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BASE INDUCED OPENING OF 2,3-EPOXYCHLORIDES : AN EFFICIENT PREPARATION OF trans-CHLOROVINYL ALCOHOLS

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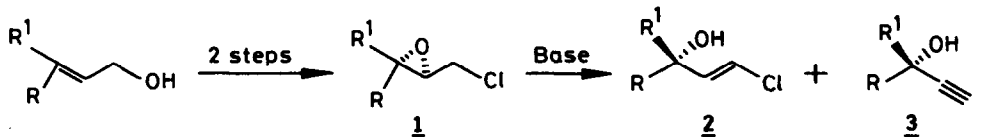
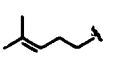
Abstract *A highly efficient protocol for the synthesis of chiral trans-1-chlorovinyl alcohols (2) from chiral 2,3-epoxychloride is described by using stoicheiometric amount of $LiNH_2$ or LDA.*

During our continuing programme[1] on biologically active hydroxy unsaturated fatty acids, we have developed a methodology to prepare optically pure terminal alkynols from chiral substrates[2] and achiral allyl alcohols[3]. During this study of chiral propargyl alcohols (3) from the corresponding chloroepoxides (1), we observed that elimination reaction under controlled conditions, particularly with 1 eq of LDA in THF or $LiNH_2$ in liq. NH_3 leads to the isolation of the chiral intermediates trans-1-chlorovinyl alcohols (2). The chiral chlorovinyl alcohols are indeed important intermediates finding diverse use in the synthesis of natural products[4], as they undergo C-C bond formation with ease. Notably, the recent discovery of the 1-chlorovinylic alcohols could be coupled stereospecifically[5] with acetylenic and vinyltin moieties with the aid of Pd catalyst under mild and essentially neutral conditions, has increased their utility greatly. These chiral chlorovinyl alcohols are presently prepared[6] by stereospecific Wittig olefination with α-hydroxyaldehydes or by using multistep processes.



a R^1 = Me, R = 
b R^1 = H, R = n-C_8H_{17}-
c R^1 = H, R = 
d R^1 = H, R = n-C_5H_{11}-

Treatment of 1 with one equivalent of LDA in THF at -78° or $LiNH_2$ in liq. NH_3 at -33° afforded 2 in quantitative yield. The elimination reaction produced trans-vinyl chlorides and was found to be highly stereoselective. The trans-configuration was confirmed by analysis of ^1H NMR spectra. In addition, this reaction appears to be general, versatile and could be performed under mild conditions as evident from the Table. Using Sharpless asymmetric epoxidation[8] as a complimentary protocol to prepare chirally defined 2,3-epoxy chlorides, this method could provide a variety of functionalized and enriched chiral building blocks in both the enantiomeric forms for the synthesis of natural products[4].

We next examined the opening of 2,3-epoxychloride (1a) with one eq. of n-BuLi at -33° in THF. It resulted in a product mixture containing approximately 43, 20 and 36 per cent of chlorovinyl alcohol (2a), propargyl alcohol (3a) and the starting 2,3-epoxychloride (1a) respectively. It

Table Preparation of trans-chlorovinyl alcohols (**2**)

Entry	Epoxy-chlorides	Base	eq	Crude yield %	Chlorovinyl alcohols*	Propargyl alcohol*
1	**1a**	$LiNH_2$ or LDA	1	92	**2a** (82)	-
2	**1a**	$LiNH_2$ or LDA	3	81	-	**3a** (77)
3	**1a**	n-BuLi	1	94§	**2a** (41)	**3a** (19)
4	**1a**	n-BuLi	3	83	-	**3a** (77)
5	**1b**	$LiNH_2$ or LDA	1	95	**2b** (85)	-
6	ent. **1c**	$LiNH_2$ or LDA	1	89	ent.**2c** (79)	-
7	**1d**	$LiNH_2$ or LDA	1	96	**2d** (87)	-
8	**1d**	n-BuLi	1	93§	**2d** (44)	**3d** (17)

* Isolated yields (%) are given in parenthesis. § Also contains their unreacted epoxychlorides.

appears that n-BuLi reacts indiscriminately with both the epoxychloride (**1a**) and chlorovinyl alcohol (**2a**), formed during the course of the reaction, thereby giving a mixture of products. However, 3 eq. of n-BuLi at -33°C in THF always produced the propargyl alcohol (**1a**) as the sole product reported earlier.[9] Thus LDA or $LiNH_2$ is the suitable base for the preparation of **2**.

In conclusion, it is worth mentioning that the ease of preparing chirally enriched trans-1-chlorovinyl alcohols (**2**) by this new method from the easily obtainable 2,3-epoxychlorides will permit one to tap the immense potential which these intermediates possess.

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