Journal of Chemistry and Technologies, 2026, *34*(1), 49-56

Journal of Chemistry and Technologies

pISSN 2663-2934 (Print), ISSN 2663-2942 (Online).

journal homepage: http://chemistry.dnu.dp.ua
editorial e-mail: chem.dnu@gmail.com

UDC 544.4:[547.311+547.56+547.304.2]:547.476

PHENOLYSIS OF 2-(CHLOROMETHYL)OXIRANE IN THE PRESENCE OF TERTIARY AMINES: NUCLEOPHILIC-ELECTROPHILIC INTERACTIONS

Stanislav V. Domanskyi[1], Elena N. Shved[1,2*], Kseniia S. Yutilova[3], Georgii M. Rozantsev[1]

[1]*Vasyl' Stus Donetsk National University, Vinnytsia, Ukraine*
[2]*L. M. Litvinenko Institute of Physical Organic and Coal Chemistry of the NAS of Ukraine, Kyiv, Ukraine*
[3]*Institute of Organic Chemistry of the NAS of Ukraine, Kyiv, Ukraine*

Received 14 December 2025; accepted 14 February 2026; available online 23 March 2026

Abstract

The aim of this work is to study the reaction series "4-nitrophenol–2-(chloromethyl)oxirane (epichlorohydrin, ECH)–*N,N*-dimethylaniline," nucleophilic-electrophilic interactions in the system to compile a kinetic model of oxiranes phenolysis. The catalytic phenolysis of epichlorohydrin was studied using kinetic methods, along with a similar acidolysis reaction for comparison. The reaction kinetics was studied in ECH excess, which acts simultaneously as substrate and solvent, as well as in its binary mixture with tetrahydrofuran. The kinetic scheme of the reaction was confirmed by studying the structure of the synthesized product using ^{1}H NMR and gas chromatography–mass spectroscopy. The regiospecificity of ECH phenololysis was concluded. The zero order of the reaction with respect to the nucleophilic reagent and the first order of the reaction with respect to the amine were established. The effect of solvent polarity on the reaction kinetics was examined. The kinetic law of the reaction is the same as for the catalytic acidolysis of epichlorohydrin. The kinetic features of the phenolysis and acidolysis of epichlorohydrin with varying solvent polarity were analyzed. It was confirmed that the initial stage of the reaction – amine quaternization – has an S_N2 character. Nucleophilic-electrophilic interactions in the system were analyzed. The mechanism of nucleophilic opening of the oxirane cycle was described in detail. Regiospecific phenolysis and regioselective acidolysis are described by a single kinetic model that corresponds to the mechanism of transfer of the anion of a nucleophilic reagent by an ion pair.

Keywords: epoxide cycle opening; 2-(chloromethyl)oxirane (epichlorohydrin); phenolysis and acidolysis; *N,N*-dimethylaniline (tertiary amine); solvent polarity; regiospecificity and regioselectivity; NMR analysis; catalysis; nucleophilic-electrophilic interactions; reaction kinetic model and mechanism.

ФЕНОЛІЗ 2-(ХЛОРМЕТИЛ)ОКСИРАНУ В ПРИСУТНОСТІ ТРЕТИННИХ АМІНІВ: НУКЛЕОФІЛЬНО-ЕЛЕСТРОФІЛЬНІ ВЗАЄМОДІЇ

Станіслав В. Доманський[1], Олена М. Швед[1,2*], Ксенія С. Ютілова[3], Георгій М. Розанцев[1]

[1]*Донецький національний університет імені Василя Стуса, Вінниця, Україна*
[2]*Інститут фізико-органічної хімії і вуглехімії ім. Л. М. Литвиненка НАН України, Київ, Україна*
[3]*Інститут органічної хімії НАН України, Київ, Україна*

Анотація

З метою розробки кінетичної моделі фенолізу оксирану досліджена реакційна серія «4-нітрофенол–2-(хлорметил)оксиран (епіхлоргідрин, ЕХГ)–*N,N*-диметиланілін» та нуклеофільно-електрофільні взаємодії в системі. Каталітичний феноліз епіхлоргідрину вивчений кінетичними методами та порівняний з аналогічними дослідженнями ацидолізу. Кінетика реакції досліджена в ЕХГ та його бінарній суміші з тетрагідрофураном в умовах значного надлишку оксирану, оскільки він одночасно виступає і субстратом, і розчинником. Кінетична схема реакції підтверджена встановленням структури синтезованого продукту методами ^{1}Н ЯМР спектроскопії та газової хромато-мас спектрометрії. Зроблений висновок щодо регіоспецифічності фенолізу ЕХГ. Встановлений нульовий порядок реакції за нуклеофільним реагентом та перший порядок реакції за аміном. Досліджений вплив полярності розчинника на кінетику реакції. Кінетичний закон реакції такий самий, як і для каталітичного ацидолізу епіхлоргідрину. Проаналізовані кінетичні особливості фенолізу та ацидолізу епіхлоргідрину зі зміною полярності розчинника. Підтверджено, що початкова стадія реакції – кватернізація аміну – має S_N2-характер. Проаналізовані нуклеофільно-електрофільні взаємодії в системі. Деталізований механізм нуклеофільного розкриття оксиранового циклу. Регіоспецифічний феноліз та регіоселективний ацидоліз описуються єдиною кінетичною моделлю, яка відповідає механізму переносу аніона нуклеофільного реагенту іонною парою.

