

THEORETICAL AND EXPERIMENTAL STUDY OF THE BEHAVIOR OF E^+-Nu^- SALTS IN THE NUCLEOPHILIC RING OPENING REACTION OF 2-(CHLOROMETHYL)OXIRANE

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Oxiranes are widely used as universal synthons and intermediates in organic synthesis. Asymmetric oxiranes, amongst them 2-(chloromethyl)oxirane (epichlorohydrin, ECH), have a high synthetic potential [1]. The strained three-membered ECH cycle is easily opened under the attack of proton-donating nucleophilic reagents E^+-Nu^- , such as carboxylic acids (Fig. 1), alcohols, phenols, salts, forming two products of "normal" and "abnormal" ring opening.

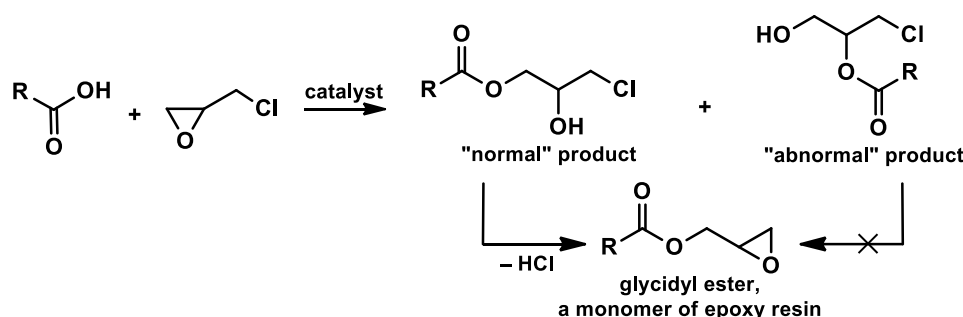


Fig. 1. Ring-opening reaction of 2-(chloromethyl)oxirane with carboxylic acids.

However, only a "normal" product is able to convert to glycidyl esters used in the synthesis of epoxy resins. Therefore, the study of factors affecting the rate and regioselectivity of reaction is important for the targeted oxirane ring opening. As shown by previous studies [2], one of the factors contributing to an increase in the rate of ECH acidolysis is the electrophilic activation of oxirane ring opening (Fig. 2, pathway B) with proton-donating reagents.

Modelling of the oxirane ring opening with E^+-Nu^- reagents, where the proton acts as an electrophile, does not allow localization of transition states on the reaction path, and leads directly to the product. In order to study the effect of the nature of the electrophile in E^+-Nu^- particles, there are promising models involving alkali metal cations as counterions for attacking nucleophiles. This approach allows studying not only the effect of the electrophilic activation on the rate and regioselectivity of the ring opening, but also assessing the impact of the cation volume on the efficiency of activation.

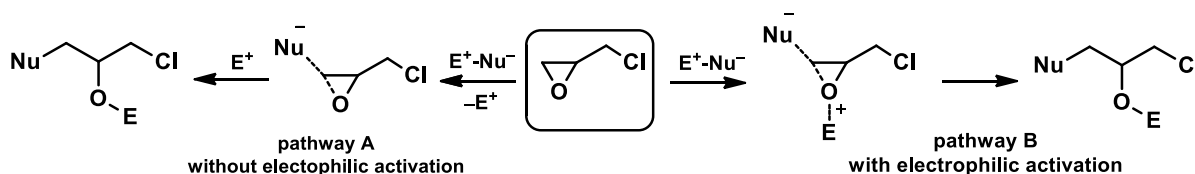


Fig. 2. Nucleophilic ring-opening reaction of 2-(chloromethyl)oxirane without (A) and with (B) electrophilic activation.

The aim of the study is to investigate the oxirane ring opening reaction of 2-(chloromethyl)oxirane by methods of quantum chemical modelling with alkali metal salts MX ($M = Li^+, Na^+, K^+$; $X = Br^-, CH_3COO^-$) and the subsequent experimental study of acetolysis of 2-(chloromethyl)oxirane in the presence of tetraalkylammonium halides R_4NX : tetraethylammonium bromide, tetraethylammonium iodide, tetra-*n*-butylammonium iodide. The computation was performed using the density functional theory (DFT) method with the B3LYP basic set. Acetolysis of ECH was studied at 333 K in a binary solvent ECH : tetrahydrofuran (50% vol.).

The studies showed that for both tetraalkylammonium and alkali metal salts, the kinetic behavior changes in the same manner, which indicates the same mechanism for the catalysis of 2-(chloromethyl)oxirane acetolysis with R_4NX and MX . It was found that the catalytic activity of R_4NX and MX increases with an increase in the nucleophilicity and electrophilicity of ions. The regioselectivity of the ECH ring opening by E^+-Nu^- particles rises with an increase in the nucleophilicity of the anion and a decrease in the cation volume. The data obtained are important both for the targeted synthesis of epoxides and for studying the mechanism of nucleophilic oxirane ring opening.

[1] G. S. Singh, K. Mollet, M. D'Hooghe et al., Epichlorohydrins in organic synthesis, *Chem. Rev.* **113**, 1441-1498 (2013).

[2] K. Yutilova, Y. Beshpalko, E. Shved, A Computational Study of 2-(chloromethyl)oxirane Ring Opening by Bromide and Acetate Anions Considering Electrophilic Activation with Cations of Alkali Metals, *Croat. Chem. Acta* **92**, 1-11 (2019).