Selenonium ylides: synthesis, characterization, and applications to photo-induced cyclopropanation reactions

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Abstract

Carbenes are important and highly reactive intermediates for the synthesis of various complex molecules. They are now an indispensable chemical species in organic chemistry and are used frequently to synthesize complex compounds in drug discovery chemistry. In general, carbenes are synthesized by a combination of transition metal catalysts and diazo compounds or by the decomposition reactions of diazo compounds. This paper reports the development of the visible light for the photochemical generation of carbenes from a novel *C,Se*-selenonium ylide. Overall, this photochemical carbene generation method using *C,Se*-selenonium ylide does not require a catalyst, is simple to perform, and enables highly efficient cyclopropanation reactions with alkenes.

Graphical abstract

Keywords Carbene · Selenonium ylide · Cyclopropanation · Photoreaction

1 Introduction

Carbenes are a neutral, six-electron carbon species with unique reactivity [1]. These compounds have been actively studied in synthetic organic chemistry, and various reactions have been developed using them [2, 2]. Although free carbenes are prepared by the thermal or photochemical decomposition of carbene precursors, control of their reactivity has significant drawbacks. Moreover, the reactivity and selectivity can be controlled by synthesizing metal carbenoids as free carbene precursors through a reaction of

diazo compounds with metal complexes [4]. Various metals, such as Rh, Cu, and Pd, can be used to produce metal carbenoids. Considerable progress has been made in elucidating the reactivity depending on the type of diazo compound and metal [2–4]. Accordingly, various reactions can be carried out using carbenes. Carbenes are a reactive chemical species essential in the total synthesis and construction of complex molecules [7]. Although diazo compounds are often used to generate metal carbenoids because of their high efficiency, there are significant problems for their large-scale applications in terms of safety and handling. Therefore, the use of main group element ylides as alternative reagents has attracted attention [5–8, 10, 13].

In 2007, Jenks et al. developed *C,S*-sulfonium ylides based on the thiophene moiety as a useful precursor for carbenes using a photochemical activation methodology (Scheme 1a) [9]. The synthesized sulfonium ylides were

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Scheme 1. **a** Jenks' sulfonium ylide strategy to generate carbenes; **b**) molecular design for novel ylide; **c**) methodology for visible-light-induced carbene generation

stable, easy to handle, and could generate free carbenes using ultraviolet (UV) irradiation without a catalyst [10, 15, 17]. These studies reported that onium ylides with relatively large conjugated systems could photochemically generate the corresponding carbene species. Furthermore, the carbenes released from these onium ylides require intense UV light. Hence, improvements are needed before they can be implemented in synthetic organic chemistry. Therefore, this study developed a highly versatile carbene precursor that can release carbenes under visible-light irradiation and milder conditions. The necessity of UV light for the excitation wavelength in *C,S*-sulfonium ylides was attributed to the C–S bond strength and the absorption wavelength of dibenzothiophene [11, 19]. Accordingly, using this ylide motif, selenium, a member of the same group as sulfur, was chosen because it can form weaker bonds than sulfur with carbon. Selenium has a larger atomic radius than sulfur. Additionally, compounds containing selenium have a narrower HOMO–LUMO gap, and the heavy atom effect stabilizes the excited triplet state (Scheme 1b) [12, 13, 21]. Therefore, it was hypothesized that the corresponding selenonium ylides could be excited by visible light to produce the carbene species efficiently. Thus, *C,Se*-selenonium ylides were synthesized, and their physical properties and reactivities as carbene precursors were evaluated. This paper reports the synthesis and characterization of novel *C,Se*-selenonium ylides and their

applications to the visible-light-responsive radical generation reaction (Scheme 1c).