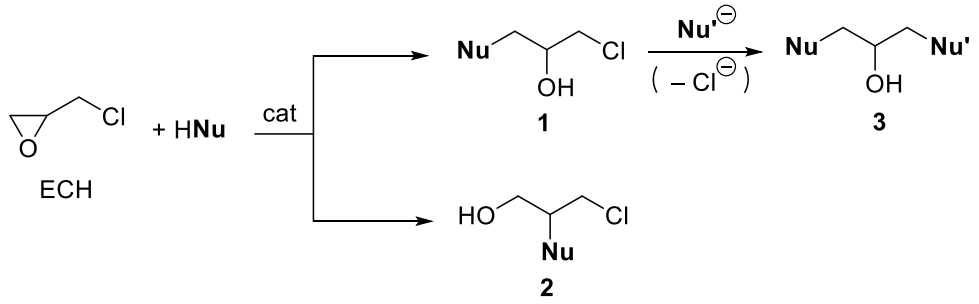
Ключові слова: розкриття епоксидного циклу; 2-(хлорметил)оксиран (епіхлоргідрин); феноліз та ацидоліз; *N,N*-диметиланілін (третинний амін); полярність розчинника; регіоспецифічність та регіоселективність; ЯМР-аналіз; каталіз; нуклеофільно-електрофільні взаємодії; кінетична модель та механізм реакції.

**Corresponding author: e-mail: shved_e@yahoo.com*
 doi: 10.15421/jchemtech.v34i1.352278

Journal of Chemistry and Technologies, 2026, *34*(1), 49-56

Introduction

The reaction of oxiranes with proton-donating nucleophiles (**HNu**), such as carboxylic acids, phenols, and alcohols, is a fundamental reaction in organic chemistry [1–4], with wide applications in the production of epoxy resins and their derivatives, dyes, and pharmaceuticals [3–6]. One of the most practically important oxiranes is epichlorohydrin (ECH, 2-(chloromethyl)oxirane). The ECH molecule contains three electrophilic centers, allowing facile synthesis of compounds **1–3** with diverse functional groups (Scheme 1). The ring-opening of ECH occurs regioselectively [1; 4; 7; 8]. Regioisomers **1** and **3** are referred to as "normal" products, whereas **2** is the "abnormal" product. Notably, product **1** serves as a synthon in the synthesis of epoxides [4; 8–11].



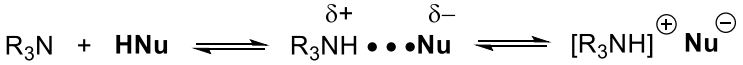
Scheme 1. 2-(Chloromethyl)oxirane ring opening by proton-donating nucleophiles

Therefore, control over the regioselectivity of the reaction is important in modern synthesis, which imposes high demands on product purity [12–16]. Tertiary amines are effective catalysts for the reaction of oxiranes with proton-donating nucleophiles, providing a high yield of isomer **1** [17; 18] and allowing a reduction in the curing temperature of epoxy resins [19].

In cases where **HNu** is a carboxylic acid, the reaction selectivity reaches 80–90 % [4; 6; 8; 17; 20]. A feature of the phenolysis of ECH is its regiospecificity [8; 13], when only the product of the "normal" opening of the oxirane cycle – chlorohydrin ether **I** – is formed, which in a subsequent stage is converted into the corresponding epoxide. Thus, the phenolysis of ECH catalyzed by tertiary amines is a promising system for the development of a kinetic model of a regiospecific reaction.

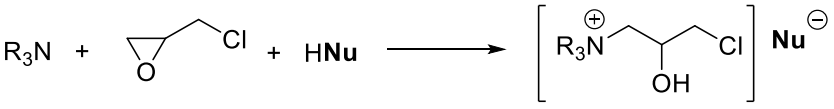
The initial task in developing such a model is to determine the reaction orders with respect to its components. For most of the studied reaction series [4; 6; 8; 21; 22; 23], the reaction order with respect to the oxirane is first, regardless of its structure, and first order with respect to the catalyst. The reaction order with respect to **HNu** varies from zero to first, depending on the reaction series and the acidity of the reagent. In the presence of an excess of oxirane, the reaction order with respect to carboxylic acids is predominantly zero, while in reagent excess, it increases up to first order. In a significant excess of oxirane, the reaction order for phenols depends on their acidity (pKa > 8 – first order; pKa < 8 – zero order) [8].

To enable comparison of results from analogous series with carboxylic acids and phenols, the reaction series "4-nitrophenol (pKa = 7.15 [24]) – ECH – *N,N*-dimethylaniline ($PhNMe_2$, pKa = 5.15 [24])" was selected. *N,N*-Dimethylaniline was chosen as the tertiary amine catalyst, whose moderate basicity minimizes its contribution to the overall reaction *via* deactivation by the acidic reagent (Scheme 2).



Scheme 2. Tertiary amine quaternization in the reaction with HNu

A key point of discussion in developing the kinetic model is the mechanism of oxirane reactions with proton-donating nucleophiles under base catalysis. Nevertheless, a common feature in the mechanisms under discussion [6; 8; 21; 22]) is the formation, by one route or another, of ammonium salts in which the anion is the nucleophile anion **Nu**$^-$ (Scheme 3).

