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Ring-opening reactions of methylenecyclopropanes with diphenyl diselenide upon heating; formation of 3-phenylselenyl-2,5-dihydrofuran derivatives†

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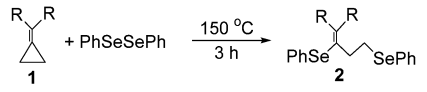
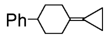
The reactions of methylenecyclopropanes 1 with diphenyl diselenide give ring-opened products 2 in good yields at 150 °C under nitrogen atmosphere for 3 h; the products 2 can further undergo oxidative cyclization with hydrogen peroxide to furnish 3-phenylselenyl-2,5-dihydrofurans 3 in moderate yields (three steps) at room temperature in CH_2Cl_2 for 5 h; a plausible reaction mechanism has been proposed.

Methylenecyclopropanes (MCPs) **1** are highly strained but readily accessible molecules that have served as useful building blocks in organic synthesis.[1,2] Recently, we have been investigating the Lewis acid-mediated ring-opening reactions of MCPs **1** with nucleophiles such as alcohols, aromatic amines and other reactants under mild conditions.[3] In order to explore the further transformations of **1**, we investigated the reactions of **1** with a variety of reactants having sulfur (S) and selenium (Se) heteroatoms.[3g] Herein, we wish to report the ring-opening reactions of **1** with diphenyl diselenide (PhSeSePh) upon heating at high temperature and the formation of 3-phenylselenyl-2,5-dihydrofurans in the presence of hydrogen peroxide. An efficient radical ring-opening process of MCPs **1** with diphenyl diselenide upon heating at 150 °C has been disclosed.[4]

Previously, Ogawa *et al.* reported that the addition of diphenyl diselenide (PhSeSePh) to a number of alkynes produced *vic*-bis(phenylselenyl)alkenes at 150–180 °C for 10 h *via* radical type scission.[5] Enlightened by their finding, we attempted to test the reactions of MCPs **1** with diphenyl diselenide at high temperature. We carried out the reactions of a variety of symmetric MCPs **1a–g** with diphenyl diselenide at 150 °C for 3 h without an organic solvent, and the results are summarized in Table 1 (entries 1–7). The corresponding ring-opened products **2** were obtained in good yields. Their structures were determined by ^{1}H and ^{13}C NMR spectroscopic data, HRMS and microanalysis (see ESI†).

Table 1 Reactions of symmetric MCPs **1a–1g** (0.3 mmol) with diphenyl diselenide (0.3 mmol) at 150 °C for 3 h



Entry	R, R	Yield[a] (%)
1	C_6H_5 (**1a**)	85 (**2a**)
2	*p*-$CH_3C_6H_4$ (**1b**)	82 (**2b**)
3	*p*-$CH_3OC_6H_4$ (**1c**)	79 (**2c**)
4	*p*-ClC_6H_4 (**1d**)	71 (**2d**)
5	*p*-FC_6H_4 (**1e**)	87 (**2e**)
6	 (**1f**)	88 (**2f**)
7	C_4H_9 (**1g**)	66 (**2g**)

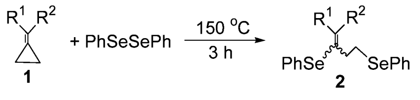
[a] Isolated yields.

Moreover, for unsymmetric MCPs **1h–1n**, the reactions with diphenyl diselenide produced a mixtures of *Z*- and *E*-isomers in 1:1 ratio in moderate to good yields under the same conditions (Table 2, entries 1–7). The configurations of the *Z*- and *E*-isomers were determined by NOESY spectroscopic data (see ESI†).

On the basis of previous investigations on the thermolysis of diphenyl diselenide,[6] a plausible mechanism for the reaction of MCPs **1** with diphenyl diselenide is outlined in Scheme 1. The phenylselenyl radical, produced by thermal cleavage of diphenyl diselenide, adds to the double bond of MCPs **1** to form the radical **A** which immediately undergoes a homoallylic rearrangement to give another radical **B**.[4,7] **B** reacts with another molecule of diphenyl diselenide *via* homolytic substitution (S_H) to produce the ring-opened product **2** and regenerate a phenylselenyl radical (Scheme 1).

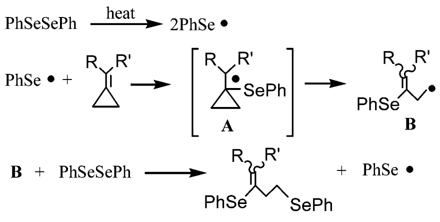
Interestingly, when product **2a** was oxidized with excess hydrogen peroxide (30% H_2O_2 aqueous solution) in dichloromethane at room temperature, 3-phenylselenyl-2,5-dihydrofuran **3a**, an oxidative cyclization product, was obtained in moderate yield (Table 3, entry 1). A variety of similar compounds, **2b–2e**,

Table 2 Reactions of unsymmetric MCPs **1h–1n** (0.3 mmol) with diphenyl diselenide (0.3 mmol) at 150 °C for 3 h



Entry	R^1, R^2	Yield[a] (%)
1	*p*-$CH_3OC_6H_4$, H (**1h**)	79 (**2h**)[b]
2	*o,p*-$(CH_3O)_2C_6H_3$, H (**1i**)	76 (**2i**)[b]
3	*m,m,p*-$(CH_3O)_3C_6H_2$, H (**1j**)	89 (**2j**)[b]
4	*p*-BrC_6H_4, H (**1k**)	72 (**2k**)[b]
5	*p*-$EtOC_6H_4$, Me (**1l**)	59 (**2l**)[b]
6	*p*-$MeOC_6H_4$, C_6H_5 (**1m**)	81 (**2m**)[b]
7	*o*-ClC_6H_4, C_6H_5 (**1n**)	73 (**2n**)[b]

[a] Isolated yields. [b] *Z*/*E* = 1/1 as determined from ^{1}H NMR spectroscopic data.



