

SELECTIVE RING-OPENING REACTION OF STYRENE OXIDE WITH LITHIUM AZIDE IN THE PRESENCE OF CYCLODEXTRINS IN AQUEOUS MEDIA

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(Received 2 January 1992)

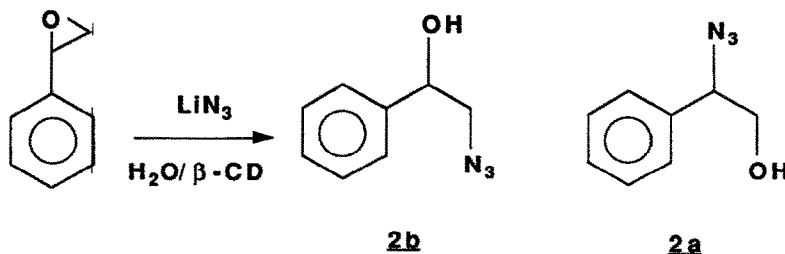
Abstract : Regioselective ring-opening of racemic styrene oxide was achieved by lithium azide in the presence of β -cyclodextrin in aqueous media. Kinetic resolution of racemic epoxide was observed and 1-phenyl-2-azido-ethanol was obtained with 78 % ee.

The complexation or host-guest interaction by cyclodextrin has attracted growing attention and many efforts have been made to control enantioselective reaction by means of inclusion phenomenon. Cyclodextrins (CD) are cyclic oligosaccharides consisting of six, seven or eight D-glucopyranose units (α , β , γ -cyclodextrins) linked by α (1 \rightarrow 4) bonds with a central cavity of 6-10 Å which can complex various organic compounds in aqueous solution inside their hydrophobic cavities ¹.

As molecular reaction vessels, CDs are expected to exert microenvironmental effects leading to selective reactions, Breslow reported the remarkable regioselectivity in the para position during the chlorination of anisole by hypochlorous acid ². Such regioselectivity were also observed by Komiyama using CDs and their derivatives in the formylation, carbonylation, dihalomethylation and allylation of phenols ³. The chiral cavity of CDs has been utilized also to perform asymmetric synthesis ¹. Asymmetric epoxidation ⁴, halogenation and hydrogenation of olefins ⁵ and asymmetric reduction of ketones ⁶ have been reported. Recently Takahashi reported the ring-opening reaction of styrene oxide with

NaBH_4 in the presence of cyclodextrins **7**. The reaction is regioselective and proceeds smoothly in aqueous media leading to partial resolution of the racemic epoxide.

Our interest was set on the regio and stereoselective ring-opening of epoxides by azide ions which depending on the experimental conditions employed, can be totally regio and stereoselectively controlled **8**. We wish to report herein some preliminary results obtained on the effects of CDs during the ring-opening reaction of epoxides with LiN_3 in aqueous media.



Conditions		Unreacted epoxide		2a (α attack)		2b (β attack)		Regioselectivity %
βCD/epoxide	Time	Yield %	e.e. ^a %	Yield %	e.e. ^a %	Yield %	e.e. ^a %	$\frac{2b}{2a + 2b}$
without βCD	17 h	7	0	85	0	8	0	8.6
0.2 βCD	1 h	51	0	47.5	0	1.5	(b)	3
0.2 βCD	18 h	2.5	(b)	94	0	3.5	(b)	3
1 βCD	4 h	59	20 (S)	24	3 (R)	17	78 (R)	41.5
2 βCD	6 h	68	18 (S)	13	16 (S)	19	78 (R)	59
2 βCD	17 h	28	30 (S)	36	6 (S)	36	78 (R)	50
2 βCD	43 h	4.5	(b)	76	12 (R)	19.5	56 (R)	20
10 βCD	53 h	1	(b)	79	10 (R)	20	57 (R)	20

a) e.e. of styrene oxide and azidoalcohols **2a** and **2b** were determined by specific rotation from literature (ref **9**); b) Not determined

Table 1 : Effects of β-CD on the Ring-Opening Reaction of Styrene Oxide

The ring-opening reaction of styrene oxide was carried out by stirring a mixture of epoxide, LiN_3 and β -CD in water at room temperature. The results obtained are shown in Table 1.

Firstly, we observed an increase in the regioselectivity of the ring-opening process. A regioselectivity of 59 % could be obtained for compound 2b when the reaction was performed in the presence of β -CD, compared to 8.6 % without the use of β -CD. Although a good selectivity can be reached with the use of β -CD as a mediator, a decrease in the regioselectivity is observed as the conversion of styrene oxide is realized ; a ratio of 20 % resulted after 43 hours of reaction.

Secondly, the kinetic resolution of racemic styrene oxide observed during the course of this reaction tells us that the selectivity comes from the combination step between the starting material and β -CD. Therefore, the unreacted styrene oxide recovered is enriched (ee 20 %) in S (-) after 41 % conversion, whereas 1-phenyl-2-azidoethanol 2b obtained from the attack at the less linkered carbon, shows an enantiomeric excess of 78 %. At the same time however, 2-phenyl-2-azidoethanol 2a formed when the attack occurs at the benzylic position affords 2a as a racemic compound.

The marked stereoselective effects noted by the use of β -CD may be interpreted by the formation of water-soluble inclusion complexes between styrene oxide and β -CD as previously showed by Takahashi. The resulting inclusion complex can be stereoselectively opened by azide ion on the β carbon leading to the azidohydrin 2b. Whereas the azidohydrin 2a is formed more rapidly outside the cyclodextrin and is produced in its racemic form.

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