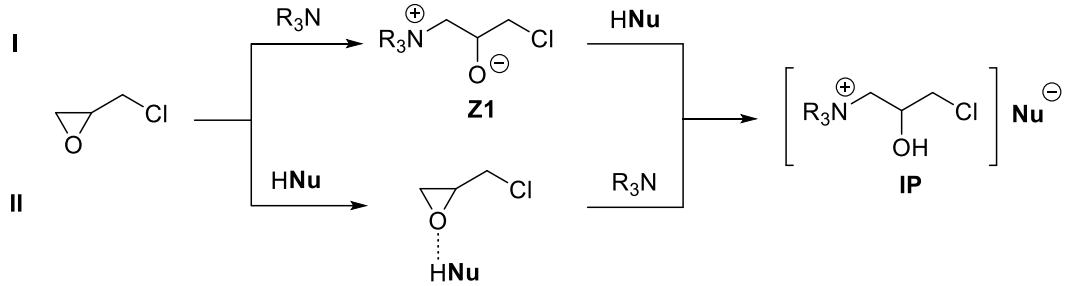


Scheme 3. Tertiary amine quaternization in the reaction with 2-(chloromethyl)oxirane and HNu

Journal of Chemistry and Technologies, 2026, *34*(1), 49-56

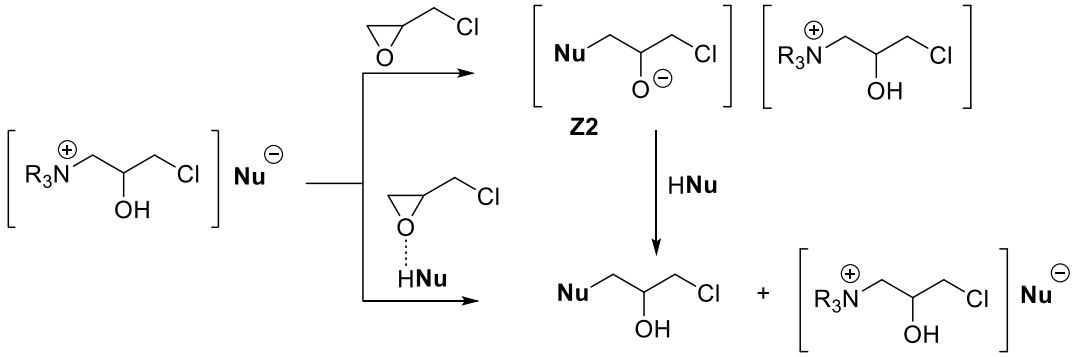
Experimentally, the quaternization stage of tertiary amines in the reaction with 2-(chloromethyl)oxirane and AcOH (**HNu**) has been confirmed by UV and visible spectroscopy for both aromatic [18] and aliphatic amines [25]. Thus, the study [18] of the reaction series "AcOH – ECH – $PhNMe_2$" by UV spectroscopy showed that the concentration of $PhNMe_2$ decreases over time. The irreversible and relatively slow conversion of the amine corresponds to the formation of the quaternary ammonium carboxylate, which can be considered the true catalyst for the oxirane ring opening, leading to the formation of the corresponding chlorohydrin esters **1** and **3**. Therefore, in the case of phenolysis, it can be assumed that the product of oxirane ring opening by tertiary amines in the presence of **HNu** is an ammonium salt in which the anion is the corresponding phenoxide anion (**Nu**$^-$).

Previous studies [6; 17; 21; 26] have shown that in reactions with oxiranes, amines exhibit nucleophilic character, with ring opening occurring *via* an S_N2 mechanism, including a contribution from the "borderline" S_N2 pathway [4; 6; 26]. The mechanism that best explains the available experimental data is the anion transfer of the nucleophilic reagent by an ion pair [6; 8; 17], in which the pathway of tertiary amine quaternization in the reaction with 2-(chloromethyl)oxirane and **HNu** is represented in Scheme 4.



Scheme 4. The paths of the tertiary amine quaternization in the reaction with 2-(chloromethyl)oxirane and HNu

Oxirane ring opening can proceed *via* two pathways. Path **I** in volves the slow interaction of the amine with the oxirane, leading to the formation of the zwitterion **Z1**, which in a fast subsequent step reacts with **HNu** to form the carboxylate/phenoxide ion pair **IP.** Path **II** initially involves electrophilic activation of the oxirane by **HNu**, followed by the quaternization of the amine to form the ion pair (**IP**). Quantum chemical studies have shown that amines open the oxirane ring only when it is activated by a proton-donating reagent [6; 8; 21]. Further participation of the **IP** in the reaction with both unactivated and activated oxirane leads to the formation of product **1** (Scheme 5).



Scheme 5. Pathways for the ion pair (IP) transformation in the reaction with 2-(chloromethyl)oxirane and HNu

The aim of this work is to study the reaction series "4-nitrophenol–ECH–*N,N*-dimethylaniline" and nucleophilic-electrophilic interactions within this system to develop a kinetic model of oxirane phenolysis.

Results and discussion

The primary task in kinetic studies is to determine the reaction order with respect to each component. As noted earlier, in a significant excess of oxirane, the reaction order for phenols depends on their acidity [8]. Therefore, an important aspect of this study is to determine the reaction order with respect to 4-nitrophenol, which has a *pKa* = 7.15 [24]. The kinetics of the reaction of 4-nitrophenol with ECH were investigated at different concentrations of

Journal of Chemistry and Technologies, 2026, *34*(1), 49-56

$PhNMe_2$ in ECH (permittivity ε = 22.6) and in its binary mixture ECH : THF (1:1 v/v, ε = 15.1). The component ratio in the ECH : THF solvent was chosen to maintain a significant excess of ECH. For reactions proceeding *via* an S_N2 mechanism, or for complex reactions with a rate-limiting S_N2 step in the case of a neutral nucleophile, a decrease in medium polarity reduces the reaction rate [4]. Thus, conducting kinetic studies in solvents of different polarity allows experimental identification of the mechanism of the $PhNMe_2$ quaternization step in ECH phenolysis. The progress of the reaction was monitored by measuring the change in reagent concentration over time according to the method described in the Experimental section. Kinetic curves illustrating the effect of varying catalyst concentration in both solvents are shown in Figure: ECH (**A**) and ECH : THF (**B**).

