Reaction of Methylenecyclopropanes and Diphenyl Diselenide under Visible-Light Irradiation

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Abstract: The reaction of methylenecyclopropanes with diphenyl diselenide promoted by visible light was investigated and a series of 2,4-diphenylselenyl-1-butenes was prepared under mild conditions. Interestingly, with the addition of oxidant such as dibenzoyl peroxide, 1-(phenylselenyl)cyclobutanols were obtained.

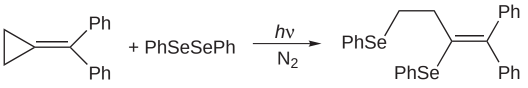
Key words: methylenecyclopropanes, selenium, radicals, radical reactions

Methylenecyclopropanes, which are highly strained but readily accessible molecules, are of current interest in synthetic organic chemistry.[1] The relief of their ring strain provides a potent thermodynamic driving force, which facilitates the construction of complex and interesting organic molecules under mild conditions.[2] During the last decade, much attention has been paid to the reactions of MCPs catalyzed by transition metal[3] or Lewis acid.[4] Recently, our group reported several free radical reactions of MCPs, providing a useful synthetic method for 1,2-dihydronaphthalenes.[5]

In the research on MCPs' free-radical-mediated reactions, Shi[6] reported heat-promoted free radical reaction of MCPs and diphenyldiselenide to synthesize 2,4-diphenylselenyl-1-butenes, which could be further transformed to 3-phenylselenyl-2,5-dihydrofuran derivatives. However, this reaction requires a high temperature (150 °C), which might limit its application in organic synthesis. It is well known that diphenyl diselenide has its maximum absorption in the near-UV range, thus irradiation with the light of wavelength longer than 300 nm can also induce homolytic cleavage of the selenium–selenium bond to generate phenylseleno radical.[7] In this paper, we wish to present the reaction of MCPs with diphenyl diselenide under visible-light irradiation.

We initially examined the reaction of (diphenylmethylene)cyclopropane (**1a**) and diphenyl diselenide in nitrogen under visible-light irradiation with benzene as solvent. After five hours, the expected product 1,1-diphenyl-2,4-diphenylselenyl-1-butene (**2a**) was obtained in 77% yield (Table 1, entry 1). Further screening demonstrated that toluene was a better solvent, and the yield of **2a** could be improved to 87% (Table 1, entry 2).

Table 1 Reaction of MCPs and Diphenyl Diselenide under Visible-Light Irradiation in Different Solvents



1a **2a**

Entry	Solvent[a]	Time (h)[b]	Yield (%)[c]
1	PhH	5	77
2	PhMe	3.5	87
3	MeCN	12	39
4	CCl_4	8	72
5	EtOH	9	70

[a] Amounts of MCP and diphenyl diselenide were both 0.3 mmol, the amount of solvent was 5 mL.
[b] The reaction was monitored by TLC.
[c] Isolated yields.

Under these conditions, a series of MCPs was employed and the corresponding products 2,4-diphenylselenyl-1-butenes were prepared in good yields[8] (Table 2). In this reaction, high temperature was not required and the reaction conditions were much milder.

Interestingly, when the reaction was proceeded without nitrogen protection in EtOH, in addition to 1,1-diphenyl-2,4-diphenylselenyl-1-butene (**2a**), an unexpected ring-expansion product 2,2-diphenyl-1-phenylselenylcyclobutanol (**3a**) was obtained in 37% yield (Scheme 1).

Further screening demonstrated that addition of dibenzoyl peroxide could avoid the formation of **2a** and the yield of **3a** could be increased to 66%. Under similar reaction conditions, various 1-(phenylselenyl)cyclobutanols were prepared in moderate yields[9] (Table 3).

Cyclobutane derivatives, which are not easily accessible, are pivotal skeletons in many natural products with interesting biological activities and are useful building blocks in synthetic organic chemistry.[10] Selenium compounds are of great interest because of their biological activities such as antitumor, antibacterial and other properties.[11]

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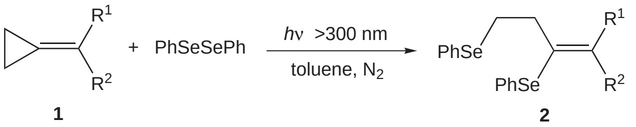
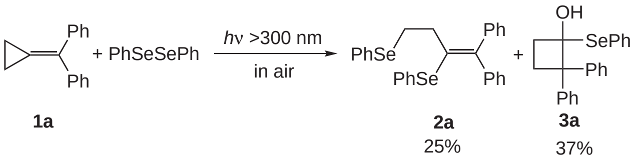
Table 2 Preparation of 2,4-Diphenylselenyl-1-butenes



