295. A New Type of *Claisen* Rearrangement Involving 1,3-Dipolar Intermediates[1])

Preliminary communication

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Summary

During the reaction of allyl ethers, allyl sulfides and allyl selenides with *in situ* prepared dichloroketene (**1**), 2 competing pathways are observed. Besides [2+2]-cycloaddition, an unprecedented [3,3]-sigmatropic *(Claisen)* rearrangement *via* a 1,3-dipolar intermediate takes place. It leads to *O*-, *S*- or *Se*-esters of a,a-dichloro-γ,δ-unsaturated acids containing an inverted allylic group. Starting from cyclic **n**-membered a-vinyl-substituted ethers, lactones with **n+4**-membered rings are formed. A very facile synthesis of the naturally occurring macrolides (±)-phoracantholide I (**10**) and (±)-phoracantholide J (**11**) illustrates the synthetic utility of this new 'ketene' *Claisen* rearrangement.

In 1912, the thermal rearrangement of phenyl allyl ethers was discovered by *Claisen* [1]. In the last 30 years, the synthetic scope of this [3,3]-sigmatropic rearrangement has been considerably broadened. In particular, the 'enolate' [2], 'amide' [3] and 'ester' [4] versions of the *Claisen* rearrangement have found very useful synthetic applications[2]). Furthermore, the presence of a negative charge at C(1) in the enolate system [3] or a positively charged heteroatom at position 3 [6] aids in lowering the activation energy of the rearrangement[3]).

We now report that the combination of *both* accelerating factors in *one* reactive 1,3-dipolar intermediate formed *in situ* from allylic *O*-, *S*- or *Se*-ethers and dichloroketene (**1**) permits the preparation of *O*-, *S*- or *Se*-esters of γ,δ-unsaturated acids at RT., and in good yields. Thus, when dichloroketene (**1**), prepared *in situ* by slow addition (4 h) of trichloroacetylchloride (0.11 M) to a suspension of Cu-activated Zn powder (0.12 M) in ether (150 ml), reacts with (2-methylbut-2-enyl)phenylsulfide (**2**) (0.10 M) at 25°, work-up after 2 h yields the [2+2]-cycloadduct **3** ($\tilde{\nu}_{C=O}$ 1808 cm^{-1},

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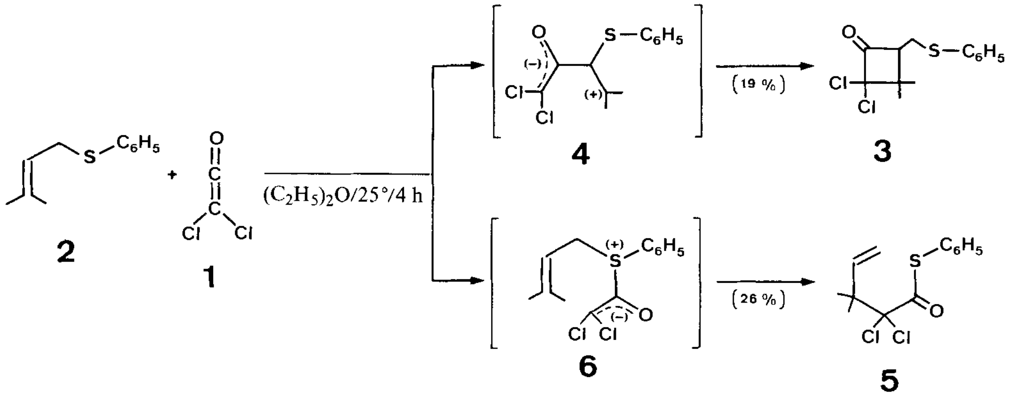
[1]) Presented at the Autumn Meeting of the Swiss Chemical Society, Bern, October 20-21, 1978.

[2]) For further references see recent reviews on *Claisen* rearrangement [5].

[3]) *E.g.* the acceleration factors (K_{H^+}/K_{Δ}) calculated from the activation parameters of the acid-catalyzed and thermal rearrangements of *N*-allylanilines are 10^5-10^7 [6].