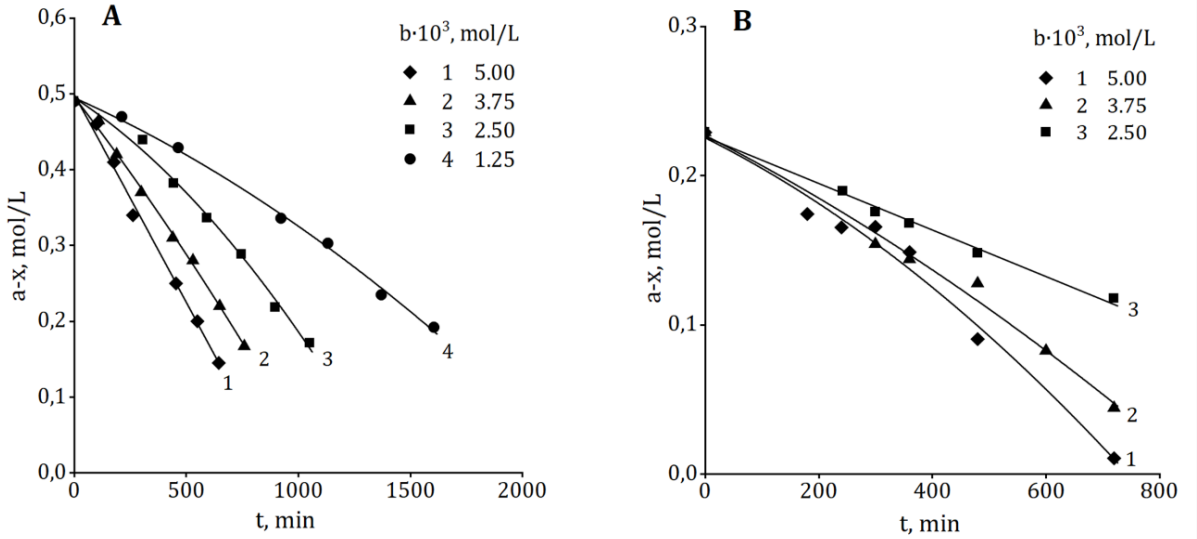


Figure. Plots of the residual concentration (a–x) *vs.* time (t) for the reaction of 4-nitrophenol [a = 0.46 (A) / 0.23 (B) mol/L] with ECH [s = 12.75 mol/L (A), 6.36 mol/L (B)] catalyzed by $PhNMe_2$ [$b = 1.25 \cdot 10^{-3} \div 5.00 \cdot 10^{-3}$ mol/L in ECH (A) and [$b = 2.50 \cdot 10^{-3} \div 5.00 \cdot 10^{-3}$ mol/L ECH : THF (1:1) (B) as solvent; 353 K

The linear relationship observed in the plots of reagent concentration versus reaction time indicates a zero-order reaction with respect to 4-nitrophenol in both solvents. Remarkably, the initial segments of the kinetic curves exhibit a slightly smaller slope, which corresponds to the hypothesis of a slow quaternization step of the tertiary amine and the formation of the ion pair (**IP**) that catalyzes the formation of chlorohydrin ether **1**. Taking into account the established zero order with respect to 4-nitrophenol and the significant excess of ECH, the observed rate constants (k_{obs}) were calculated using the following formula:

$$k_{\text{obs}} = \frac{a-(a-x)}{st}, \qquad (1)$$

The reaction order with respect to the catalyst was determined by comparing the observed rate constants with the corresponding catalyst concentrations according to the following equation:

$$k_{obs} = k_{non} + k_{cat} b, \qquad (2)$$

where k_{non} and k_{cat} are the rate constants of the non-catalyzed (s^{-1}) and catalyzed (L/(mol·s)) reactions, respectively.

Calculations according to equation (2) allowed the determination of the catalytic and non-catalytic reaction rate constants:

Solvent ECH
$$k_{obs} = (1.21 \pm 0.16) \cdot 10^{-7} + (1.30 \pm 0.06) \cdot 10^{-4} \cdot b \qquad (3)$$
r = 0.999; SD =$0.1 \cdot 10^{-7}$; N = 4

Solvent ECH:THF
$$k_{obs} = (1.96 \pm 1.10) \cdot 10^{-7} + (1.04 \pm 0.28) \cdot 10^{-4} \cdot b \qquad (4)$$
r = 0.990; SD = $0.5 \cdot 10^{-7}$; N = 3

According to equations (3) and (4), a linear dependence of k_{obs} on the concentration of $PhNMe_2$ is observed, indicating the first order of the reaction with respect to the catalyst.

The correlation between k_{non} and k_{cat} shows that the catalytic process proceeds much faster than the non-catalytic one ($k_{non} << k_{cat}$,). This allows k_{cat} to be calculated using a simplified formula:

$$k_{obs} = k_{cat} b \qquad (5)$$

Journal of Chemistry and Technologies, 2026, *34*(1), 49-56

The rate constants for the catalytic phenolysis of ECH (k_{obs} and k_{cat}) are given in Table 1 and compared with the corresponding constants for benzoic acid with higher acidity (pKa = 4.18 [24]).

