO$_4^-$ (5 mol %), Co(dmgH)$_2$PyCl (15 mol %), and DCE (2 mL) were stirred in a tube irradiated using 5 W blue LEDs at rt for 72 h. [b] Isolated yields.

corresponding C(sp^2)−H/C(sp^2)−H cross-coupling products **3q** and **3r** were also obtained, although methylstyrene **1p** as the acyclic internal alkene did not react with **2a** to form the corresponding **3p**, due to probably the steric hindrance of **1p**. When 1,1-diarylethylenes (**1s**−**1u**) were applied, the desired **3s**−**3u** were produced, and functional groups such as fluoro (**1t**) and methyl (**1u**) can be well tolerated.

Next, the scope of ketene dithioacetals **2** as the internal alkenes was investigated (Scheme 3). It was proven that styrene **1a** can react with a wide variety of α-oxo ketene dithioacetals, including those having phenyl (**2a**), electron-deficient aryl (**2a**−**2f**), electron-rich aryl (**2g**−**2j**), naphthyl (**2k**), and hetero aromatic groups (**2l** and **2m**), to afford the desired 1,3-dienes **4a**−**4m** in good to excellent yields. Notably, the reactions of α-ethoxycarbony ketene dithioacetal **2n** and α-cyano ketene dithioacetal **2o** with **1a** also gave the expected **4n** and **4o**, respectively, in good yields. In addition, α-oxo ketene dithioacetal **2p** with the 1,3-dithiane moiety afforded the corresponding 1,3-diene **4p** in 70% yield.

Scheme 3. Scope of Internal Alkenes 2 in the C(sp^2)−H/C(sp^2)−H Cross-Coupling Reaction[a,b]

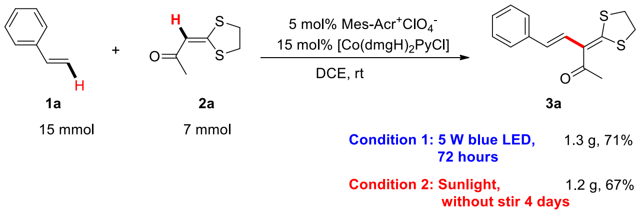


[a]Styrene **1a** (1.5 mmol), ketene dithioacetal **2** (0.5 mmol), Mes-Acr$^+$ClO$_4^-$ (5 mol %), Co(dmgH)$_2$PyCl (15 mol %), and DCE (2 mL) were stirred in a tube irradiated using 5 W blue LEDs at rt for 72 h. [b]Isolated yield.

It is noteworthy that for the photoinduced C(sp^2)−H/C(sp^2)−H cross-coupling reaction mentioned above, only the regio- and stereospecific *E* isomers **3** and **4** are constructed. These results indicate the reaction proceeds in a regio- and stereospecific manner.

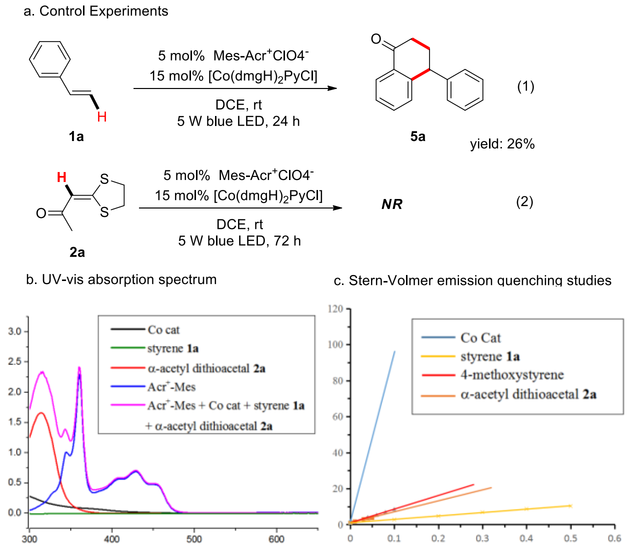
In our research, it was demonstrated that **3a** can be prepared on gram-scale in good yields (Scheme 4) under standard conditions or even induced by natural sunlight under ambient conditions, showing this C(sp^2)−H/C(sp^2)−H cross-coupling reaction is practical.