Scheme 1



19%) (*via* **4**), along with the *S*-phenyl ester of 2,2-dichloro-3,3-dimethylpent-4-enoic acid (**5**) (b.p. 120°/0.001 Torr; $\tilde{\nu}_{C=O}$ 1704 cm^{-1}; 26%)[4]). Apparently, the nucleophilic sulfur atom in **2** competes successfully with the double bond for the electrophilic dichloroketene. The 1,3-dipolar intermediate **6** thus formed is beautifully set up for a [3,3]-rearrangement leading to **5**.

Table. *Yields of competitive reactions of allyl ethers* **7a–e**, *allyl sulfides* **7f–g** *and allyl selenide* **7h** *with dichloroketene* (**1**)

Entry	X	R_1	R_2	R_3	R_4	R_5	**8** Yield[a])	**9** Yield[b])
a	O	Me	H	H	Me	H	63%	-
b	O	Me	Me	H	Me	H	45%	-
c	O	Me	H	H	Me	Me	48%	25%
d	O	Me	H	H	Ph	H	60%	-
e	O	$SiMe_3$	H	H	Me	H	40%[c])	-
f	S	Et	H	Me	Me	H	60%	-
g	S	Et	H	H	H	H	40%	-
h	Se	Ph	H	H	Me	Me	38%	19%

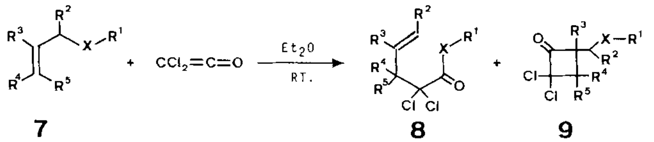
[a]) Yields of isolated products.

[b]) Yields calculated from integrated ^{1}H-NMR. spectra of crude reaction products.

[c]) Yield of free acid (**8e**; $R_1 = H$) after work-up.

We thank Prof. *A. Eschenmoser* for suggesting this experiment.

Scheme 2



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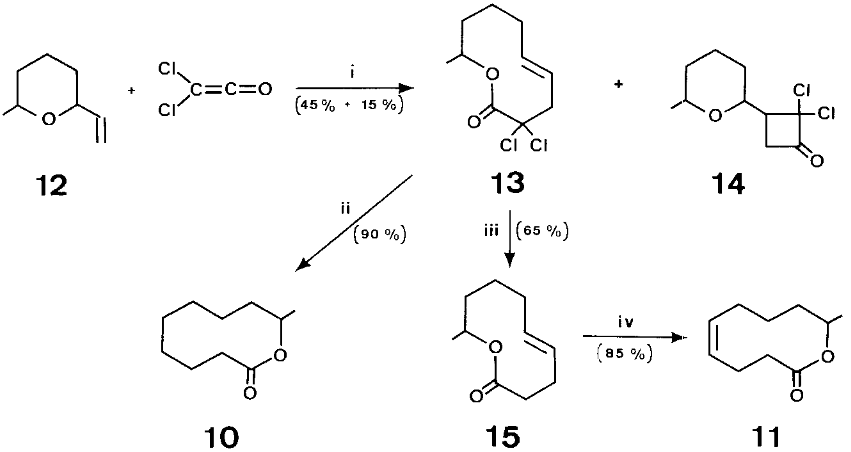
[4]) Satisfactory spectroscopic analyses have been obtained for all new compounds.

The facility of this rearrangement is particularly striking in the case of *O*-allyl ethers (**7**; X=0). Some representative examples of a series of simple *O*-, *S*- and *Se*-esters are presented in the *Table*. As is common for *Claisen* rearrangements [5], the esters **8** contain an inverted allylic group. The stereochemistry of the resultant double bond in the rearrangement of the secondary ether **7b** displays high selectivity (≥95% by NMR.) for the (*E*)-isomer. In most cases, the esters **8** are the only isolable products[5]).