Entry	R^1, R^2	Yield (%)[a]
1	Ph, Ph (**1a**)	87 (**2a**)
2	*p*-MeC_6H_4, *p*-MeC_6H_4 (**1b**)	80 (**2b**)
3	*p*-$MeOC_6H_4$, *p*-$MeOC_6H_4$ (**1c**)	75 (**2c**)
4	*p*-FC_6H_4, *p*-FC_6H_4 (**1d**)	72 (**2d**)
5	*p*-ClC_6H_4, *p*-ClC_6H_4 (**1e**)	71 (**2e**)
6	-$CH_2CH_2CH(Ph)CH_2CH_2$- (**1f**)	90 (**2f**)
7	-$(CH_2)_5$- (**1g**)	72 (**2g**)
8	*p*-BrC_6H_4, H (**1h**)	76[b] (**2h**)

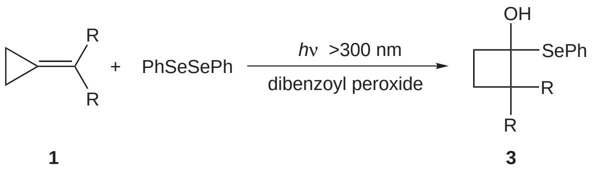
[a] Isolated yields.

[b] *Z*/*E* = 1:1 as determined by ^1H NMR.



Scheme 1

Table 3 Preparation of 1-(Phenylselenyl)cyclobutanols



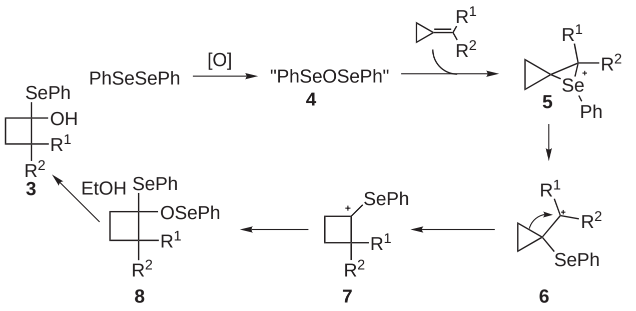
Entry	R, R	Yield (%)[a]
1	Ph (**1a**)	66
2	*p*-MeC_6H_4 (**1b**)	69
3	*p*-$MeOC_6H_4$ (**1c**)	60
4	*p*-FC_6H_4 (**1d**)	54
5	*p*-ClC_6H_4 (**1e**)	58

[a] Isolated yields.

1-(Phenylselenyl)cyclobutanols, containing both cyclobutane structural unit and selenium atom, may have potential biochemical activity and applications in organic synthesis.[12]

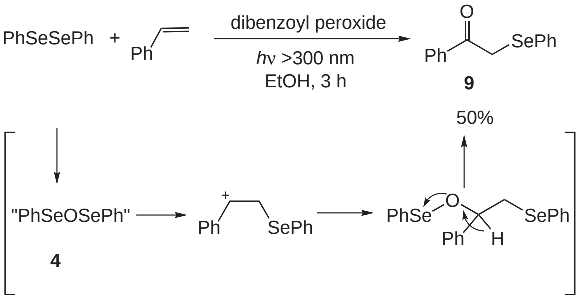
This methodology is only suitable for diaryl-substituted MCPs. When alkyl-substituted MCPs were employed, a series of side products was obtained instead of the desired 1-(phenylselenyl)cyclobutanols.

A plausible mechanism was suggested as follows: the diphenyl diselenide was first oxidized to benzeneselenenic anhydride **4**,[13] which added to the C=C double bound of the MCPs to form the cyclopropyl cationic intermediates **5** and **6**. Rearrangement of carbonium ion **6** gave ring-expanded cyclobutyl cation **7**,[14] which reacted with benzeneselenenic anion to give the intermediate **8**. Alcoholysis of **8** gave the final product **3** (Scheme 2).



