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The Stereochemistry of Solvolysis of an Acyclic Allylic Epoxide

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Abstract: In contrast to solvolysis of cyclic allylic epoxides, the acid-catalyzed solvolyses of optically pure 1,2-epoxy-3-butene using water or alcohols show a high degree of inversion stereoselectivity.

Epoxides generally afford inversion of configuration when undergoing ring-opening reactions.[1] However, retention of configuration or stereochemical scrambling has sometimes been observed, especially if a potential carbocation intermediate can be delocalized into a neighboring π-system.[1] Allylic epoxides are capable of this type of delocalization, and stereorandom acid-catalyzed epoxide hydrolysis has been observed for several cyclic allylic epoxides.[2] For example, the acid-catalyzed hydrolytic ring opening of cyclopentadiene monoepoxide gives a stereorandom mixture of all four *syn* and *anti* 1,2 and 1,4 water addition products.[2a]

In contrast, acyclic allylic epoxide solvolysis stereochemistry has been little studied. This is probably caused by the challenge in acyclic systems of obtaining the required absolute stereochemical knowledge. Ideally, a substrate with minimal substitution would be used for a study of this sort to avoid substituent-derived stereochemical perturbation. Thus, we decided to investigate the stereochemistry of solvolysis of the simplest acyclic allylic epoxide, 1,2-epoxy-3-butene (**1**).

This epoxide can be readily prepared in optically active form. For example, glyceraldehyde acetonide (obtained from the chiral pool) can be converted by a sequence of olefination, acetonide removal, derivatization of the resulting 3-butene-1,2-diol to 2-hydroxy-3-butenyl tosylate, and then elimination to the desired epoxide **1**.[3] Alternately, 2-hydroxy-3-butenyl tosylate can be resolved, either through Sharpless epoxidation of the olefin,[4] or through an enzymatic resolution of the secondary alcohol.[5] We used the latter procedure to prepare *S*-2-hydroxy-3-butenyl tosylate of >99% ee, and, by ring closure, 1,2-epoxy-3-butene of the same configuration without loss of stereochemical purity.[3]

Treatment of the epoxide *S*-**1** with aqueous base resulted in a slow reaction to 3-butene-1,2-diol (**2a**) with major loss of stereochemical purity (Table 1, entries 1 and 2).[6] This probably reflects the propensity of **1** to react at both the allylic (inversion) and terminal (retention) epoxide carbons under basic conditions.[1a,7] Under neutral conditions, the stereoselectivity of the hydrolysis was much improved (Table 1, entry 3), although the reaction was unacceptably slow (incomplete after 10 days) and increasing the temperature, while increasing the rate, decreased the stereoselectivity.

The hydrolysis of **1** under acidic conditions is known to be a facile process, presumably proceeding through the carbocation since discrete amounts of the isomeric 2-butene-1,4-diol (**3a**) are formed[2,8] (Table 1, entries 4 and 5). Unexpectedly, these rapid reactions demonstrated the highest observed degree of inversion stereoselectivity.[6] A small amount of aqueous acid at 5°C (reaction time 45 min) gave the best hydrolysis

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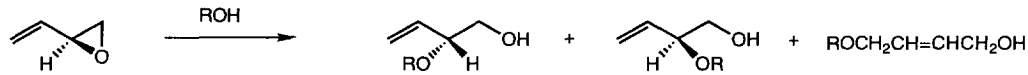
stereoselectivity (Table 1, entry 4, 97% inversion), but even with a full molar equivalent of sulfuric acid (pH 0) at ambient temperature **2a** was obtained with 82% ee! These results are greatly at variance with the solvolysis reactions of the cyclic cousins of **1**.

High stereoselectivity was also observed for solvolysis reactions performed in alcohol solvents (Table 1, entries 6-8).[9] The highest inversion stereoselectivity, >98% ee *R*-**2b**, was observed for methanol, with the stereoselectivity decreasing (along with reaction rate) for increasing alcohol size.

Although a cationic intermediate is indicated by the speed of the reactions and the presence of the allylic isomer **3**, the high inversion stereoselectivity suggests that this reaction might more likely proceed through a protonated epoxide species rather than a free carbocation, with backside S_N2 and S_N2' attack at the resulting weakened C(3)-O bond leading to the observed products.



S-1 *R*-2 *S*-2 3

a: R = H, **b**: R = Me, **c**: R = Et, **d**: R = *i*-Pr

Table 1

Entry	R	Conditions	Total Yield (2 + 3)	Relative Amounts 2:3[a]	% (*R*)-2[b]	% (*S*)-2[b]
(1)	H	1 *N* aq NaOH, RT	80%	>99:1	47.5	52.5
(2)	H	1.5 equiv K_2CO_3, H_2O, RT	78%	>99:1	73	27
(3)	H	H_2O, RT, 10 d	65%	>99:1	92	8
(4)	H	1 mol% H_2SO_4, H_2O, 5°C, 45 min	75%	95:5	97	3
(5)	H	100 mol% H_2SO_4, H_2O, RT	77%	89:11	91	9
(6)	Me	1 mol% H_2SO_4, MeOH, 0°-RT	79%	95:5	99.2	0.8
(7)	Et	1 mol% H_2SO_4, EtOH, 0°-RT	78%	92:8	97.8	2.2
(8)	*i*-Pr	1 mol% H_2SO_4, *i*-PrOH, RT, 20 h	70%	84:16	94.2	5.8

(a) Determined by ^1H NMR. (b) For R = H, determined by conversion to 1-tosyloxy-3-buten-2-yl *R*-α-methoxy-α-trifluoromethylphenylacetate and ^1H NMR integration of the methoxy peaks. For R = Me, Et, *i*-Pr, determined by GC analysis on a CYCLODEX-B chiral GC column (J&W Scientific).

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9. The absolute configuration of **2b** was determined by independent synthesis from *R*-**2a**. The absolute configurations of **2c** and **2d** were tentatively assigned by analogy with **2b**.

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