Stereo- and Regioselective Zinc-Mediated Ring-Opening of Epoxides with Diselenides

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Abstract: Two convenient rapid, efficient, stereoselective and highly regioselective methods for the synthesis of β -hydroxy selenides by the direct opening of epoxides with diselenides in acetonitrile in the presence of either Zn/AlCl₃ or zinc powder in aqueous sodium hydroxide solution are described. These methods appear to be competitive with the other methods previously reported.

Key words: β -hydroxy selenides, diselenides, epoxides, zinc, zinc selenolate

 β -Hydroxy selenides are valuable selenium intermediates in organic synthesis;¹ they can be converted to allylic alcohols, olefins, bromohydrins, vinyl selenides and epoxides.²⁻⁵ Several methods are available for the preparation of β-hydroxy selenides. These hydroxy compounds have been found as the addition products of selenenic acids to olefins with a good regioselectivity.⁶ The $S_N 2$ displacement of bromine from β -bromoselenides by hydroxide ion is another stereoselective method.⁷ The alkaline hydrolysis of β-acetoxyselenides has been described.⁸ A convenient method for the synthesis of β -hydroxy selenide uses N-phenylselenophthalimide (NPSP) in the presence of water.⁹ Another important method is the reaction of aldehydes and ketones with seleniumstabilized carbanions.¹⁰ The reduction¹¹ or nucleophilic addition of Grignard reagents,¹¹ alkyllithium, a-selenoalkyllithiums¹² to α -selenoaldehydes or β -selenoketones provide other methods for access to β -hydroxy selenides.

The $S_N 2$ ring-opening of epoxides, using selenolate anions, is a common method for preparing β -hydroxy selenides. This method provides an excellent preparative route to allylic alcohols via selenoxide elimination.² Other effective reagents for epoxide-opening include phenyl trimethylsilyl selenide,¹³ aluminum selenolates,¹⁴ selenoboranes,¹⁵ and benzeneselenol in the presence of alumina.¹⁶ Attack by the selenolates generally occurs at the less hindered epoxide carbon and is *anti* stereospecific. In cyclic systems, a strong preference for approach from the axial direction may outweigh other factors.

Herein, we report that alkyl and arylselenide ions can be easily generated from the corresponding diselenides in the presence of either $Zn/AlCl_3$ under neutral conditions or with zinc powder in aqueous sodium hydroxide solution.

SYNLETT 2005, No. 8, pp 1316–1318 Advanced online publication: 21.04.2005 DOI: 10.1055/s-2005-865224; Art ID: D00605ST © Georg Thieme Verlag Stuttgart · New York The anion can then react, under mild and atmospheric conditions, with different classes of epoxides to give β -hydroxy selenides, formed via *trans*-opening of the epoxides, in moderate to excellent yields (Scheme 1). Table 1 shows the results obtained in the reactions of a series of representative epoxides with diphenyl- and dibenzyl diselenides in the presence of Zn/AlCl₃ system in anhydrous acetonitrile (method A), compared with the results obtained in the results obtained in the presence of zn/AlCl₃ system is anhydrous acetonitrile (method A).



From the results in Table 1 it is quite evident that, in the case of unsymmetrical epoxides, the reaction proceeds with a remarkable regioselectivity because in most cases selenolate anions exclusively attack the less hindered carbon of the epoxide to give the regioisomer (2, Scheme 1). The exceptions are given by styrene oxide (entries 13 and 14) and 1,2-epoxy-3-phenoxypropane (entry 15) where mixtures of the two regioisomers are obtained. Under neutral conditions, styrene oxide reacted with diphenyl diselenide to give regioisomers (2h) and (3h) in 64:36 ratio (83% total isolated yield); whereas, the same reaction under alkaline conditions gave the two regioisomers (2h) and (3h) as an 80:20 mixture (81% total isolated yield). This regioselectivity is presumably due to partial stabilization of developing positive charge at the more hindered site of the epoxide. In the reaction of 1,2-epoxy-3-phenoxypropane with diphenyl diselenide under both reaction conditions, while only one regioisomer (2i) was obtained in alkaline medium (entry 16), equal quantities of both regioisomers were detected under neutral conditions. The reactions are completely anti-stereoselective as shown by the reactions carried out on cyclohexene- and cyclooctene oxides (entries 8-12), where no trace of the syn-adducts were detected by ¹H NMR spectroscopy.

