

A PhSeCl-Mediated Allylic Oxidation of Prenyl Moiety: A Convenient Method for the Construction of 3-Isopenten-2-ol Unit

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A phenylselenenyl chloride (PhSeCl)-mediated allylic oxidation to give allylically rearranged alcohol has been developed. A possible mechanism for the present reaction is generation of allylic selenide from prenyl moiety via [1,3]-sigmatropic rearrangement, followed by oxidation and [2,3]-sigmatropic rearrangement to afford 3-isopenten-2-ol.

Key words allylic oxidation; trisubstituted alkene; sigmatropic rearrangement; phenylselenenyl chloride; prenyl moiety; 3-isopenten-2-ol

A number of methodologies for the oxidation of alkenes to allylic alcohols have been developed (Fig. 1).¹⁾ For example, selenium dioxide and chromate reagents generally oxidize the allylic position without rearrangement of the carbon–carbon double bond. In contrast, singlet oxygen affords the allylic alcohol with the rearrangement of the carbon–carbon double bond. Epoxidation of alkenes followed by epoxide opening with metal amide is also well-known.^{2–6)}

During the course of the synthetic investigation of diversifolin, we found that treatment of γ,δ -unsaturated carboxylic acid **1** with 2.0 eq of phenylselenenyl chloride (PhSeCl) in pyridine at 50 °C, followed by oxidation with hydrogen peroxide, provided γ -butyrolactone **2** in 44% yield (Chart 1).⁷⁾ This result means that allylic oxidation of the trisubstituted alkene proceeded in addition to the planned selenolactonization of the 4-alkenoic acid moiety. Herein we wish to report the scope and limitations of the phenylselenenyl chloride-

mediated allylic oxidation of alkenes.

At first, we investigated the optimization of this oxidation using citronellyl acetate **3** as a model substrate. As shown in Table 1, the reaction of **3** proceeded in a similar manner (PhSeCl–pyridine, 50 °C) as **1** to give the corresponding allyl alcohol **4** in 66% yield (entry 1).⁸⁾ When other readily available phenylselenium reagents were applied in the reaction, neither phenylselenenyl bromide (PhSeBr) nor *N*-PSP (*N*-phenylselenenylphthalimide) were effective for this transformation (entries 2, 3). Although the reactions in benzene, triethylamine, and 2,6-lutidine yielded poor results, the reaction in acetonitrile gave **4** in 31% yield (entries 4–7). As shown in entries 8 and 9, higher reaction temperatures resulted in a slight decrease in the yield probably due to decomposition of **4**. These results indicate that treatment with PhSeCl in pyridine at 50 °C gave the best result.

With optimum conditions established, we next carried out the oxidation of a variety of other substrates **5a–j** as shown in Table 2.⁸⁾ The reaction of 2-methyl-2-undecene (**5a**) gave the corresponding allyl alcohol **6a** in 55% yield (entry 1), while 1,1-diethyl substituted derivative **5b** gave **6b** in a very low yield due to steric hindrance around the trisubstituted olefin (entry 2). In contrast, cyclohexylidene derivative **5c** produced **6c** in higher yield than in the case of **5b** (entry 3). This result might be attributed to inflexibility of the cyclohexane ring in **5c**. Although the allylic oxidations of nerol **5d** and citronerol **5f** afforded the corresponding diols **6d** and **6f**