Table 1

Observed (k_{obs}) and catalytic (k_{cat}) rate constants for the reaction of 4-nitrophenol / benzoic acid (a, mol/L) and ECH (s, mol/L) catalyzed by *N,N*-dimethylaniline (PhNMe$_2$, b, mol/L) in ECH (ε = 22.6) and ECH:THF (1:1 v/v, ε = 15.1) as solvents

$b\cdot10^2$, mol/L	$k_{obs}\cdot10^6$, s^{-1}	$k_{cat}\cdot10^4$, L/(mol·s)	$k_{obs}\cdot10^6$, s^{-1}	$k_{cat}\cdot10^4$, L/(mol·s)
	4-Nitrophenol, 353 K			
	ECH (a = 0.46; s = 12.75)		ECH : THF (a = 0.23; s = 6.36)	
0.500	0.75±0.01	1.30±0.06	0.70±0.11	1.0±0.3
0.375	0.62±0.01		0.63±0.05	
0.250	0.44±0.10		0.44±0.02	
0.125	0.275±0.009		–	
$b\cdot10^2$, mol/L	Benzoic acid, 333 K			
	ECH (a = 0.300; s = 12.75)		ECH:THF (a = 0.300; s = 6.36)	
0.500	1.23±0.11	1.7±0.1	0.49± 0,03 [20]	0.99±0.05[a]
0.375	0.95±0.04			
0.250	0.71±0.03			
0.125	0.46±0.02			

[a] k_{cat} is calculated by the formula (7)

For both acidic reagents, a decrease in solvent polarity leads to a reduction in the reaction rate constants, which is consistent with the behavior of processes proceeding *via* an S_N2 mechanism in the case of a neutral nucleophile. The reactivity of 4-nitrophenol (pKa = 7.15) is noticeably lower than that of benzoic acid (pKa = 4.18). Thus, in analogous reaction series, an increase in the acidity of **HNu** promotes the nucleophilic opening of the oxirane ring.

An important aspect of studying nucleophilic–electrophilic interactions in the "ECH – **HNu** – R_3N/**IP**" system is the comparison of trends in reaction rate constants as solvent polarity decreases and reagent acidity varies. A comparative analysis was performed for 4-$NO_2C_6H_4$–OH, AcOH, and PhCOOH, whose acidity constants differ by three orders of magnitude (Table 2).

Table 2

Catalytic rate constants (k_{cat}) for the reaction of HNu (pK_a) and ECH (s, mol/L) catalyzed by PhNMe$_2$/Bu$_3$N/*n*-Bu$_4$NI in the ECH (k'_{cat}) / ECH:THF (1:1 v/v) (k''_{cat}) solvents, and the ratio k'_{cat}/k''_{cat}

HNu / pK_a	catalyst	T, K	$k'_{cat}\cdot10^4$, L/(mol·s)	$k''_{cat}\cdot10^4$, L/(mol·s)	k'_{cat}/k''_{cat}
4-$NO_2C_6H_4$–OH / 7.15	PhNMe$_2$	353	1.30±0.06	1.0±0.3	1.25
	n-Bu$_4$NI	353	1.4±0.2	2.0±0.2	0.70
AcOH / 4.75	PhNMe$_2$	333	0.58±0.03	–	–
	Bu$_3$N	333	1.23±0.02	0.81±0.04 [17]	1.52
	n-Bu$_4$NI	333	2.2±0.2	3.3±0.1 [27]	0.67
PhCOOH / 4.18	PhNMe$_2$	333	1.7±0.1	0.99±0.05 [20]	1.76
	n-Bu$_4$NI	333	6.7±0.5	9.2±0.4[27]	0.73

The effect of changes in solvent polarity on the reactivity of proton-donating nucleophiles can be assessed by comparing the corresponding rate constants with the pK_a values of the reagents. However, phenolysis and acidolysis were studied at 353 and 333 K, respectively. Therefore, a convenient parameter for evaluating the influence of solvent nature on the phenolysis/acidolysis of ECH is the ratio k'_{cat}/k''_{cat}, which depends primarily on the nature of **HNu** rather than on temperature. Correlation equation (6) demonstrates that the sensitivity of the reaction catalyzed by PhNMe$_2$ (and by Bu$_3$N in the case of AcOH) to changes in the acidity of the reagent

$$k'_{cat}/k''_{cat} = (2.3 \pm 0.3) + (-0.15 \pm 0.04)pK_a \quad (6)$$
$$r = 0.954;\ SD = 0.107$$

is relatively low; however, the statistical correlation parameters, r and SD, confirm the presence of a linear relationship between k'_{cat}/k''_{cat} and pK_a. The negative sign of the sensitivity parameter indicates that increasing the acidity of the reagent enhances the effect of increased solvent polarity on the catalytic rate. Indeed, in more polar media, the extent of acid self-association decreases, resulting in a higher proportion of the monomeric form [28]. This observation is consistent with the involvement of electrophilic activation in the reaction between

Journal of Chemistry and Technologies, 2026, *34*(1), 49-56

HNu and the oxirane under tertiary amine catalysis (Scheme 4). Taking into account the more complex mechanism of oxirane ring opening (Schemes 4 and 5), at the initial stage of the reaction, when attacked by the initial nucleophile, the **Nu**$^-$ anion is formed *in situ* from the acidic reagent. The nucleophilicity of this anion is determined by the nature of the acid, *i.e.*, the higher the *pKa* value of the reagent, the greater the nucleophilicity of the anion. The data in Table 2 and equation (6) suggest that the rate of oxirane ring opening by **HNu** reagents, when a tertiary amine is present in the initial reaction system, depends to a greater extent on the acidity of the reagent than on the nucleophilicity of **Nu**$^-$. Furthermore, the significant role of electrophilic assistance indicates that the amine quaternization step is slow, and its rate depends both on the nucleophilic properties of the amine and on the degree of acid activation of the oxirane ring.

