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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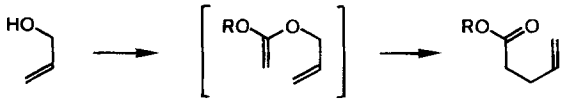
Summary

Regiospecific addition of benzeneselenenyl bromide to ethyl vinyl ether followed by alcoholysis of the initially formed β-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 γ,δ-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[1]). 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 γ,δ-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)*.

Scheme 1



Although the addition of phenylselenenyl halides to internal [7] and terminal olefins [8][2]) is a well established process, similar reactions with enolethers have, to our knowledge, not been reported[3]). 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 β-methallylalcohol **2d** (1 mol-equiv.) and diisopropylamine (1.65 mol-equiv.) in dry THF furnished after chromatography[4]) (alumina activity

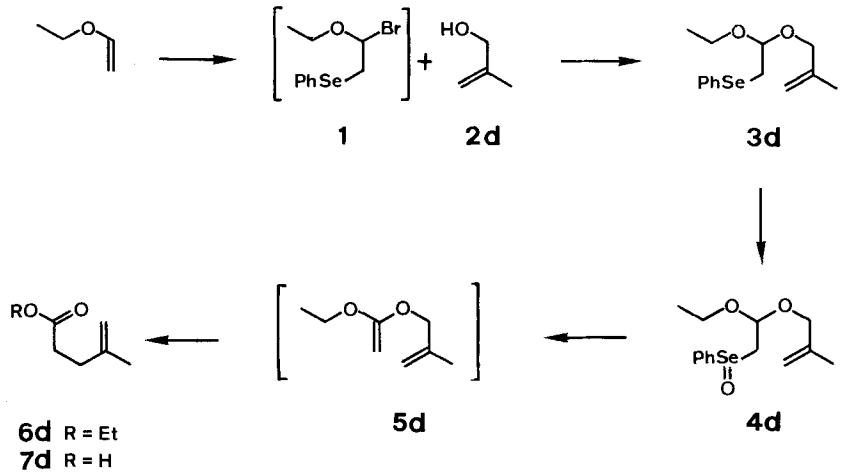
[1]) For recent reviews see [2] [3].

[2]) The degree of regioselectivity in the formation of β-haloalkyl phenylselenides is dependent on the leaving group X = Cl, Br, the solvent and the reaction temperature [8a].

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

[4]) 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**[5]) in 99% yield *(Scheme 2)*[6])[7]). 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 $NaIO_4$ (1.5 mol-equiv.) and $NaHCO_3$ (1.1 mol-equiv.) in $MeOH/H_2O$ 6:1 (1 h/25°) afforded the corresponding selenoxide **4d**[5]) as a colourless viscous oil in quantitative yield. Unlike other primary alkyl selenoxides carrying no β-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 β-alkoxy substituents[8]). However, under more forcing conditions, *i.e.* heating the selenoxide **4d** in refluxing *m*-xylene (b.p. 139°) in the presence of hexylamine[9]) (3 mol-equiv.) and dry $MgSO_4$ (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,

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[5]) All new compounds possessed IR., NMR. and mass spectral data consistent with their assigned structures.

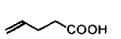
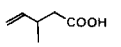
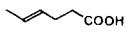
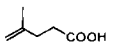
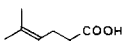
[6]) Neat ethyl vinyl ether (1.65 mmol) was added at once to a solution of benzeneselenenyl bromide [10] (1.5 mmol) in 10 ml of dry THF at 25°. Immediately afterwards a solution of β-methallyl alcohol (1 mmol) and diisopropylamine (1.65 mmol) in 2 ml of dry THF was added over 1 min to the vigorously stirred, clear yellow solution. A voluminous white precipitate was quickly formed. After stirring an additional 10 min the reaction mixture was poured into aq. $NaHCO_3$-solution and extracted with ether. The organic layers were washed with water and brine, dried over K_2CO_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**[5]) (99%).

[7]) The corresponding regioisomer was not observed under these conditions.

[8]) For a kinetic study of the effect of α- or β-substituents on the rate of selenoxide *syn* elimination see [11].

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

Table. *Yields of the γ,δ-unsaturated acids* **7a–7e** *and their precursors*

Starting allylic alcohol		Selenide Yield[a])		Selenoxide Yield[a])		Acid		Yield[a])
	**2a**	**3a**	100%	**4a**	93%		**7a**	78%
	**2b**	**3b**	93%	**4b**	99%		**7b**	95%
	**2c**	**3c**	87%	**4c**	95%		**7c**[b])	80%
	**2d**	**3d**	99%	**4d**	100%		**7d**	96%
	**2e**	**3e**	81%	**4e**	96%		**7e**	100%

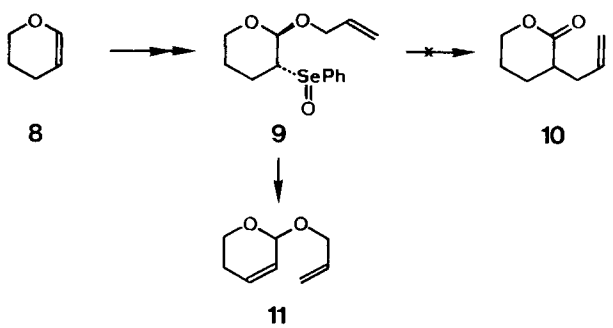
[a]) Yields are based on isolated products. [b]) No *Z*-isomer was detected.

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

This new procedure for the preparation of γ,δ-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 α-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 CCl_4 in the presence of $CaCO_3$ the substituted 3,4-dihydropyran **11**[5]) was formed exclusively (91%). This demonstrates that, if possible, elimination away from the heteroatoms is clearly favoured (see also [11]).

Scheme 3



8 **9** **10**

11

[10]) 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.

[11]) A mixture of selenoxide **4d** (1 mmol), hexylamine[9]) (3 mmol) and dry $MgSO_4$ (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 ($MgSO_4$) and concentration *in vacuo* afforded pure **7d**[5]) (96%).

The described three-step procedure for the preparation of γ,δ-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**[12]).

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[12]) If desired, expensive diphenyldiselenide may be recovered in a large part.