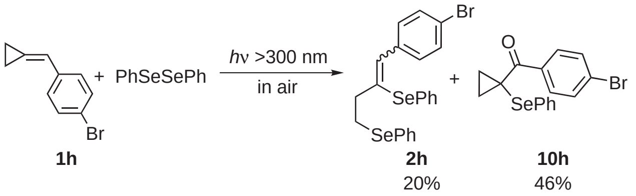
Scheme 2

For proving the above mechanism that benzeneselenenic anhydride (**4**) was formed at first and then underwent electrophilic addition to carbon–carbon double bond. We examined the reaction of styrene under the same reaction conditions. Experimental results showed that the expected product α-phenylselenyl acetophenone (**9**) was produced in 50% yield after irradiation for three hours. Obviously, the diphenyl diselenide was firstly oxidized to benzeneselenenic anhydride (**4**), then added to the double bond of the olefin, further elimination of PhSeH produced α-phenylselenyl acetophenone (**9**)[13] (Scheme 3).



Scheme 3

In order to gain more mechanistic insights into this ring-expansion reaction, we employed monosubstituted MCP 1-bromo-4-(cyclopropylidenemethyl)benzene (**1h**) as substrate. However, when dibenzoyl peroxide was employed as oxidant in this reaction, a series of unidentified products was obtained instead of the expected 4-bromophenyl 1-(phenylselenyl)cyclopropyl ketone (**10h**), this was probably because that the oxidizability of dibenzoyl peroxide was too strong. Thus, we used air as weaker oxidant. Even as we expected, 4-bromophenyl 1-(phenylselenyl)cyclopropyl ketone (**10h**) was obtained when monosubstituted MCP 1-bromo-4-(cyclopropylidenemethyl)benzene (**1h**) and diphenyl diselenide were irradiated in air with EtOH as solvent (Scheme 4). Elimination of PhSeH became feasible because of the presence of a hydrogen atom adjacent to the carbocation. When diaryl-substituted MCPs were employed, there was no hydrogen atom linked to the cationic carbon, so elimination of PhSeH was impossible and the rearrangement of carbonium ion happened.



Scheme 4

In conclusion, we reported here an efficient transformation of MCPs to the corresponding 2,4-diphenylselenyl-1-butenes under visible-light irradiation. We also developed a novel and convenient method for the synthesis of 1-(phenylselenyl)cyclobutanols. The reaction mechanism and synthetic applications of this methodology are under further investigations in our laboratory.

Acknowledgment

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(8) **2,4-Diphenylselenyl-1-butenes 2 – Typical Procedure.** A solution of(diphenylmethylene)cyclopropane (**1a**, 0.062 g, 0.3 mmol) and diphenyl diselenide (0.094 g, 0.3 mmol) in 5 mL of toluene was irradiated with a tungsten lamp (300 W) under nitrogen atmosphere. The temperature rose to 40 °C because of the irradiation. The reaction was monitored by TLC (eluent: PE). After 3.5 h, the reaction terminated, the solvent was evaporated under vacuum and the residue was subjected to preparative TLC (eluent: PE) to afford **2a** (0.135 g, 87%). The melting point and spectra data were consistent with literature.[6] Other 2,4-diphenylselenyl-1-butenes were prepared in a similar way.

(9) **1-Phenylselenylcyclobutanol 3 – Typical Procedure.** A solution of(diphenylmethylene)cyclopropane (**1a**, 0.062 g, 0.3 mmol), diphenyl diselenide (0.094 g, 0.3 mmol) and dibenzoyl peroxide (0.073 g, 0.3 mmol) in 5 mL of EtOH was irradiated with a tungsten lamp (300 W) in air. The temperature rose to 40 °C because of the irradiation. The reaction was monitored by TLC (eluent: PE). After 5 h, the reaction terminated, the solvent was evaporated under vacuum and the residue was subjected to preparative TLC (eluent: EtOAc) to afford **3a** (0.075 g, 66%). Other 1-(phenylselenyl)cyclobutanols were prepared in a similar way.
Selected Data for 3a: White solid, mp 106–107 °C. ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 7.23–7.57$ (m, 15 H), 5.80 (s, 1 H, exchanged with D$_2$O), 1.26–1.32 (m, 1 H), 0.64–0.70 (m, 2 H), 0.42–0.46 (m, 1 H). ^{13}C NMR (100 MHz, CDCl$_3$): $\delta = 6.1$, 9.0, 51.1, 81.3, 127.0, 127.1, 127.3, 127.5, 127.7, 128.0, 128.2, 129.1, 131.0, 131.1, 140.1, 143.8. IR (KBr): $\delta = 3057$, 1491, 1044, 806, 745, 703 cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 380 (4) [M$^+$ + H], 379 (1) [M$^+$], 198 (33), 183 (40), 105 (100).

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