Table 2 presents the catalytic rate constants for the reaction under discussion when the initial catalyst is *n*-Bu_4NI – an ionic compound in which the nucleophilic center is I^-. Since the nucleophilic opening of the oxirane ring follows patterns characteristic of an S_N2 mechanism, a decrease in solvent polarity in the case of a charged nucleophile leads to an increase in the reaction rate. Indeed, the reduced solvation of the anionic nucleophile in a less polar solvent facilitates the reaction. However, the acidity of the reagent has little effect on the ratio $k'_{cat}/k''_{cat} \approx 0.7$. That is, in the case of tetraalkylammonium salts, the rate of oxirane ring opening is primarily influenced by the nucleophilicity of I^-/**Nu**$^-$ rather than by the acidity of the reagent. Therefore, the interaction of the oxirane with a proton-donating nucleophile in the presence of an ionic catalyst can proceed *via* both Path **I** and Path **II** (Schemes 4 and 5), with the contribution of Path **I** being greater due to the significant excess of ECH. At the same time, the contribution of Path **II** to the overall reaction increases with increasing acidity of the reagent. Indeed, the ratio $k'_{cat}(n\text{-}Bu_4NI)/k'_{cat}(PhNMe_2)$, which quantitatively characterizes the influence of the nucleophilic properties of the initial catalyst on the rate of ring opening, depends on the acidity of the **HNu** reagent, as shown by equation (7).

$$k'_{\text{cat}}\,(n-\text{Bu}_4\text{NI})/k'_{cat}\,(\text{PhNMe}_2) = (8.2 \pm 0.8) + (-1.0 \pm 0.2)\,pK_a \qquad (7)$$
$$r = 0.989;\quad SD = 0.335$$

The relatively high value of the coefficient associated with *pKa* (–0.993 ± 0.150) and its negative sign indicate an increased contribution of Path **II** to the overall reaction for more acidic proton-donating nucleophiles.

Therefore, the effect of solvent polarity on the rates of oxirane phenolysis and acidolysis confirms that the oxirane ring-opening step proceeds *via* an S_N2 mechanism. Phenolysis and acidolysis of epichlorohydrin follow the same kinetic patterns, which is consistent with a unified catalytic mechanism – namely, the anion transfer by an ion pair mechanism (Schemes 4 and 5). When a tertiary amine serves as the initial catalyst, nucleophilic opening of the oxirane ring occurs predominantly through interaction with the oxirane activated by **HNu**. In the case of an ionic catalyst, ring opening proceeds *via* both pathways. Higher acidity of the reagent favors the reaction to a greater extent than an increase in the nucleophilicity of the **Nu**$^-$ anion formed *in situ* during the reaction.

Experimental

Purification of substances.

4-Nitrophenol was recrystallized from water (m.p. 114–115 °C; lit. 114 °C [29]).

Benzoic acid was recrystallized from water in the presence of activated carbon (m.p. 121–122.5 °C; lit. 123 °C [29]).

N,N-dimethylaniline was dried for 24 hours over NaOH (10 g of granulated NaOH was taken per 100 ml of amine) and distilled under reduced pressure (b.p. 193 °C, n_D= 1.5578; lit. b. p. 193–194 °C, n_D = 1.5581 [29]).

ECH was dried by double distillation over sodium sulfate for 20 hours, and the fraction with b.p. 116–116.5 °C was collected; lit. 116 °C [29].

Tetrahydrofuran was purified from peroxides as follows: a 10 % aqueous solution of Na_2SO_3 was added, shaken, and left for 20–30 minutes. The inorganic layer was separated using a separatory funnel, dry NaOH was added to the organic layer, and the mixture was left overnight. Tetrahydrofuran was then decanted from the alkali and distilled over sodium at atmospheric pressure (b.p. 65–65.5 °C; lit. 66 °C [29]).

Kinetic measurements. To study the reaction kinetics, 4-nitrophenol (or carboxylic acid) and catalyst solutions were prepared in the solvent (ECH or ECH : THF) using accurately weighed amounts. Then, 2 mL of the 4-nitrophenol solution and 1 mL of the catalyst solution were placed in a two-compartment flask. The flask was immersed in a water heating bath for 10 min at the desired

Journal of Chemistry and Technologies, 2026, *34*(1), 49-56

temperature. The two solutions were then quickly mixed inside the flask and returned to the bath for the required reaction time. The initial time of the reaction was defined as the moment of solution mixing. At the end of the required exact time, the reaction was stopped by addition of 10 mL of cold (0 ÷ 5 °C) isopropanol : water mixture (1 : 1 v/v). The contents of the flask were quantitatively transferred to the titration vessel and diluted with water. The amount of unreacted 4-nitrophenol was determined by pH-potentiometric acid-base titration with a 0.1 mol/L NaOH solution.

Analysis of reaction products. ^{1}H NMR spectra were recorded at 298 K on a Varian Mercury Plus 300 MHz device in deuterated chloroform. Chemical shifts were determined on the δ scale from tetramethylsilane as an internal standard. The authenticity of the obtained spectra of corresponding reaction products was confirmed by the chemical shift calculations using the ACD/ChemSketch software package. The formation of only product I (3-chloro-2-hydroxypropyl ether of 4-nitrophenol) was established. ^{1}H NMR spectra (300 MHz $CDCl_3$), δ, ppm: 7.56 d/d (4H, C_6H_4), 4.15 m (1H, CH), 3.95 d/tr (2H, CH_2), 3.50 d/tr (2H, CH_2Cl).

