

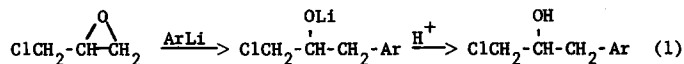
THE STEREOSPECIFIC RING OPENING REARRANGEMENT OF
EPICHLOROHYDRIN WITH n-BUTYLLITHIUM

by

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The reactions of epoxide ring systems with a wide range of electrophilic and nucleophilic reagents have been studied in the past and several excellent reviews are available.¹ Included in these studies have been several involving the reactions of organolithium compounds with epihalohydrins, which are reported to follow the "classical reaction course" of addition to the oxirane ring resulting in the formation of saturated alcohols.^{2,3} As an example, Gilman, Hofferth and Honeycutt have reported the synthesis of secondary alcohols from epichlorohydrin and aryllithium compounds (1).³

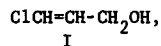


(Ar = phenyl, *p*-tolyl, 1-naphthyl and *p*-dimethylaminophenyl)

Recent work in this laboratory, however, had established that tetrahydrofuran exerts an extraordinary directional influence upon the reactions of alkyllithium compounds with aryl substituted chloromethanes.⁴ The data indicated that at low temperatures in this solvent, the reaction proceeded exclusively via α -hydrogen-metal interconversion (formation of aryl-chloromethyl carbanion) as contrasted with other solvents in which halogen-metal interconversion was the primary reaction path.^{4,5} As an extension of this work, the effect of tetrahydrofuran upon the reaction of n-butyllithium with a wide variety of substituted halomethanes, including epihalohydrins, has been under study.

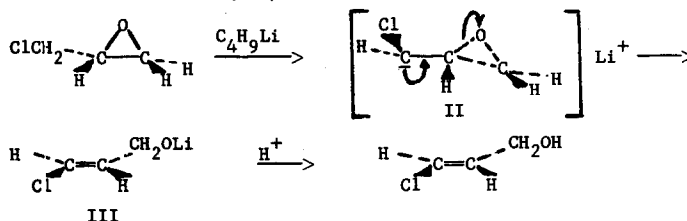
We now wish to report that under the conditions of our experiments (-80 to -100°C in tetrahydrofuran), n-butyllithium does not add to the oxirane ring. Rather than obtaining the saturated alcohol, the only

isolable product, after hydrolysis, was the β, γ -unsaturated primary alcohol, 3-chloro-2-propen-1-ol (I):⁶



isolated in 40-60% yields (b.p. 123, 104-105°; b.p. 744, 150-151°; n_D^{20} 1.4676, Calcd. for $\text{C}_3\text{H}_5\text{ClO}$: C, 38.9, H, 5.5, Cl, 38.3, O, 17.3; Found: C, 38.9, H, 5.8, Cl, 38.0, O, 18.4; phenylurethan m.p. 76-76.5, Calcd. for $\text{C}_{10}\text{H}_{10}\text{ClNO}_2$: C, 56.7, H, 4.73, Cl, 16.8, N, 6.62, O, 15.1; Found: C, 56.8, H, 4.84, Cl, 16.5, N, 6.86, O, 15.0; 3,5-dinitrobenzoate ester m.p. 86.5-88°, Calcd. for $\text{C}_{10}\text{H}_7\text{Cl}_2\text{N}_2\text{O}_6$: Cl, 12.4; Found: Cl, 13.0; the 60 megacycle NMR spectrum indicated methylene proton resonance signals at 5.97 and 6.04 τ , olefinic proton resonance at 4.25, 4.17, 4.03, 3.95, 3.88 (2) and 3.64 τ , and a hydroxyl proton signal which shifted on dilution or by changing the sample temperature; the proton count was 2:2:1, respectively. This product, moreover, which gas-liquid chromatography (GLC) indicated contained only one component, was found to be identical to the trans- γ -chloroallyl alcohol obtained from the hydrolysis (with sodium hydroxide) of trans-1,3-dichloropropene,^{7,8} and the properties noted above were in good agreement with the properties observed by Julia and Surzur for the trans isomer of γ -chloroallyl alcohol (b.p. 90-95-97°, b.p. 754-153-154°, n_D^{20} 1.4680, phenylurethan m.p. 75°) prepared via the stereospecific partial reduction of 3-chloro-2-propyn-1-ol.⁹

It is suggested that rather than the "classical" addition to the oxirane ring, the n-butyllithium attacks the protons of the chloromethyl group (a hydrogen-metal interconversion reaction) leading to the formation of an unstable chlorocarbanion (II), which rearranges with ring opening to form the stable alkoxide (III):



That the exclusive formation of the trans isomer of γ -chloroallyl alcohol was due to a stereospecific ring opening of II and not due to a post reaction isomerization of the cis to the trans-alcohol was estab-

lished by the observation that a synthetic mixture of the cis and trans- γ -chloroallyl alcohol (30% cis, 70% trans) was essentially unaltered by these reaction and workup conditions.¹⁰

The specificity of this ring opening rearrangement, as indicated by a study of molecular models (Stuart-Briegleb), is postulated to be the formation of the least strained conformation of the chlorocarbanion II (both for steric and polar effects) in which the halogen atom is furthest removed from the oxirane ring. Provided the chlorocarbanion is long-lived enough, achievement of this conformation assures a trans- product.

At room temperature, the same reaction occurs, but both cis and trans-alcohol result (ca. 70% trans by GLC measurement). The specificity also appears dependent to a small extent on solvent, the yield of trans-alcohol decreases in the order THF > ethyl ether > hexane (in the hexane, the overall yield of γ -chloroallyl alcohol was significantly less than in ether or THF).

We hope to report on these studies in greater detail at a later date.

References

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10. These reactions typically contained ca. 50 m.moles of epichlorohydrin dissolved in 100 ml. of pure, dry tetrahydrofuran under an argon atmosphere. At the prescribed temperature, an equimolar amount of *n*-butyllithium was added slowly as a solution (1.5M) in hexane. After the allotted reaction period (2-3 hrs.), the reaction was dumped into 200 ml. of water and the upper organic phase was separated. The aqueous phase was made slightly acidic and extracted with ethyl ether. The organic phases were combined, dried over Na₂SO₄, and the solvent was removed by vacuum stripping. The residue was then distilled.