

## 217. A Convenient High Yield Version of the Ester *Claisen* Rearrangement

Preliminary Communication

by **Martin Petrzilka**

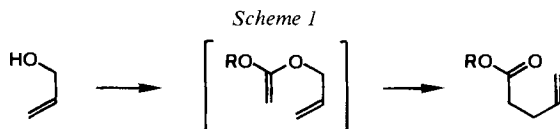
Département de Chimie Organique, Université de Genève, CH-1211 Genève 4

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### Summary

Regiospecific addition of benzeneselenenyl bromide to ethyl vinyl ether followed by alcoholysis of the initially formed  $\beta$ -bromoalkyl selenide **1** by primary, secondary or tertiary allylic alcohols **2a-e** gave the mixed acetals **3a-e**. Subsequent oxidation and thermal treatment of the corresponding selenoxides **4a-e** furnished after saponification the  $\gamma, \delta$ -unsaturated acids **7a-e** in excellent overall yields. The entire sequence (*Scheme 2*) represents a new version of the ester *Claisen* rearrangement.

Since its discovery in 1912 [1] several new variations of the *Claisen* rearrangement have been introduced for synthesis<sup>1)</sup>. Among these the ortho ester process developed by *Johnson et al.* [4] and the allyl ester enolate rearrangement developed by *Arnold et al.* [5] and *Ireland et al.* [6] have served successfully for the preparation of  $\gamma, \delta$ -unsaturated esters and acids. The present communication describes another procedure which provides access to the requisite ketene acetal, the key intermediate of the ester *Claisen* rearrangement (*Scheme 1*).



Although the addition of phenylselenenyl halides to internal [7] and terminal olefins [8]<sup>2)</sup> is a well established process, similar reactions with enolethers have, to our knowledge, not been reported<sup>3)</sup>. Addition of ethyl vinyl ether (1.65 mol-equiv.) to benzeneselenenyl bromide [10] (1.5 mol-equiv.) in dry THF at 25° followed by addition of a solution of  $\beta$ -methallyl alcohol **2d** (1 mol-equiv.) and diisopropylamine (1.65 mol-equiv.) in dry THF furnished after chromatography<sup>4)</sup> (alumina activity

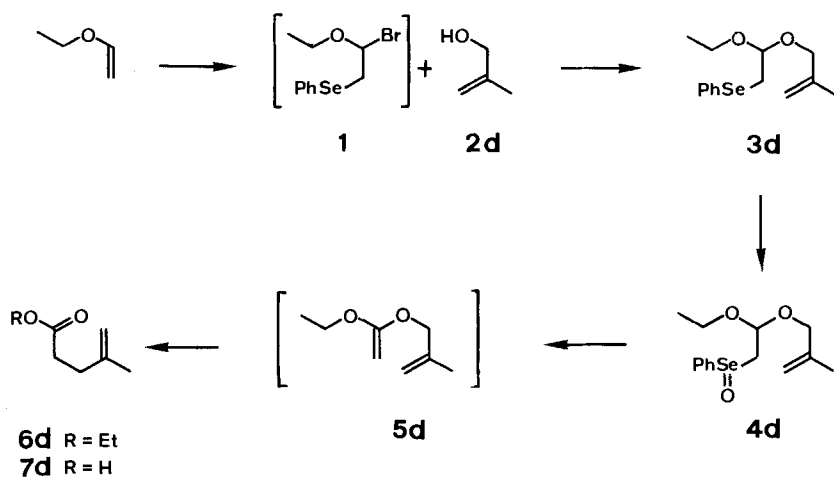
<sup>1)</sup> For recent reviews see [2] [3].

<sup>2)</sup> The degree of regioselectivity in the formation of  $\beta$ -haloalkyl phenylselenides is dependent on the leaving group X = Cl, Br, the solvent and the reaction temperature [8a].

<sup>3)</sup> For a recent comprehensive review article on modern organoselenium chemistry see [9].

<sup>4)</sup> This purification step serves mainly to remove some diphenyldiselenide which is formed during the reaction. If omitted, however, it has no significant influence on the overall yield of acids **7a-e**.

Scheme 2



III) the phenylselenide **3d**<sup>5)</sup> in 99% yield (Scheme 2)<sup>6) 7)</sup>. Characteristically these oily mixed acetals **3a–e** exhibit in their NMR. spectra a triplet ( $J=6$  Hz, 1H) at  $\delta \sim 4.8$  ppm due to the acetal proton and a doublet ( $J=6$  Hz, 2H) at  $\delta \sim 3.15$  ppm due to the two protons next to the phenylseleno group. Subsequent oxidation using  $\text{NaIO}_4$  (1.5 mol-equiv.) and  $\text{NaHCO}_3$  (1.1 mol-equiv.) in  $\text{MeOH}/\text{H}_2\text{O}$  6:1 (1 h/ $25^\circ$ ) afforded the corresponding selenoxide **4d**<sup>5)</sup> as a colourless viscous oil in quantitative yield. Unlike other primary alkyl selenoxides carrying no  $\beta$ -heteroatom substituents the compounds **4a–e** are remarkably stable and may be stored for weeks at ambient temperature without any decomposition. This is certainly due to a strongly retarded *syn* elimination of benzeneselenenic acid towards the two  $\beta$ -alkoxy substituents<sup>8)</sup>. However, under more forcing conditions, *i. e.* heating the selenoxide **4d** in refluxing *m*-xylene (b. p.  $139^\circ$ ) in the presence of hexylamine<sup>9)</sup> (3 mol-equiv.) and dry  $\text{MgSO}_4$  (500 mg/mmol) for 4 h clean elimination of benzeneselenenic acid occurred to give the ethyl ester **6d**, the *Claisen* rearrangement product of ketene acetal **5d**; this,

<sup>5)</sup> All new compounds possessed IR., NMR. and mass spectral data consistent with their assigned structures.


