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Visible-light-induced [4+2] Cycloaddition of Pentafulvenes by Organic Photoredox Catalysis

Kenta Tanaka,*a Yosuke Asada,^b Yujiro Hoshino*^b and Kiyoshi Honda*^b

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We have developed thioxanthylium photoredox catalyzed [4+2] cycloaddition of pentafulvenes at room temperature under green light irradiation, which affords the tetrahydrocyclopenta[b]chromenes with high regioselectivities. The present reaction provides a sustainable approach to carry out cycloaddition of pentafulvenes without the use of transition metal catalysts or high-temperature condtions. This procedure enables a mild and straightforward access 1,3a,9,9ato tetrahydrocyclopenta[b]chromenes. The quantum yield of the reaction (Φ = 0.15) indicates that the reaction would mainly proceeds via photocatalytic pathways.

Cycloaddition of pentafulvenes potentially have the powerful approaches to various polycyclic compounds.¹ In the past few decades, a variety of cycloaddition reactions such as [2 + 2], [3 + 2], [4 + 2], [6 + 2], [6 + 3] and [6 + 4] cycloadditions have been successfully developed due to their ability to display multiple cycloaddition profiles.² More recently, a chiral scandium-complex-catalyzed asymmetric [4+2] cycloaddition with fulvenes was also reported.³ However, previously reported cycloaddition metal catalysts or under high temperature conditions (Scheme 1 (a)),⁴ hence, development of more efficient and milder methods was highly desirable.

Being one such efficient protocol, photochemical reaction is an attractive method in organic synthetic chemistry, and especially, visible-light-induced photoredox reaction has become a powerful tool in organic synthesis over the past decades.⁵. However, only few examples of UV light-induced cycloaddition reactions of pentafulvenes have been developed.⁶

In the course of our study on [4+2] cycloaddition reactions,⁷ we recently synthesized the thioxanthylium organic photoredox catalysts, which have high excited state reduction potentials and are able to be used under irradiation with green light.⁸

Compared with transition-metal photoredox catalysts, organic photoredox catalysts have some merit that their use represents a more cost-effective and sustainable approach.^{9,10} In 2019, we reported that thioxanthylium photoredox catalysts efficiently promoted oxa-[4+2] cycloaddition of ortho-quinone methides with styrenes to furnish chromanes.¹⁰ Based on the aforementioned background, we assumed that the photocatalytic systems can be applied to not only styrenes but also other various dienophiles such as fulvenes. Moreover, only few hetero-[4+2] cycloaddition reactions of fulvene have so far been reported.^{3,11} Therefore, in order to expand to the utility of the reaction of fulvene, herein, we report thioxanthylium organic photoredox catalyzed [4+2] cycloaddition of pentafulvene under green light irradiation at room temperature (Scheme 1(b)).



Initially we screened the reaction of *ortho*-quinone methide (**1a**) with pentafulvene (**2a**) in the presence of thioxanthylium photoredox catalyst using various solvents at room temperature under green light irradiation (Table 1). When medium to non-polar solvents such as THF and toluene were used, the reaction did not afford any of the target product (**3a**) (entries 1–2). On the other hand, while polar solvents such as

^{a.} Faculty of Pharmaceutical Science, Tokyo University of Science, 2641 Yamazaki, Noda-city, Chiba, 278-8510, Japan.

^{b.} Graduate School of Environment and Information Sciences, Yokohama National University, Tokiwadai, Hodogaya-ku, Yokohama 240-8501, Japan.

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DMF and CH₃CN were not suitable for the reaction (entries 3–



4), reactions with CF₃CH₂OH, CH₃NO₂ and CH₂Cl₂ furnished the desired [4+2] cycloadduct (entries 5-7), whereby especially CH_2Cl_2 effectively increased the product yield to 98% (dr = 1.4:1). These solvents were often used for radical cation cycloadditions, and they would stabilize radical cation intermediates, suggesting that this reaction system may be through the radical cation pathway.¹² Fortunately, single crystals of each diastereomer 3a, which are suitable for an X-ray diffraction analysis, could be obtained by recrystallization. Therefore, the relative stereochemistry of endo- and exochromanes 3a could be determined by single crystal X-ray diffraction analysis. From the blank experiments, the reaction effectively proceeds in the only case of using photocatalyst, light source, and air (entries 8-10). Finally, the photocycloaddition reactions using the representative organophotocatalysts under otherwise identical reaction conditions were examined (see Supporting Information, page S5). As a result, miserable outcomes were obtained, and it was found that for the present photoredox catalysis TXT arcatalyst DOI: 10.1039/D0OB01151G specifically works well.