When diselenides were reacted with $Zn/AlCl_3$ in dry MeCN (method A), the zinc powder almost disappeared within 1.5 hours; this indicates a reductive cleavage of the Se-Se bond¹⁷ leading to the zinc selenolate [(R²Se)₂Zn] intermediate which further undergoes nucleophilic attack

Entry	R ¹ or epoxide	\mathbb{R}^2	Method ^a	Reaction time (h)	Product ^{b,c}	Yield (%) ^d
1 2	CH ₃	Ph	A B	1.5 0.5	2a ²¹ 2a	90 91
3 4	<i>n</i> -C ₆ H ₁₃	Ph	A B	3 1	2b ²¹ 2b	61 86
5 6	HOCH ₂	Ph	A B	4 1	2c ²¹ 2c	76 80
7	CICH ₂	Ph	А	3	2d ²²	70
8 9	o	Ph	A B	5 3	SePh ""OH	68 65
10 11 12	O	Ph Ph	A B	2 0.5	2e ²⁰ SePh ""OH 2f ²⁰	78 80
		PhCH ₂	В	4	SeCH ₂ Ph	60
13 14	Ph	Ph	A B	4 1	25 2h/3h ²⁰ 2h/3h	83 ^e 81 ^f
15 16	PhOCH ₂	Ph	A B	1.5 0.5	2i/3i ²⁴ 2i	91 ^g 91
17	PhOCH ₂	PhCH ₂	В	2	$2j^{24}$	70
18 19	$n-C_4H_9$	Ph	A B	3 1	2k ²⁵ 2k	70 89

Table 1 Reaction of Epoxides with Diselenides in the Presence of Zinc under Neutral and Alkaline Conditions

^aA: Zn/AlCl₃ system in anhyd MeCN; B: Zn in MeCN-NaOH (aq).

^b All products are known compounds.

^c References of the known compounds.

^d Isolated yields.

^e Ratio **2h/3h** = 1.8:1.

^f Ratio 2h/3h = 4:1.

^g Ratio **2i/3i** = 1:1.

on the epoxide.¹⁸ It seems that, in aqueous sodium hydroxide medium, zinc selenolate turns into the sodium salt (R²Se⁻Na⁺) which is a more reactive selenolate ion towards nucleophilic ring-opening of epoxides.¹⁹ Interestingly, no corresponding diols were detected using this method.

In conclusion, the new method described here appears to be highly competitive with other methods reported in the literature, and in some cases better results are obtained, especially in terms of reaction time and yields.^{15,20} It has been shown that the methods here reported are very effective for the opening of epoxides, with high regioselectivity, under simple and relatively mild conditions. The other advantages of these methods are simple work-up, lower toxicity, and low costs.

Acknowledgment

This work was supported by the K. N. Toosi University of Technology Research Council.

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- (18) General Experimental Procedure: Method A. A stirred solution of the diselenide (0.5 mmol) in anhydrous MeCN (15 mL) was treated with activated zinc powder (2.5 mmol). The mixture was refluxed for 1.5 h, during which time the zinc powder was almost completely consumed. Then, finely ground anhydrous AlCl₃ (1.2 mmol) and the epoxide (1.5 mmol) were added to the solution and stirring

was continued for the specified time (Table 1) without protection from the atmosphere. Progress of the reaction was monitored by TLC. After completion of the reaction, the solvent was evaporated and the residue was acidified to pH 4 with HCl (10%). The organic phase was extracted with Et_2O (2 × 15 mL), dried (Na₂SO₄), and concentrated. The pure products were obtained by preparative TLC (silica gel, eluent, CCl₄/Et₂O = 2:1) to afford the desired β -hydroxy selenides.

(19) General Experimental Procedure: Method B.

- A mixture of diselenide (0.5 mmol) and activated zinc powder (2.5 mmol) was suspended in MeCN (15 mL). The mixture was refluxed, with stirring, for 10 min. To this mixture was added 25% NaOH (3 mL, 18.8 mmol), and the mixture was stirred for further 5 min, during which time the yellow solution turned to colorless. Then, the epoxide (1 mmol) was added in one portion to the solution and stirring was continued for the length of time indicated in Table 1. When the reaction was complete, the organic solvent was evaporated, and the residue was acidified to pH 4 with HCI (10%). The organic layer was extracted with Et₂O (2×20 mL), dried (Na₂SO₄), and evaporated. Preparative TLC yielded the pure products.
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