Gas chromatography mass spectrometry (GS-MS) of product I (3-chloro-2-hydroxypropyl ether of 4-nitrophenol was recorded using an Agilent 5809 Series II 5972 instrument (electron impact ionization), eluent: methylene chloride. Observed *m/e* (*I*, %): 81 (23.1) $[CH(OH)CH_2{}^{37}Cl]^+$; 79 (71.0) $[CH(OH)CH_2{}^{35}Cl]^+$; 61 (77.6) $[CH{=}CH^{35}Cl]^+$; 51 (9.0) $[CH_2{}^{37}Cl]^+$; 49 (28.0) $[CH_2{}^{35}Cl]^+$

Conclusions

The kinetic behavior of the phenolysis of 2-(chloromethyl)oxirane in the "4-nitrophenol – ECH – *N,N*-dimethylaniline" system was investigated in both ECH and the less polar solvent mixture ECH:THF. A zero-order dependence on the proton-donating reagent and a first-order dependence on the amine were established. Similar reaction orders were determined for the acidolysis series "PhCOOH/AcOH – ECH – *N,N*-dimethylaniline" in the same solvents. For both series, it was shown that decreasing solvent polarity reduces the reaction rate in the presence of a tertiary amine catalyst, indicating that the oxirane ring-opening step proceeds *via* an S_N2 mechanism. This conclusion was further supported by the behavior of an ionic catalyst (Bu_4NI) in analogous phenolysis and acidolysis series: in the case of a charged nucleophile, the catalytic rate increases with decreasing solvent polarity. Thus, regioselective phenolysis and regioselective acidolysis can be described by a unified kinetic model corresponding to the anion-transfer mechanism by an ion pair. This mechanism accounts for the possible nucleophilic–electrophilic interactions in the system, the multistep nature of the process, and the *in situ* generation of an ion pair that both catalyzes product formation and is generated during the reaction.

Experimentally, it was confirmed that increasing the acidity of the reagent accelerates oxirane ring opening. The effect of reagent acidity is decisive when a tertiary amine serves as the initial catalyst, indicating the necessity of electrophilic activation of the oxirane at the initial stage of amine quaternization. In contrast, an increase in the nucleophilicity of the reagent anion has a comparatively smaller effect on the reaction rate. Overall, the proposed kinetic model provides a reliable basis for the development of controlled syntheses using oxirane reactions with proton-donating reagents.

Acknowledgements

The study was conducted within the Fundamental Research Program of the Ministry of Education and Science of Ukraine (Project No. 0123U101422, Project No. 0125U002751)

The authors are grateful to the Institute of Organic Chemistry of NAS of Ukraine for assistance with spectroscopic measurements.

The authors are grateful to the European Chemistry School for Ukrainians II for the informative lecture series that contributed to the preparation of this article.

References

[1] Haslewood, M. N. D., Farmer, T. J., North, M. (2023). Synthesis and chemoselective crosslinking of functionalized polyesters from bio-based epoxides and cyclic anhydrides. *J. Polym. Sci.*, *61*(4), 311–322. doi.org/10.1002/pol.20220552

[2] Muniappan Thirumalaikumar. (2022). Ring Opening Reactions of Epoxides. A Review. *Organic Preparations and Procedures International*, *54*(1), 1–39. doi.org/10.1080/00304948.2021.1979357

[3] Chen, J., Nie, X., Liu, Z, Mi, Z., Zhou, Y. (2015). Synthesis and application of polyepoxide cardanol glycidyl ether as biobased polyepoxide reactive diluent for epoxy resin. *ACS Sustain. Chem. Eng.*, *3*(6), 1164–1171. doi.org/10.1021/acssuschemeng.5b00095

[4] Kasian, L. I., Kasian, A. O., Okovityi, S. I., Tarabara, I. N. (2003). [*Alicyclic epoxy compounds. Reactivity*]. Dnipropetrovsk, Ukraine: Izdatelstvo Dnepropetrovskogo universiteta (in Russian).

[5] Soni, H., Verma, K., Singh, K., Priya, S. D., Bhattu, M., Singh, J. (2025). Waste derived 0D nanomaterials for the catalysis reduction of p-nitrophenol: A technological progress and developments. *J. Mol. Struct.*, *1322*(3), 140532. doi.org/10.1016/j.molstruc.2024.140532

[6] Hanif, M., Mansha, A., Ali, K.G., Saeed, M. A., Mahmood, S., Chaudhry, A. R., Irfan, A., Mushtaq, A., Zahoor, A. F. (2025). Ring opening of epoxides: a facile approach towards the synthesis of polyketides and related stereoenriched natural products: a review. *Mol. Divers.*, *29*(5), 4919–4952. doi.org/10.1007/s11030-024-11057-7

[7] Bespalko, Y., Sinel'nikova, M., Shved, E., Bakhalova, E. (2021). Experimental and computational studies of the mechanism of base-catalyzed ring opening of 2-(chloromethyl)oxirane by benzoic acid. *Int. J. Chem. Kinet*., *53*(3), 356–368. doi.org/10.1002/kin.21448

[8] Shved, E. N. (2014). [*Unpublished doctoral dissertation abstract*]. Ukrainian State University of Chemical Technology, Dnipropetrovsk, Ukraine. (In Ukrainian).

