

NEW REGIOSPECIFIC AND STEREOSSELECTIVE ROUTE TO β -HYDROXY SELENIDES

A (C,C) CONNECTIVE AND STEREOSPECIFIC ROUTE TO OLEFINS AND EPOXIDES

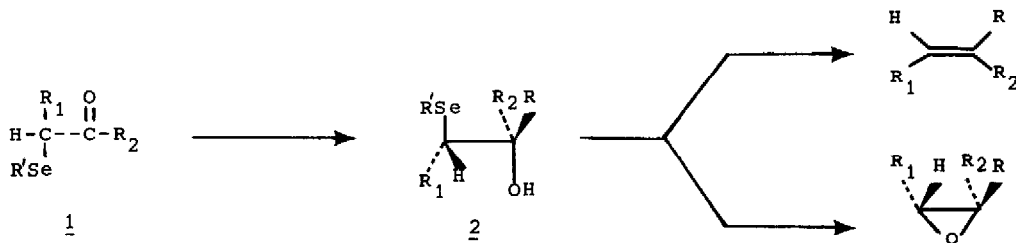
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β -Hydroxy selenides 2 are used extensively for the synthesis of allyl alcohols^{1,2}, β -halogenohydrins³, as well as for the stereospecific synthesis of olefins⁴ or epoxides⁵. These compounds 2 have already been synthesized by (C-C) connective routes from α -seleno carbanions^{2,4,5} and a carbonyl compound, or stereospecifically^{1,4a} from an epoxide and alkyl or phenyl selenolate.

This paper reports a new synthon for the synthesis of β -hydroxy selenides which allows both a connective (C-C) bond formation and a stereoselective arrangement of the hydroxyl and selenyl functions by reacting α -seleno carbonyl compounds and organometallics (Scheme 1).

Scheme 1



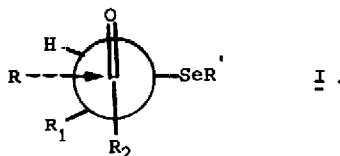
Lithium aluminum hydride⁶ in ether (-15°C) for instance adds the carbonyl group of α -seleno aldehydes or ketones^{7,8} producing the β -hydroxy selenides 2 in up to 65% yield, moreover in the later case the "threo" derivative 2 is stereoselectively formed (threo / erythro : 80/20). (See : scheme 1 (R : H), TABLE 1).

β -Hydroxy selenides are also synthesized in 65% yield by reacting Grignard reagents⁹ in THF or ether with α -seleno aldehydes. In this case, the "erythro" isomer 2 is stereoselectively formed (erythro / threo : 94/6). (See : scheme 1 (R : alkyl), TABLE 1).

Unfortunately, except in the case of α -seleno acetone, Grignard reagents do not add to α -seleno ketones under standard conditions.

The high selectivity of our reaction can be explained by the Felkin model¹¹ I (Scheme II) in which the separation between the selenyl group and the incoming organometallic is the greatest. It is not surprising then that the more polar selenophenyl group leads to a better stereochemical control (erythro/threo: 94/6) than does the selenomethyl group (erythro/threo: 85/15). Several examples of such a kind of stereoselective induction, on α -heterosubstituted carbonyl compounds have been extensively described in the literature¹¹⁻¹⁷ and several reports have been devoted to tentatively explain^{11-17,18,19} the experimental results.

Scheme II



The reaction we describe in Scheme I is a parallel to the well known Cornforth synthesis¹⁷ of disubstituted epoxides and olefins. The main advantages of our method for the synthesis of olefins and epoxides are listed below:

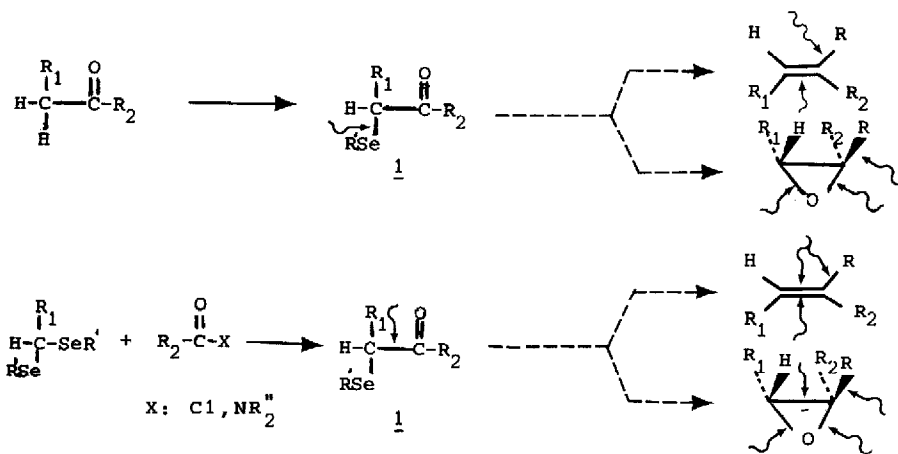
I) the inertness of the β -hydroxy selenides under the reaction conditions in which they are formed

II) the easy and selective activation of β -hydroxy selenides which allows their stereospecific conversion either to an epoxide⁵ or an olefin⁴. The later transformation being easier compared to the Cornforth transformation (β -chlorohydrin \longrightarrow olefin).

