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TIME DEPENDENT STEREOSELECTIVITY IN THE REDUCTION OF STYRENE OXIDE BY A CHIRAL LITHIUM ALUMINUM HYDRIDE COMPLEX

Lawrence J. Altman* and Yen Li
Department of Chemistry, State University of New York at Stony Brook
Stony Brook, New York 11794

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We should like to report some interesting observations made during a study of the reduction of styrene oxide by a chiral reducing agent -- a lithium aluminum hydride -(-)-α-phenethylamine complex.[1] The Results are summarized in Table I.

The chiral complex was initially prepared by the addition of an ethereal solution of (-)-α-phenethylamine (71.6% ee) to a LAH slurry at room temperature. The precipitated complex was stirred for two hours after which time the temperature was adjusted to the final reaction temperature and an ethereal solution of styrene oxide was added. After stirring the reaction mixture for the prescribed length of time, the reaction was quenched and the 1-phenylethanol isolated by multiple preparative layer chromotographic separations. Surprisingly, chiral 1-phenylethanol was obtained even when the reduction was carried to completion! This kinetic resolution can only be explained by assuming that each enantiomer of the styrene oxide was reduced to produce a different ratio of 1-phenylethanol to 2-phenylethanol. In addition, a remarkable reversal in the stereoselectivity of the reduction was obtained when the temperature was changed from -40° to 36°. These observations are reminiscent of similar observations made by Yamaguchi and Mosher[2] and by Sandman, Mislow, *et al.*[3]

The age of the reagent proved to play a major role in determining the steric course of the reduction. Using a chiral complex prepared from a clarified LAH solution immediately after its preparation gave 1-phenylethanol whose enantiomeric purity increased as the extent of

Table I. Stereoselectivity in the Reduction of Styrene Oxide by a Chiral Lithium Aluminum Hydride Complex

	Molar Ratios							Stereoselectivity[b]	
Run	$LiAlH_4$	$R*NH_2$[a]	Styrene Oxide	Reaction Temp (°C)	Time (Hr)	Extent (%)	1/2[g] Ratio	Config.	e.e. (%)
1	1.0[c]	1.00	0.25[e]	-40	36	Q	6.9	S	6.5 ± 0.6
2	1.0[c]	1.00	0.23[e]	36	30	Q	2.7	R	2.0 ± 0.8
3	1.0[c]	1.00	0.25[e]	36	36	Q	3.3	R	3.6 ± 0.9
4	1.0[d]	1.30	1.33[e]	RT	0.3	50	3.4	S	6.5 ± 0.9
5	1.0[d]	1.33	1.33[e]	RT	1.2	70	7.9	S	1.6 ± 1.6
6	1.0[d]	1.30	1.30[f]	RT	0.1	30	5.5	S	8.1 ± 0.8
7	1.0[d]	1.33	1.33[f]	RT	2	50	8.6	S	9.9 ± 0.7
8	1.0[d]	1.33	1.33[f]	RT	1.2	70	16.8	S	14.7 ± 1.1
9	1.0[d]	1.30	1.30[f]	-76	50	30	4.2	S	25.5 ± 1.1

(a) (-)-α-phenethyl amine of 71.6% ee was used in all runs. (b) The stereoselectivities refer to isolated 1-phenylethanol. Rotations were measured on a Perkin-Elmer Model 241 digital polarimeter. (c) An ethereal slurry of LAH was used. (d) A clarified ethereal solution of LAH was used. (e) An ethereal solution of styrene oxide was added after the initial chiral complex had aged for two hours. (f) The ethereal solution of styrene oxide was added within three minutes of the preparation of the chiral complex. (g) The gas chromatographically determined ratio of 1-phenylethanol to 2-phenylethanol.

the reduction increased. However, allowing the chiral complex to age for two hours before use yielded 1-phenylethanol whose enantiomeric purity decreased with the course of the reaction. The 1-phenylethanol to 2-phenylethanol ratio increased with the extent of the reaction, independent of the age of the reagent.

