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Facile Access to 2-Alkylidene 3-Oxy Propanals and Propionic Acids from Conjugated Enals

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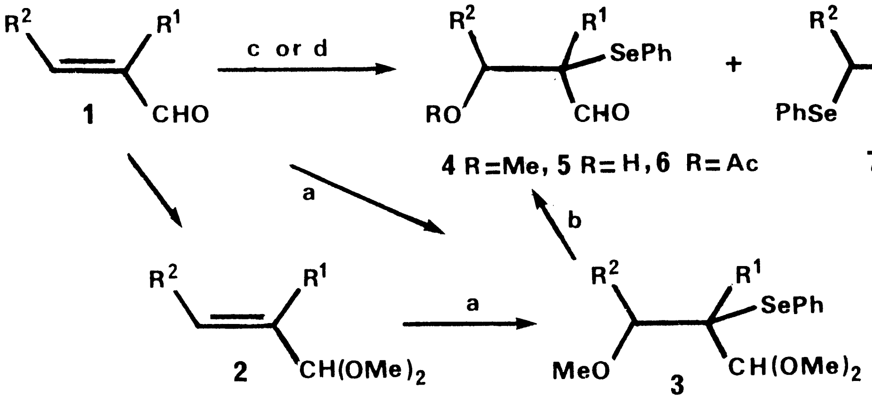
Conjugated enals or their methyl acetals react with benzeneselenenyl chloride in the presence.of an oxygen nucleophile to give Michael-type adducts. The latter are oxidized into 2-alkylidene 3-oxy propanals and propionic acids.

α-Phenylseleno α,β-unsaturated aldehydes [1)] are easily prepared by addition of morpholino benzeneselenenamide on conjugated enals followed byelimination of morpholine [2)] We decided to study the reaction using a selenium electrophile (PhSeCl) and various oxygen or nitrogen nucleophiles on conjugated enals (or their methyl acetals) bearing various substituents on the α- and β-carbons. We present our first results concerning the use of oxygen nucleo-philes (MeOH, H_2O, AcO^-) in the reactions with enals 1 or acetals 2.



a) PhSeCl, MeOH, -30°C, 3 h (1 h for 2) then $NaHCO_3$, -30°C → 20°C ; b) H_3O^+
c) PhSeCl, $MeCN/H_2O$ (3/1), 20°C, 8 h; d) PhSeCl, KOAc, Ac_2O, AcOH, 20°C, 8 h.

Scheme 1.

Regarding the additions of selenium electrophile on enals, we only noted the reactions of acrylaldehyde and crotonaldehyde with phenyl selenocyanate (MeOH, CuCl2 or CuCl)[3] and benzeneselenenyl halides in chloroform[4] or methylene chloride.[5] We first studied the reaction of PhSeCl with enals 1 in methanol. Diastereomeric mixtures of acetals 3 were isolated after treatment with sodium carbonate at-30°C(Scheme 1).The same adducts 3 were obtained from the acetals 2[6] in comparable yields and diastereomeric ratios (Table 1). Starting from the aldehydes 1, we observed that the acetals 2 first appear and that the regioisomers of 3 are not formed. These observations can be interpreted by the reversible formation of an intermediate seleniranium cation derived from 2 as previously proposed,[5] followed by the nucleophilic attack of the less hindered and more activated β-carbon. The acidic hydrolysis of the acetals 3 gave the aldehydes 4 (R= Me) in good yields (Table 1).

Table 1. Acetals 3, aldehydes 4, 5, 6,and 7[a]

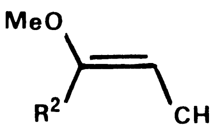
No.			3	4	5	6,7	
1 - 7	R^1	R^2	Yield/% b)	Yield/% b)	Yield/%	Yield/%	Regio. Comp.6/7
a	H	H	35[c]	-[c]	-[f]	74	40/60
b	H	Me	90[c] (68/32)	79[c] (64/36)	87 (57/43)		
c	H	nPr	81 (75/25)	85 (82/18)	81 (52/48)		
d	H	Ph	91 (100/0)	92 (100/0)	-[g]		
e	Me	H	91	84	80		
f	Me	Me	83 (60/40)	85 (55/45)	78 (59/41)	68	68/32 (35/45) (30/70)
g	Me	Et	75 (57/43)	93 (55/45)	69 (53/47)	74	72/28 (58/42) (56/44)
h	Me	Ph	-[e]	90 (70/30)	-[g]		
i	Et	Me	78 (54/46)	79 (63/37)	58 (62/38)		
j	$-(CH_2)_4-$		55 (64/36)	75 (65/35)	-[h]		

a) All compounds were fully characterized (^1H NMR, Mass, and IR spectra) and gave satisfactory microanalyses. b) Diasteromeric Composition.
c) Compounds already described See Ref.3 d) Not isolated in pure form.
e) Partially hydrolyzed. f) Mixture of compounds not analyzed.
g) The addition reaction is unsuccessful. h) Reaction not achieved.