Scheme 3



i $(C_2H_5)_2O$/25°/4 h
ii H_2/Pd-C 5%/dioxane/$(C_2H_5)_3N$ (2 equiv.)/25°
iii Zn/CH_3COOH/80°/6 h
iv $(C_6H_5S)_2$ (0.05 equiv.)/hexane/hν/20°

The extremely facile synthesis of the naturally occurring 10-membered ring macrolides (±)-phoracantholide I (**10**) and (±)-phoracantholide J (**11**)[6]) exemplifies the applicability of this new rearrangement for the transformation of cyclic, **n**-membered, α-vinylsubstituted ethers into unsaturated, **n**+**4**-membered lactones.

Treatment of **12**[7]) with 1.2 equiv. of dichloroketene (**1**) under the usual exper. conditions (see above) produces a 3:1 mixture (by NMR.) of **13** and **14**[4]). Chromatographic separation gives pure **13** (45%) as an oil. Spectral data show that **13**

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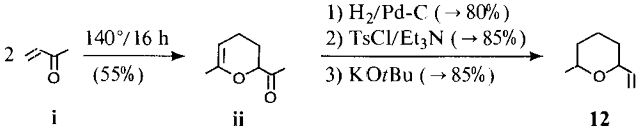
[5]) If **8** is isolated by distillation, the most volatile fractions contain some starting material **7** and the corresponding alkyl dichloroacetate (up to 15%).

[6]) Compounds **10** and **11** were found in the metasternal secretion of the eucalypt longicorn *Phoracantha synonyma* [7]. Both macrolides were first totally synthetized by *Gerlach et al.* [8]. Recently, *Petrzilka* [9] synthesized **11** using his version [4c] of the 'ester' *Claisen* rearrangement.

[7]) Compound **12** was prepared *via* the [4+2]-dimer **ii** of butenone **i** [10] in 4 very simple steps as follows:



and the dechlorinated product **15** are isomerically pure (*E*)-lactones[8]. Catalytic reduction of **13** yields the saturated dechlorinated lactone **10**, identical (IR.; NMR.[8]) and GC. behaviour) with an authentic sample of (±)-phoracantholide I[9]).

Compound **15** is converted to a 1:20 mixture of **15** and **11** using the method of (*E*)/(*Z*)-isomerization developed by *Schulte-Elte & Ohloff* [11]. Thus, irradiation of a 0.2M hexane solution of **15** in the presence of 0.05 equiv. of diphenyldisulfide, followed by preparative GC. (SE 30; 20%; 200°) affords **11** in 85% yield[8])[9]). This synthesis of (±)-phoracantholide J (**11**) and especially that of **10** has the advantage over previous syntheses in that it involves few steps, proceeds in good yield and utilizes readily available starting materials.

Noteworthy features of the new 'ketene' *Claisen* rearrangement are: (a) neither high temperatures nor exotic and expensive reagents are necessary to create the reactive intermediates; (b) for the first time, the ring enlargement by 4 carbon atoms (cyclic ether → lactone transformation) can be accomplished by means of a *Claisen* rearrangement; (c) the chlorine atoms in the α-position of products such as **8** or **13** can be conveniently removed by metal (Zn, Fe) reduction; and (d) as far as dichloroketene (**1**) is concerned, this rearrangement represents a hitherto unknown reaction mode of this well investigated [12] ketene[10]).

We thank our colleague, Dr. *H. Greuter*, for many stimulating discussions.

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[8] The vicinal coupling constants *J* between olefinic protons determined by 360 MHz ^{1}H-NMR. ($CDCl_3$) are: 15.5 Hz in **13** and in **15** ((*E*)–C=C) and 11.2 Hz in **11** ((*Z*)–C=C). We thank Dr. *G. Rist* for these careful NMR. spectra measurements.

[9] We thank Prof. *H. Gerlach*, ETH Zürich, for providing the samples of **10** and **11**, and Dr. *M. Petrzilka*, University of Geneva, for a sample of a mixture of **15** and **11**.

[10] Monochloroketene and cyanochloroketene can be used analogously to **1**; however, the yields of esters of type **8** are lower.