A reduction was carried out at -76° using freshly prepared chiral complex (a clear LAH solution was used). The course of the reduction was followed by gc. The results are presented in Figure 1. It appears as if there are two reagents with differing reactivities present in the mixture. The more reactive reagent yields largely 2-phenylethanol whereas the less reactive reagent yields largely 1-phenylethanol. After the reaction had proceeded to 30% completion, the reaction was quenched and the 1-phenylethanol was isolated and showed a 25% ee! There have been reports of kinetic resolutions employing styrene oxide but only low selectivities were observed.[4]

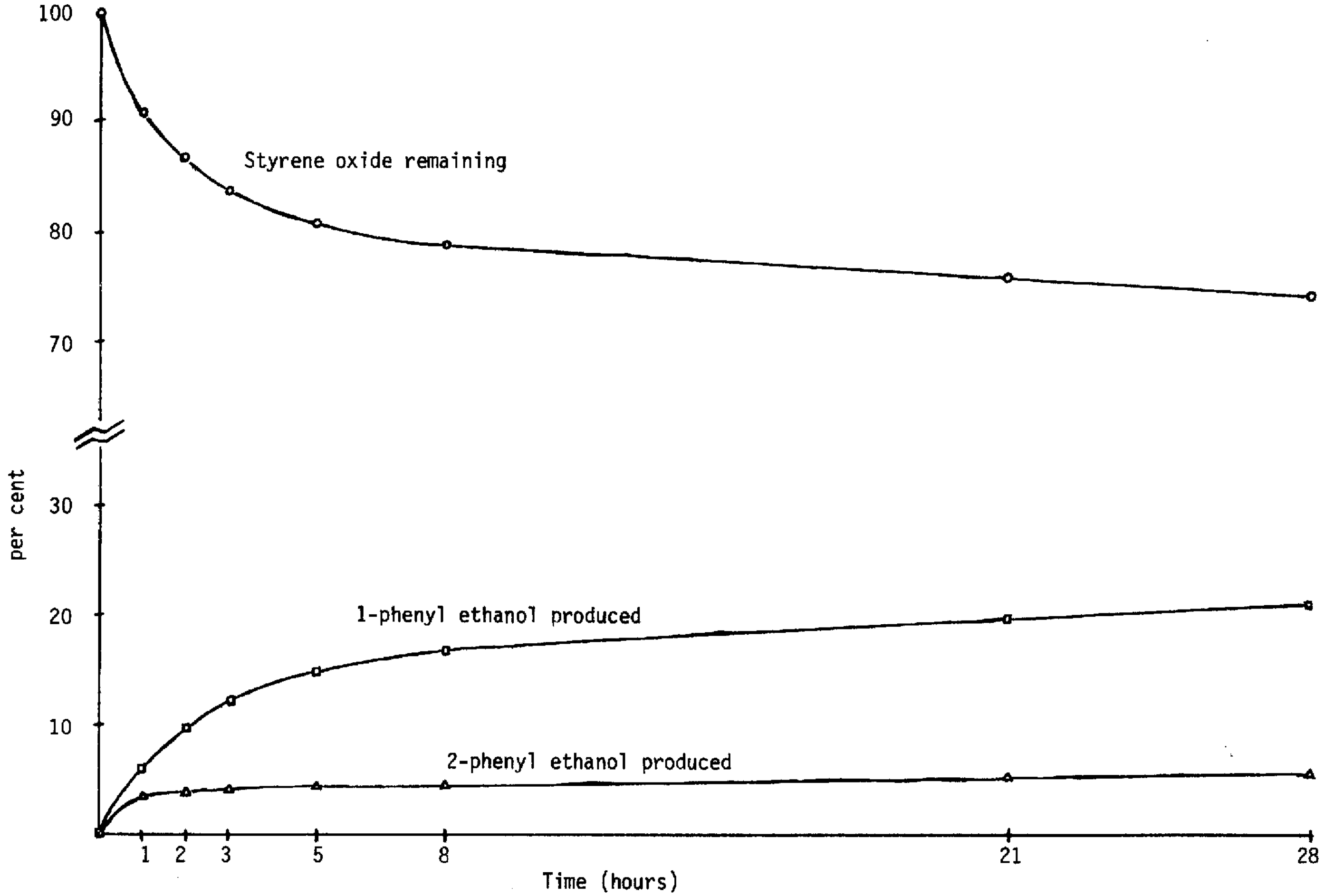

Figure I. Time course of the Reduction of Styrene Oxide by a Chiral Lithium Aluminum Hydride - α-phenethyl amine Complex in Ether at -78°.

The unusual time dependence in the stereoselectivity of the reduction remains to be satisfactorily explained.

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