The addition of PhSeCl to 1 in a mixture MeCN/H_2O (3/1) leads to the β-hydroxy α-phenylseleno-aldehydes 5 (R=H) without any traces of regioisomers. The reaction time is longer than for the methoxyselenenylation. Starting from the acetals 2, the fast hydrolysis of the intermediate acetal adducts occurs in the media and the formation of the two diastereoisomers of 5 was observed.

The two regioisomers 6 and 7 are formed in the course of the acetoxyselenenylation of enals 1. The two diastereoisomers are characterized for both compounds. It is to be noted that in the case of enals 1, with no alkyl group in the α-position, the corresponding α-phenylseleno α,β-unsaturated aldehydes[1)] were isolated. The β-acetoxy derivatives 6 were also prepared by esterification of the β-hydroxy aldehydes 5.[7)]

The periodate oxidation[8)] of α-seleno aldehydes 4b and 4d with no substituent on the α-carbon (R^1=H) gave, after thermal decomposition of the stable selenoxides, the β-methoxy enals 8a (R^2=Me)[9)] and 8b (R^2=Ph),[10)] respectively.



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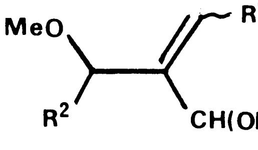

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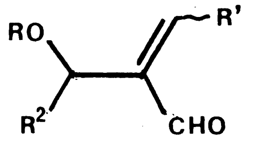
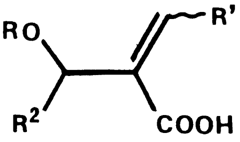


10, 11, 12
R = Me, H, Ac



13, 14, 15
R = Me, H, Ac

Table 2. Acetals 9, aldehydes 10,12, and carboxylic acids 13-15

No.			Yield/%						
9-15	R'	R^2	9	10	11	12	13	14	15
a	H	H	55	58	51				
b	H	Me	60	74	65	61	79	58	62
c	H	Et	70	72	54	65	73	54	60
d	H	Ph	-	88			86		
e	Me	Me	74[a)]	78[b)]			75[c)]		
f	$-(CH_2)_3-$		60	65			90		

a-c) Mixture of Z-E isomers : a) 59/42 c) 72/28.

Under the same oxidative conditions,[8)] the α-seleno acetals 3 gave directly the unsaturated acetals 9 while the α-seleno aldehydes 4, 5, and 6 with an α-alkyl substituent R^1=CH_2R' lead to the conjugated enals 10, 11, and 12, respectively[8)] (Table 2).

As previously described for simple α-seleno aldehydes,11) the hydrogen peroxide oxidation of the adducts 4, 5, and 6 (R^1= CH_2R') allows the facile access to the α,β-unsaturated carboxylic acids 13, 14 and 15 bearing respectively a methoxymethyl, an hydroxymethyl and an acetoxymethyl group on the α-carbon. All the olefinic compounds were prepared in fair to good yields (Table 2).

Other transformations of the adducts 3-7 are now under investigation. The use of nitrogen nucleophiles in the addition reaction on conjugated enals has been also studied in our laboratory.12)

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7) Ac_2O, pyridine, 70°C, 8 h : 6a, 82 % ; 8f : 78 % (61/39) ; 8g : 70 % (56/44).
8) Oxidation of 3 and 4 : $NaIO_4$ (2 equiv.), MeOH:H_2O (3/1), $NaHCO_3$, 0 °C, 1h. The selenoxides derived from 4 (R^1=H) are stable compounds characterized by ^1H NMR. The oxidation of hydroxy aldehydes 5 and acetates 6 was achieved in pure methanol. The thermal decomposition of selenoxides leading to enol ethers 8 was carried out in CCl_4 at reflux in the presence of DABCO. 8a (R^2=Me) : 30 % yield. 8b (R^2=Ph): 71 % yield. The stereochemistry of these known compounds was determined (Ref. 9 and 10).
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