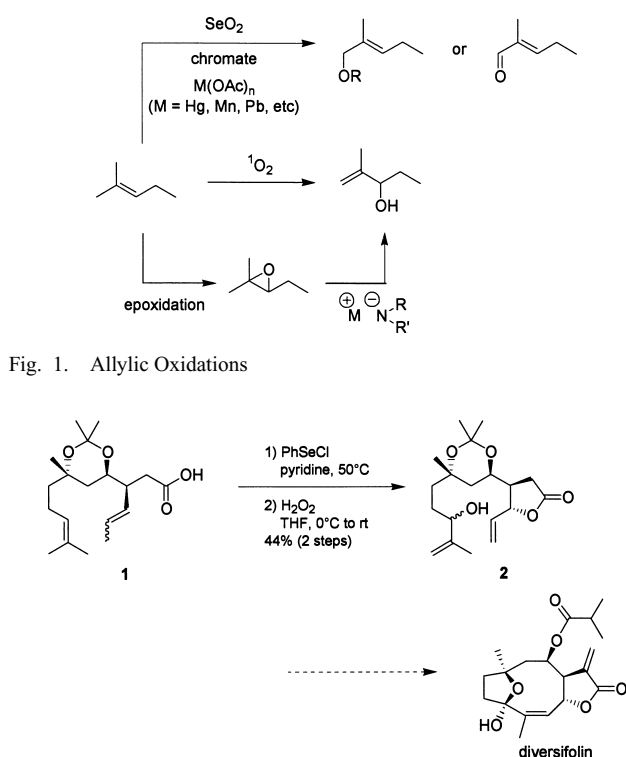


Fig. 1. Allylic Oxidations

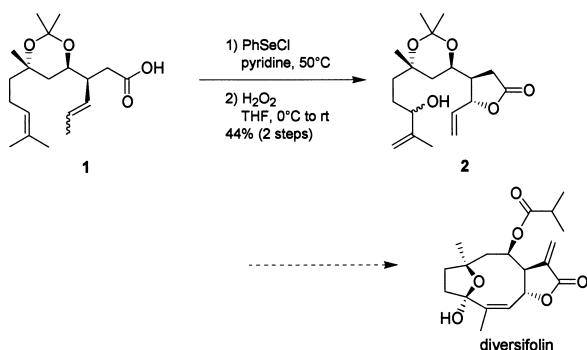


Chart 1

Table 1. Optimization

Entry	PhSeX	Solvent	Temp. (°C)	Yield (%)
1	PhSeCl	Pyridine	50	66
2	PhSeBr	Pyridine	50	6
3	<i>N</i> -PSP ^{a)}	Pyridine	50	N.R. ^{b)}
4	PhSeCl	MeCN	50	31
5	PhSeCl	Benzene	50	3
6	PhSeCl	2,6-Lutidine	50	N.R. ^{b)}
7	PhSeCl	Et ₃ N	50	N.R. ^{b)}
8	PhSeCl	Pyridine	80	62
9	PhSeCl	Pyridine	100	48

a) *N*-Phenylselenenylphthalimide. b) No reaction.

Table 2. Limitation

Entry ^{a)}	Substrate	Product	Yield (%)
1			55
2			6 ^{b)}
3			37
4			28
5			64
6			26
7			66
8			0 ^{d)}
9			59
10			6 ^{c,d)}
11			10

a) i) PhSeCl (1 eq), pyridine (0.1 M), 50 °C; ii) H₂O₂, THF (0.1 M), 0 °C to rt. b) Small amount of the eliminated diene and unrearranged allyl alcohol was obtained. c) Approximately 30% of starting material was recovered. d) Selenoetherified products were obtained.

only in 28% and 26% yields, respectively (entries 4, 6). Yields were increased when the hydroxyl groups in substrates were protected (entries 5, 7). When olefinic alcohol **5g** was treated with PhSeCl, selenoetherification proceeded and no allylic alcohol **6g** was formed, but the corresponding allylic alcohol could be obtained in 59% yield by protecting the hydroxyl group (entries 8, 9). The oxidation of cyclic trisubstituted *endo*-alkenes such as α -terpineol (**5i**) and its silyl derivative (**5j**) gave the corresponding allyl alcohols in poor yield along with approximately 30% recovery of starting alkene (entries 10, 11). From these results on the scope and limitations of this reaction, the present PhSeCl–pyridine methodology was found to be effective for the oxidation of a prenyl unit to a 3-isopenten-2-ol unit.

Further experimentation was also undertaken to elucidate the mechanism of the above allylic oxidation (Chart 2). Thus, the treatment of 2-methyl-2-undecene (**5a**) with PhSeCl in pyridine afforded allyl selenide **7** as an inseparable mixture of geometric isomers (*E/Z* = ca. 2 : 1). Two singlet peaks at δ 3.51 and 3.56 in ¹H-NMR spectra are assigned to an allylic methylene group adjacent to the phenylselenenyl group of *E*-**7** and *Z*-**7**, respectively. The geometry of each isomer was determined by nuclear Overhauser effect (NOE) experiments as shown in Chart 2. The resulting allyl selenide **7** was treated with hydrogen peroxide to afford 2-methyl-1-undecen-3-ol (**6a**).