Scheme 4. Gram Synthesis



To gain further insight into the photocatalytic process of the reaction, a series of mechanism studies were performed including control experiments, cyclic voltammetry,[22] UV−vis monitoring and Stern−Volmer studies (Scheme 5). As shown in Scheme 5 (a), the reaction of **1a**, in the absence of **2a**, under the standard conditions (Table 1, entry 1) give the cyclodimerization−oxygenation product **5a** in 26% yield.[23] As a comparison, **2a** was not reacted under otherwise identical conditions in the absence of **1a**. These results suggested that in the cross-coupling reaction styrene **1** should be oxidized by the excited state of the photosensitizer to generate a styrene radical cation intermediate. As described in Scheme 5 (b), the UV−vis absorption spectrum confirms that Mes-Acr$^+$ClO$_4^-$ is the only visible-light photosensitizer in the reaction. According to the linear Stern−Volmer behavior (Scheme 5, (c)), either styrene **1a**, α-acetyl dithioacetal **2a**, or Co(dmgH)$_2$PyCl can quench the excited photosensitizer Mes-Acr$^+$ClO$_4^-$ in the emission-quenching experiments, meaning the electron transfer among Mes-Acr$^+$ClO$_4^-$, **1a** and Co(dmgH)$_2$PyCl. It worth mention that 4-MeO styrene has a larger quenching rate than both of **1a**

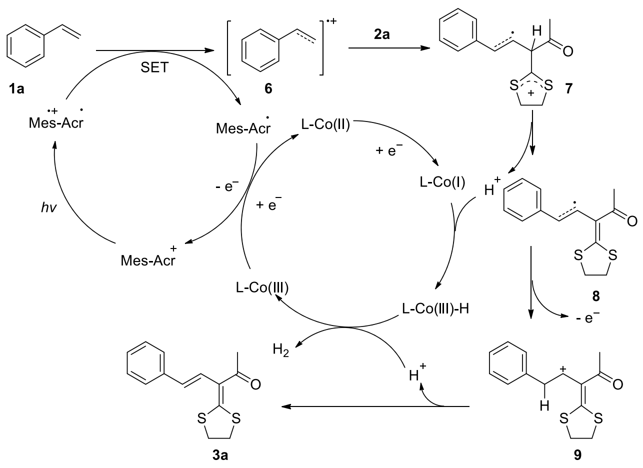
Scheme 5. Mechanistic Studies



and **2a** (Scheme 5 (b)), exhibiting the excited state of the photosensitizer is to be inactive in this case.

In light of the experimental results and mechanistic elucidations,[12−15,18,22−26] a plausible mechanistic cycle for the photoinduced direct $C(sp^2)-H/C(sp^2)-H$ cross-coupling reaction (with **1a** and **2a** as an example) is outlined in Scheme 6. The process starts from the generation of excited state of photosensitizer under blue LED irradiation. Then the styrene radical cation **6** can be formed upon the electron transfer from the styrene **1** to $Mes\text{-}Acr^+ClO_4^-$. The nucleophilic attack of **2** at radical cation **6** would furnish a distonic radical cation **7**, which deprotonated to form a radical intermediate **8**. Subsequently, a SET process between **8** and cobal should occur to form carbocation species **9**. Finally, 1,3-diene **3** is produced from **9** with the release of the proton. For the cobalt cycle part, Co(I) species can generate by reduction of Co(III). Reaction of Co(I) with H^+ gives Co(III) hydride species, which reacts with the second H^+ to release H_2 to close the cobalt catalyst cycle.

Scheme 6. Plausible Mechanism



To summarize, we have developed the first visible-light photoredox-catalyzed $C(sp^2)-H/C(sp^2)-H$ manner cross-coupling reaction between two kinds of alkenes. The reaction can be carried out using photocatalyst and cobalt dual catalyst without using noble metal and external oxidants in good to high yields in a regio- and stereospecific manner. It is an ideal reaction pathway to Csp^2-Csp^2 bond formation with high atom economy with hydrogen gas as the only byproduct. Further studies are in progress.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.9b04201.

Full experimental details, mechanistic studies and characterization of new compounds (PDF)

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Notes

The authors declare no competing financial interest.

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