Another main interest arises from the *flexibility* of the synthetic routes proposed in Scheme III, due to the powerful synthetic methods of formation of the starting α -seleno carbonyl compounds 1 compare to those described for their α -chloro analogs, e.g. route B allows the regioselective synthesis of α -seleno ketones even when R_1 and R_2 are both alkyl groups.

Scheme III propose different methodologies and different building blocks which can be used for the synthesis either of Z or E olefins as well as for Cis or Trans epoxides.

Scheme III



Refers to the bonds which are formed .

TABLE I

α -seleno carbonyl compound <u>1</u>				Incoming organometallic	β -hydroxy selenide <u>2</u>	olefin	epoxide		
R ₁	R ₂	R'	Yield % () ^a	R ^b	Yield %	Yield % () ^c	E/Z ratio ^d	Yield %	Trans/cis ratio
C ₉ H ₁₉	H	C ₆ H ₅	62 (A)	CH ₃	67	92 (A)	97/3		
C ₅ H ₁₁	H	C ₆ H ₅	67 (A)	C ₆ H ₁₃	75	36 (A)	-		
C ₅ H ₁₁	H	C ₆ H ₅	67 (A)	C ₁₀ H ₂₁	65	76 (A)	94/6		
C ₂ H ₅	H	C ₆ H ₅	60 (A)	C ₃ H ₇	80	85 (B)	97/3		
H	CH ₃	C ₆ H ₅	37 (A)	C ₁₀ H ₂₁	24	90 (B)	-		
C ₁₀ H ₂₁	H	CH ₃	65 (B)	CH ₃	75	60 (A)	-	90	
C ₁₀ H ₂₁	H	CH ₃	65 (B)	C ₁₀ H ₂₁	68	67 (A)	85/15	70	85/15
C ₆ H ₁₃	H	CH ₃	40 (B)	C ₁₀ H ₂₁	50	67 (A)	81/19		
C ₅ H ₁₁	H	C ₆ H ₅	62 (A)	H	60	-	-		
C ₅ H ₁₁	H	C ₆ H ₅	67 (A)	H	60	-	-		
C ₂ H ₅	C ₃ H ₇	C ₆ H ₅	73 (A)	H	71	85 (B)	23/77		
C ₉ H ₁₉	C ₁₀ H ₂₁	C ₆ H ₅	45 (A)	H	60	80 (B)	16/84		

Unless otherwise noted, the yields refer to purified compounds. Spectroscopic data (IR, NMR, Mass spectra) fully agreement the proposed structures.

a) Refers to the synthetic method used :

A. C₆H₅SeCl in ethyl acetate on the corresponding carbonyl compound according to Sharpless procedure⁷.

B. Obtained from an α -seleno carbanion and dimethyl formamide according to our previously described method⁸.

b) R : alkyl, refers to the reaction of the corresponding Grignard reagent on the compound 1.

R : H, refers to the reaction of lithium aluminum hydride on the compound 1.

c) Refers to the synthetic method used :

A. p-toluene sulfonic acid in pentane according to our previously described method^{4a}.

B. Thionyl chloride and triethyl amine in methylene chloride²⁰.

d) Stereochemistry of the products as well as the percentage of isomers have been deduced from the corresponding thiono carbonates²¹.

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- 6a) Typical experiment : α -seleno carbonyl compound (3 mmoles) in ether (5 ml) is slowly added to a precooled (-15°C) suspension of lithium aluminum hydride (2 eq.) in the same solvent (4 ml). After stirring 2 hrs. at this temperature then 1 more hr. at 25°C, a KOH (50%) solution (3-8 drops) is slowly added. The resulting suspension is diluted in ether, filtered over cellite, washed with brine and dried. The β -hydroxy-selenide is purified by PLC (Preparative thick layer chromatography, SiO₂, ether-pentane : 1-9).
 - b) Reductions have also been performed by lithium aluminum hydride in THF or DME, or sodium borohydride in ethanol. In both cases, products resulting from the cleavage of the C - Se bond are observed beside the β -hydroxy-selenide.
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- 9) Typical experiment : α -seleno-aldehyde (3 mmoles) in ether (3 ml) is added to a precooled (-110°C) solution of Grignard reagent ¹⁰ (3.5 mmoles) in ether. Stirring is continued at -110°C for 2 hrs. then at -78°C for an additional hr. Acetic acid (1 ml) is added at this temperature. After hydrolysis (10 ml, 0°C), the organic layer is extracted and dried. The purification was done as described in ref. 6a.
- 10) When organolithium compounds are used in place of Grignard reagents, the yield of β -hydroxy-selenide is rather low (8 %) (Stereochemical control E/Z : 90/10). Starting material is also recovered (15%).
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