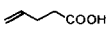

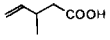

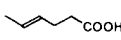

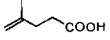

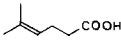
<sup>6)</sup> Neat ethyl vinyl ether (1.65 mmol) was added at once to a solution of benzeneselenenyl bromide [10] (1.5 mmol) in 10 ml of dry THF at  $25^\circ$ . Immediately afterwards a solution of  $\beta$ -methallyl alcohol (1 mmol) and diisopropylamine (1.65 mmol) in 2 ml of dry THF was added over 1 min to the vigorously stirred, clear yellow solution. A voluminous white precipitate was quickly formed. After stirring an additional 10 min the reaction mixture was poured into aq.  $\text{NaHCO}_3$ -solution and extracted with ether. The organic layers were washed with water and brine, dried over  $\text{K}_2\text{CO}_3$  and concentrated *in vacuo*. Chromatography on alumina activity III with hexane (until the yellow diphenyldiselenide was eluted) and hexane/ether 8:1 afforded **3d**<sup>5)</sup> (99%).

<sup>7)</sup> The corresponding regioisomer was not observed under these conditions.

<sup>8)</sup> For a kinetic study of the effect of  $\alpha$ - or  $\beta$ -substituents on the rate of selenoxide *syn* elimination see [11].

<sup>9)</sup> This base was added to prevent any *Pummerer*-like reactions [10].

Table. Yields of the  $\gamma, \delta$ -unsaturated acids **7a-7e** and their precursors

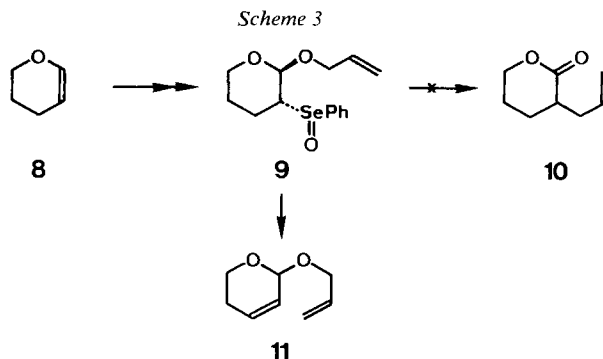
Starting allylic alcohol	Selenide Yield <sup>a)</sup>	Selenoxide Yield <sup>a)</sup>	Acid	Yield <sup>a)</sup>
 <b>2a</b>	<b>3a</b> 100%	<b>4a</b> 93%	 <b>7a</b>	78%
 <b>2b</b>	<b>3b</b> 93%	<b>4b</b> 99%	 <b>7b</b>	95%
 <b>2c</b>	<b>3c</b> 87%	<b>4c</b> 95%	 <b>7c<sup>b)</sup></b>	80%
 <b>2d</b>	<b>3d</b> 99%	<b>4d</b> 100%	 <b>7d</b>	96%
 <b>2e</b>	<b>3e</b> 81%	<b>4e</b> 96%	 <b>7e</b>	100%

<sup>a)</sup> Yields are based on isolated products. <sup>b)</sup> No Z-isomer was detected.

without isolation, was directly saponified<sup>10)</sup> (aq. 2N KOH) to afford 4-methyl-4-pentenoic acid (**7d**) in 96% yield<sup>11)</sup>.

This new procedure for the preparation of  $\gamma, \delta$ -unsaturated acids has also been successfully applied to secondary (**2c**) and tertiary (**2e**) allylic alcohols. These results are summarized in the above Table.

In addition, a cyclic enolether, dihydropyran **8**, was briefly examined as a possible precursor to the  $\alpha$ -substituted lactone **10** (Scheme 3). However, if the selenoxide **9**, prepared according to the given procedure (*vide supra*), was heated for 5 min in refluxing  $\text{CCl}_4$  in the presence of  $\text{CaCO}_3$  the substituted 3,4-dihydropyran **11**<sup>5)</sup> was formed exclusively (91%). This demonstrates that, if possible, elimination away from the heteroatoms is clearly favoured (see also [11]).



<sup>10)</sup> This saponification step was added since the fruity smelling ethyl esters **6a-e** proved to be rather volatile compounds and could not be separated easily from the solvent.

<sup>11)</sup> A mixture of selenoxide **4d** (1 mmol), hexylamine<sup>9)</sup> (3 mmol) and dry  $\text{MgSO}_4$  (500 mg) in 10 ml of *m*-xylene was heated under reflux for 4 h. Then 12 ml of 2N KOH were added and refluxing was continued for 12 h. The separated aq. phase was acidified with conc. HCl-solution and extracted with dichloromethane. Drying ( $\text{MgSO}_4$ ) and concentration *in vacuo* afforded pure **7d**<sup>5)</sup> (96%).

The described three-step procedure for the preparation of  $\gamma, \delta$ -unsaturated esters or acids offers a convenient alternative to the standard methods and allows for the isolation of a stable masked ketene acetal intermediate **4**<sup>12</sup>).

I wish to thank Mr. *J.-P. Saulnier* and Mrs. *F. Klöti* for careful <sup>1</sup>H-NMR. and mass spectra measurements.

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<sup>12</sup>) If desired, expensive diphenyldiselenide may be recovered in a large part.