Scheme 1 Plausible reaction mechanism of MCPs **1** with diphenyl diselenide at 150 °C.

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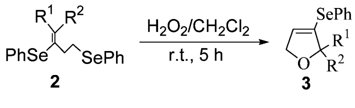
† Electronic supplementary information (ESI) available: Spectroscopic data (^{1}H and ^{13}C NMR) and analytical data of the compounds shown in Tables 1–3 and Schemes 1–3 and detailed description of experimental procedures. See http://www.rsc.org/suppdata/cc/b4/b412823k/

DOI: 10.1039/b412823k

Table 3 The reactions of **2** (0.2 mmol) in the presence of hydrogen peroxide (1.0 mmol) in dichloromethane at room temperature



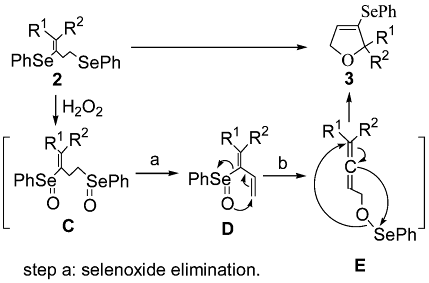
Entry	R^1, R^2	Yield[a] (%)
1	C_6H_5, C_6H_5 (**2a**)	51 (**3a**)
2	*p*-$CH_3C_6H_4$, *p*-$CH_3C_6H_4$ (**2b**)	51 (**3b**)
3	*p*-$CH_3OC_6H_4$, *p*-$CH_3OC_6H_4$ (**2c**)	52 (**3c**)
4	*p*-ClC_6H_4, *p*-ClC_6H_4 (**2d**)	53 (**3d**)
5	*p*-FC_6H_4, *p*-FC_6H_4 (**2e**)	50 (**3e**)
6	*p*-$CH_3OC_6H_4$, C_6H_5 (**2m**)	56 (**3m**)
7	*p*-ClC_6H_4, C_6H_5 (**2n**)	48 (**3n**)

[a] Isolated yields.

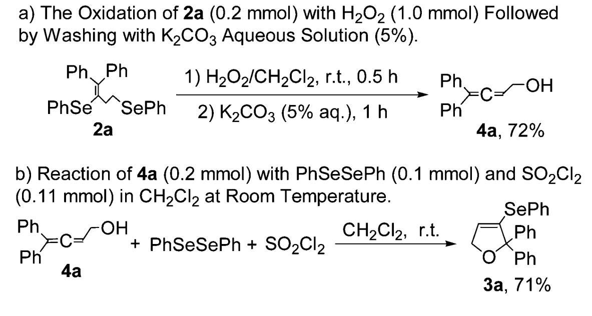
were oxidized under the same conditions to give the corresponding 3-phenylselenyl-2,5-dihydrofuran products **3b–3e** in moderate yields (Table 3, entries 2–5). When product **2m** or **2n**, a mixtures of *Z*- and *E*-isomers, was oxidized with hydrogen peroxide under the same conditions, oxidative cyclization product, **3m** or **3n**, was obtained in moderate yield (Table 3, entries 6 and 7). Their structures were determined by ^1H, ^{13}C NMR spectroscopic data and HRMS (see Supporting Information).

The mechanism for the formation of 3-phenylselenyl-2,5-dihydrofuran **3** can be recognized through a selenoxide elimination[8] and a [2,3]-sigmatropic rearrangement on the basis of previous investigation (Scheme 2).[9] Selenide **2** is oxidized by H_2O_2 to form intermediate **C** which undergoes selenoxide elimination (step a) affording intermediate **D**. Then, a [2,3]-sigmatropic rearrangement of **D** produces intermediate **E** (step b). The intramolecular nucleophilic attack in **E** generates product **3**.

To confirm the mechanistic assumption shown in Scheme 2, two control experiments were performed. Using compound **2a** as the substrate, a 5% aqueous solution of K_2CO_3 was added to the reaction mixture after oxidation with hydrogen peroxide for 0.5 h. The allene product **4a** was isolated in 72% yield (Scheme 3, conditions a).[10] This result suggests that the intermediate **E** indeed exists in the reaction mixture and can be cleaved by alkaline solution. In addition, the treatment of compound **4a** with diphenyl diselenide and SO_2Cl_2 in CH_2Cl_2 at room temperature produces compound **3a** in good yield (Scheme 3, conditions b).[11] All these evidences suggest that the formation of **3** indeed proceeds *via* the pathway shown in Scheme 2.



Scheme 2 Plausible mechanism for the formation of **3**.



Scheme 3 Control experiments.

In conclusion, we have found that the thermolysis of a variety of MCPs **1** with diphenyl diselenide gives the ring-opened products **2** in good yields at 150 °C. For aromatic group substituted products **2**, the oxidative cyclization with hydrogen peroxide give 3-phenylselenyl-2,5-dihydrofuran products **3** in moderate yields (three steps).

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