Table 1 Optimization of the reaction conditions^a

^a All reactions were carried out with **1a** (0.250 mmol), **2a** (0.125 mmol), catalyst (1.0 mol%) in solvent (2.0 mL) at room temperature for 4 h under irradiation with green light. ^b ¹H NMR yield. The ratio is endo/exo. ^c No catalyst. ^d No light. ^e Under Ar. PMP : *p*-methoxyphenyl

With the optimized conditions in hand, the scope of pentafulvenes was examined (Table 2). When diarylfulvenes bearing halogen functionalities such as chloro, bromo and fluoro groups were used as a dienophile, excellent yields of the desired products were obtained (3a-3c). 6,6-Diphenyl fulvene was well tolerated in the reaction (3d). Diarylfulvene bearing electron donating groups furnished the corresponding products in moderate to good yields (3e-3g). Next, we investigated fulvenes bearing aliphatic groups. When 6,6-dipropylfulvene was used, the reaction smoothly proceeded under the same reaction conditions leading to the formation of the desired cycloadduct in good yield (3h). Pentafulvenes bearing cyclopentyl, cyclohexyl and cycloheptyl groups were also good substrates for the formation of the desired cycloadducts (3i-3k). In addition, stereoselectivity of the product was effectively improved when 5-cyclopentylidenecyclopenta-1,3-diene was used as a substrate. ortho-Quinone methide bearing dimethoxy groups furnished the desired product in high yield (31). When the reaction was carried out with ortho-quinone methide bearing *p*-tolyl group instead of PMP, the corresponding cycloadduct was also obtained in good yields (3m-3o). Finally, monosubstituted fulvene at the C-6 position was examined. When the photocycloaddition reaction of 6-phenylfulvene was carried out in EtOAc at rt for 24 h in the presence of TXT (5.0 mol%), the corresponding cycloadduct 3p was obtained in 44% yield. Unfortunately, cis-trans isomers were also produced as a non-separable mixture along with low diastereoselectivity, giving the complex mixture of isomers that were hard to accurately analyze the structure and selectivity of them. These results indicate that the reaction can be applied to various 6,6disubstituted pentafulvenes bearing both aromatic and aliphatic groups.

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 $^{\rm a}$ 8 h. $^{\rm b}$ TXT (5.0 mol%) was used. $^{\rm C}$ Reaction conditions: TXT (5.0 mol%), EtOAc, rt, 24 h.

A plausible reaction mechanism for the reaction of pentafulvene with *ortho*-quinone methide is represented in Scheme 2. The photoredox catalyst (PC^{+*}; $E_{1/2}$ (C^{*}/C⁻) = +1.76 V vs SCE)¹⁰ which can be activated by irradiation with green light enables the oxidation of *ortho*-quinone methide **1a** ($E_{p/2}$ = +1.19 V vs SCE). Based on the Stern–Volmer experiments (Figure 1), the single electron transfer from *ortho*-quinone methide **1a** to the photoredox catalyst should occur. Since the reaction seems to require oxygen to promote the catalytic cycle (Table 1, entry 10), the reduced photocatalyst (PC⁻) would be regenerated into

the photoredox catalyst (PC⁺) via single-electron transfer to O₂. To support the generation of O₂·⁻, the control experiment in the presence of benzoquinone, which is known as a trap agent of O₂·⁻, was carried out under the same reaction conditions (see Supporting Information, page S4). As expected, no reaction occurred, suggesting the important role of O₂·⁻ in the catalytic cycle. Pentafulvene **2a** could undergo an [4+2] cycloaddition with the resulting radical cation **A** providing radical cation **B**.¹³ To confirm the radical chain processes in the catalysis, we determined the quantum yield of the reaction ($\Phi = 0.15$),¹⁴ which suggests that the reaction mainly proceeds via

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photocatalytic pathways. Thus, single electron transfer from the superoxide radical (O_2^{-}) to radical cation intermediate **B** would occur to afford the cycloadduct **3a**.



Scheme 2 Proposed reaction mechanism. PMP: p-methoxyphenyl



In conclusion, we have developed organic photoredox catalyzed [4+2] cycloaddition of pentafulvenes under visible light irradiation. The various pentafulvenes reacted with *ortho*-quinone methides in the presence of thioxanthylium organic photoredox catalyst (TXT) under green light irradiation furnished the corresponding [4+2] cycloadducts in good yields. Pentafulvenes bearing aromatic and aliphatic groups could be successfully applied to the reaction. Based on the quantum yield of the reaction ($\Phi = 0.15$), the reaction mainly proceeds via photocatalytic pathways. We hope that the reaction system provides an efficient and sustainable method for cycloaddition reaction of fulvenes.

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Conflicts of interest

There are no conflicts to declare.

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