2 Results and discussion

2.1 Synthesis of dibenzoselenophene-based selenonium ylide

The synthesis of the selenonium ylide was started with a reaction of diazomalonate **2** with dibenzoselenophene (Table 1) [23]. After the optimization study, the desired dibenzoselenophene-based selenonium ylide **3a** was obtained in good yield through a rhodium acetate dimer-catalyzed carbenoid addition reaction with selenophene [14]. The corresponding dibenzylmalonate derivative **3b** was also prepared under the optimized reaction conditions. The desired ylide using dibenzoselenophene was synthesized with electron-withdrawing or electron-donating substituents to control the absorption wavelength of selenonium ylide. Both reactions gave the corresponding products (**3b** and **3c**) without any loss of yield. The ylidization reaction also proceeded under these conditions for compounds with extended conjugation systems, giving the corresponding products in moderate yield.

Table 1 Synthesis of selenonium ylide **3**^a ^a Isolated yield.

2.2 UV/Visible spectra of selenonium ylide **3**

A series of selenonium ylides **3** were synthesized and their photochemical properties were assessed to realize the photochemical carbene-formation reaction using **3**. Figure 1 shows the spectra of the measured compounds.

Photophysical studies showed that the substituents have a significant influence on absorption (Table 2). The λ_{abs} values of selenonium ylide-bearing electron-donating groups on the dibenzoselenophene ring, such as **3c** (276, 298, and

Fig. 1 Ultraviolet/Visible spectra of the selenonium ylide **3**^a. ^a Measured in MeCN**Table 2** Ultraviolet/Visible absorption of selenonium ylide **3**

Entry	Ylides	UV/Vis	
		λ_{max} (nm)	log ϵ
1	3b	274	4.43
		330 (sh)	3.00
2	3c	276	4.25
		298	4.03
3	3d	320 (sh)	3.32
		275	3.91
		325	4.15
		385 (sh)	3.53
4	3e	280	4.21
		304	3.92
		320	3.54
		334	3.34
		350	3.37

320 nm), revealed a similar absorption spectrum to those of the parent, unsubstituted ylide **3b** (274, 330 nm). Those with electron-withdrawing substituents, such as **3d** (275, 325, and 385 nm), were red-shifted significantly (entries 1–3). Furthermore, the UV/visible absorption spectra of **3e**, a compound with a benzo[*b*]naphtho[2, 1-*d*]selenophene system, showed complex absorption spectra derived from the mother framework. On the other hand, the strong absorption peak at 280 nm, which was attributed to the ylide, showed no shift. The shoulder peaks of the absorption spectra of selenonium ylide **3** were strong enough in the visible-light region to be considered for photochemical studies using **3**.

2.3 Optimization of the reaction condition for the cyclopropanation of styrene with selenonium ylide **3**

Based on the results described above, attention was then focused on carbene generation using selenonium ylide **3** under visible-light irradiation (Table 3). The initial optimization study showed that a reaction of **3** with **4a** (10 equiv) in MeCN as a solvent was crucial for the photo-induced generation of the desired carbene [25]. The reaction of the dimethyl malonate-derived selenonium ylide **3a** with styrene **4b** under 365 nm LED irradiation for 20 h furnished the corresponding cyclopropane **5aa** in 32% NMR yield (entry 1). The reaction proceeded depending on the wavelength irradiated with the LED. The yield was improved greatly to 57% when irradiated with a longer wavelength, e.g., 400 nm, while it decreased when irradiated with 420 nm LED radiation (entries 2 and 3). This trend was also observed for the dibenzyl ester derivative **3b**, where 365–420 nm light gave the product **5ba** with the highest NMR yield of 66% (56% isolated yield) for the 400 nm light source (entries 4–6).

Table 3 Optimization study for the cyclopropanation of styrene **4a** with **3**^a

entry	3	X (nm)	5	yield (%)
1	3a	365	5aa	32
2	3a	400	5aa	57(55)
3	3a	420	5aa	50
4	3b	365	5ba	40
5	3b	400	5ba	66(56)
6	3b	420	5ba	40
7	3c	400	5ba	43
8	3d	400	5ba	56
9	3e	400	5ba	57

^a Yield was determined by ¹H NMR analysis of the crude reaction mixture using 1,1,2,2-tetrachloroethane as an internal standard. The numbers in parentheses are the isolated yields.