Based on the above results, a plausible mechanism of the present allylic oxidation is shown in Chart 3. *exo*-Alkenyl al-

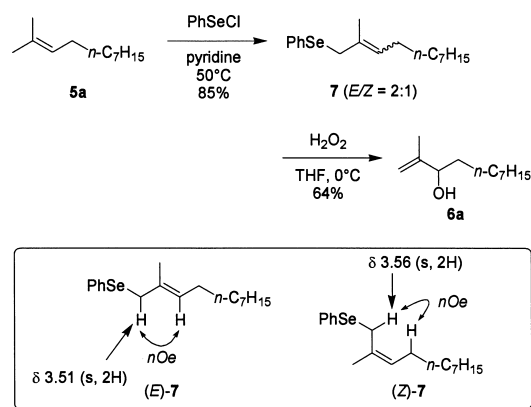


Chart 2. NOE Experiments

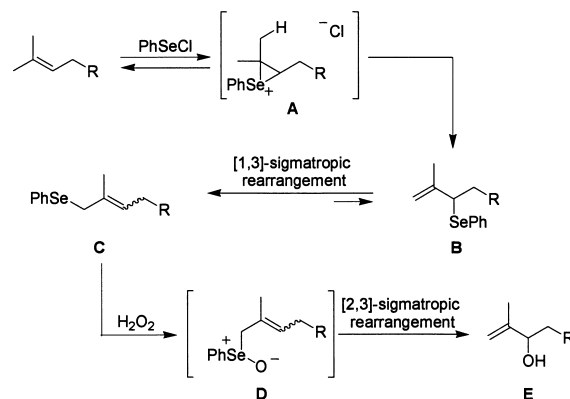


Chart 3. A Plausible Mechanism

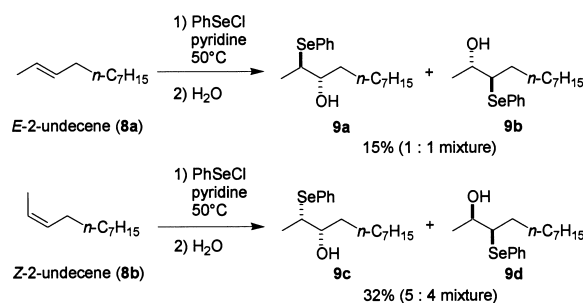


Chart 4

lylic selenide **B**,⁹⁾ formed by reaction of the trisubstituted alkene with phenylselenenyl chloride in pyridine, is in equilibrium with thermodynamically more stable *endo*-alkenyl allylic selenide **C** via a [1,3]-sigmatropic rearrangement.^{10,11)} The *endo*-alkenyl selenide **C** is oxidized by H₂O₂ to selenoxide **D**, which simultaneously undergoes [2,3]-sigmatropic rearrangement^{12–14)} to afford 3-isopenten-2-ol **E**. It should be emphasized that one-pot transformation of trisubstituted alkenes to *endo*-alkenyl allylic selenides involving [1,3]-sigmatropic rearrangement has not been reported.¹⁵⁾

In summary, we have described a method for a transformation of trisubstituted olefins to allylic alcohol.¹⁶⁾ This method is particularly useful for converting the prenyl group into a 3-isopenten-2-ol unit.

General Procedure Phenylselenenyl chloride was added to the solution of 2-methyl-2-undecene (**5a**) in pyridine at 0 °C. The mixture was stirred at 50 °C for 12 h. The resulting

mixture was poured into a saturated aqueous copper sulfate, and extracted with diethyl ether. The combined organic layer was dried over anhydrous sodium sulfate, concentrated, and purified by a short-path silica gel column chromatography (hexane) to afford allyl selenide **7**. The resulting allylic selenide **7** was treated by 30% aqueous hydrogen peroxide solution in tetrahydrofuran at 0 °C. The reaction mixture was extracted with diethyl ether, washed with brine, dried over anhydrous sodium sulfate, concentrated under the reduced pressure, and purified by a silica gel column chromatography to afford allylic alcohol **6a** (55% yield).

References and Notes

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- 16) In the case of disubstituted olefins **8a** and **8b**, each gave rise to an approximate 1 : 1 mixture of β-phenylseleno alcohols **9a**, **9b** and **9c**, **9d**, respectively, instead of the corresponding allyl selenide (Chart 4). The planar structure of **9** was determined by NMR (¹H and ¹³C), IR and HR-MS. When the stereochemistry of **9** was speculated as shown based on the reaction mechanism. Additionally, when a mixture of **5a** and **8b** was treated with PhSeCl, allylic selenide **7** derived from **5a** was obtained, and a significant amount of **8b** was recovered. This result shows that this reaction might be useful for the chemoselective transformation of trisubstituted olefins by PhSeCl.