However, the reaction proceeded in response to the shoulder peak, which is a weak absorption band because the maximum absorption wavelength was approximately 300 nm. This reaction was also applied to various substituted compounds **3**. No improvement in yield was observed using a dibenzoselenophene with an electron-donating functional group **3c** (entry 7). On the other hand, the reaction using **3d**, which has a more red-shifted absorption wavelength, gave the product in similar yield compared to the case of **3b** (entry 8). Although the benzo[*b*]naphtho[2,1-*d*]selenophene system-derived ylide was also applied to the carbene generation reaction, the desired cyclopropane **5ba** was obtained in 57% yield (entry 9). Overall, using **3b** as a carbene precursor under 400 nm irradiation conditions is optimal for the present reaction.

2.4 Substrate scope for the cyclopropanation of olefins with selenonium ylide **3**

Encouraged by the optimization study, the general applicability of this cyclopropanation reaction was evaluated, and the influence of a reaction partner was studied. Therefore, a set of differently substituted styrenes were first studied under optimized reaction conditions (Table 4, also see Tables S3–7 in ESI for full detailed substrate scope.). When *para*-methoxy styrene **4b** was used as a donor component, the desired product **5bb** was isolated in a lower yield (29%). The introduction of a *para*-bromo substituent (**4c**) led to a slight decrease in reactivity. In contrast, the developed cyclopropanation reaction using **3b** proceeded in a good yield for the *ortho* (**4d**), *meta* (**4e**), and *para* (**4f**)-methyl substituent on styrene. In the case of the *t*-butyl group (**4g**) and methyl group, the reaction proceeded smoothly, and the corresponding carbene adducts were obtained in moderate yield. This reaction was also applicable to vinyl naphthalenes, which are π -expanded aromatic carbons,

showed a red shift in the absorption band, and furnished the corresponding products in moderate yield. The reactions between **3b** and α -olefins **4** were then examined. In this case, treatment of a mixture of **3b** and 1-decene **4j** in MeCN under 400 nm LED irradiation gave **5bj** in 50% yield. The developed reaction condition using **3b** was also applied to various olefins, such as those bearing a bromo group **4k**, sterically hindered substrate at the allyl position **5l**, methyl ester **5m**, and acetyl group **5n**, and furnished the desired cyclopropanation product in moderate yield. Interestingly, this cyclopropanation reaction proceeded even in the presence of free hydroxyl groups, giving the corresponding products **3bo** in low yields.

This process was extended to other unsaturated molecules, such as internal alkenes (Table 5). Interestingly, ethyl cinnamate (**4p**) gave the corresponding cyclopropane **5bp** in 37% yield with complete *anti*-diastereoselectivity. With other internal olefins, such as cyclohexene (**3q**) and cyclohexadiene (**3r**), the developed photo-induced cyclopropanation reaction proceeded smoothly to give the product in 43% and 30% yield, respectively. Interestingly, previous experiments on the generation of carbenes from thiophene-based ylides reported the carbene insertion into the allylic C–H bond [15]. In the present reaction, however, the cyclopropanation reaction proceeded predominantly. This suggests that the singlet carbene is generated preferentially in the present system and that singlet to triplet intersystem crossing (ISC) does not occur [15]. Furthermore, norbornene (**3s**) underwent the required transformation to furnish *exo*-cyclopropanation products in good yield.

3 Conclusion

An efficient synthetic method was developed to prepare selenonium ylides from readily available dibenzoselenophenes. The selenonium ylides prepared were excited

Table 4 Reaction of various olefins **4** with the selenonium ylide **3b**^a ^a Isolated yield.**Table 5** Reaction of various internal alkenes **4** with selenonium ylide **3b**^a ^a Isolated yield.

by visible light without the need for sensitizers or photocatalysts to give the corresponding carbenes. In addition, this photo-induced carbene generation method from selenonium ylides revealed a reaction with various olefins to furnish the corresponding cyclopropane products.

The carbene species produced in this reaction were preferentially singlet carbenes, and the ISC did not proceed because of the reaction with visible light. The method of photochemically generating active species from such heavy main group element-based ylides is interesting. The synthesis of ylides for the generation of nitrenes is currently under investigation.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s43630-021-00155-2>.

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Declarations

Conflict of interest The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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