[9] Potts, D. S., Locht, H., Kim, S., Lercher, J. A., Hu, J. Z., Flaherty, D. W. (2025). In Situ NMR and Kinetics Reveal Origins of Regioselectivity Differences for Epichlorohydrin Ring-Opening in Lewis and Brønsted Acid Zeolites. *Angew. Chem. Int. Ed.*, *64* (50), e202511944. doi.org/10.1002/anie.202511944

[10] Kumar, V., Chimni, S. S. (2023). Metal-Free Ring-Opening of Epoxides. *Chemistry Select*, *8*(35), e202301963. doi.org/10.1002/slct.202301963

[11] Liu, J. W., Tang, W., Wang, C. (2023). Nickel-Catalyzed Regio- and Enantioselective Ring Opening of 3,4-Epoxy Amides and Esters with Aromatic Amines. *Chem. Eur. J.*, *29*(31), e202300704. doi.org/10.1002/chem.202300704

[12] Golsanamlou, S., Tarlani, A., Narimani, K., Hassani, E, Aghapoor, K. (2024). Regioselective ROH-Epoxystyrene-Opening over MWCNTs-[N4] Macrocycle Comprising Cu(II), Fe(III) or Cr(III). *J Iran Chem Soc., 21*(12), 2961–2973. doi.org/10.1007/s13738-024-03123-6

[13] Makhin, M. N, Klebanov, M. S. (2020). Reaction kinetics of dehydrochlorination of the chlorohydrin esters of Bisphenol A. *Kinet Catal., 61*(2), 238–241. doi.org/10.1134/S0023158420020081

[14] Zhang, Q., Zhou, Y. B., Chen, Y., Zhao, J. P. (2021). Ethoxylation of Phenols Catalyzed by Metal-Free Lewis Pairs: Living/Controlled Polymerization in a Slow-Initiation Mode†. *Chin. J. Chem.*, *39* (9), 2579–2587. doi.org/10.1002/cjoc.202100289

[15] Gansäuer, A. (2021). From Enantioselective to Regiodivergent Epoxide Opening and Radical Arylation - Useful or Just Interesting? *Synlett*, *32*(05), 447–456. doi.org/10.1055/s-0040-1706407

[16] Hansen, T., Vermeeren, P., Haim, A., van Dorp, M. J. H, Codée, J. D. C., Bickelhaupt, F. M., Hamlin, T. A. (2020). Regioselectivity of Epoxide Ring-Openings via S_N2 Reactions Under Basic and Acidic Conditions. *European Journal of Organic Chemistry*. *25*, 3822-3828. doi.org/10.1002/ejoc.202000590.

[17] Yutilova, K., Tkach, A., Tarasenko, V., Shved, E. (2024). Finding the Right Balance between Tertiary Amine Steric Effect and Solvent Polarity for the Regioselectivity and Kinetics of Epichlorohydrin Acetolysis. *J. Phys. Org. Chem., 37*(1), e4573. doi.org/10.1002/poc.4573

[18] Bakhtin, S., Shved, E., Bespalko, Y., Tyurina, T., Palchykov, V. (2020). *Detailing* the elementary stages in the oxirane ring opening reactions with carboxylic acids catalyzed by tertiary amines. *J. Phys. Org. Chem., 33*, 4071. doi.org/10.1002/poc.4071

[19] Liu, F. H., Wu, X. M., Chen, K., Yao, J. B., Ran, Q. C. (2025). The Effect of Tertiary Amines as Catalysts on the Ring-Opening Polymerization of Benzoxazines. *Polymers*, *17*(11), 1431. doi.org/10.3390/polym17111431

[20] Bakhalova, Y. A. (2023). *Benzoic acids as the proton-donating nucleophiles in reaction with 2-(chloromethyl)oxirane in the presence of bases* [Doctoral thesis, Vasyl' Stus Donetsk National University]. (In Ukrainian).

[21] Bakhtin, S., Shved, E., Bespal'ko, Y., Stepanova, Y. (2019). Behavior modelling of organic bases in the oxyalkylation reaction of Proton-Containing nucleophiles. *Prog. React. Kinet. Mech*., *43* (2), 121–135. doi.org/10.3184/146867818X15161889114501

[22] Yan, Z., Ma, Z., Deng, J., Luo, G. (2021). Mechanism and Kinetics of Epoxide Ring-Opening with Carboxylic Acids Catalyzed by the Corresponding Carboxylates. *Chemical Engineering Science, 242*, 116746. doi.org/10.1016/j.ces.2021.116746

[23] Yutilova, K., Sokolovskyi, D., Shved, E., Gorden, A. E. V. (2026). Steric and Electronic Control of Regioselectivity in Salophen Metal Complex-Catalyzed Epichlorohydrin Acetolysis. *J. Org. Chem., 91* (1), 163–176. doi.org/10.1021/acs.joc.5c02193

[24] Lide, D. R. (2004). *Ed. CRC Handbook of Chemistry and Physics*. CRC Press.

[25] Yutilova, K., Shved, E., & Chervonchenko, I. (2022). *Sposib oderzhannia 2-(khlormetyl)oksyranu [Method of obtaining 2-(chloromethyl)oxirane]* (Ukraine Patent No. 152096). Vasyl' Stus Donetsk National University.

[26] Yutilova, K. S., Martseniuk, N. S., Shved, E. N. (2023). Quantum Chemicai Study of the Steric Effect of Substituent on the Reactivity of Tertiary Amines in the Reaction with 2-(Chloromethyl)oxirane. *Journal of Chemistry and Technologies, 31*(3), 451–459. doi.org/10.15421/jchemtech.v31i3.283788

[27] Yutilova, K. S., Bakhalova, E. A., Shved, E. N., Kravchuk, A.V., Lisova, L. S. (2023). Nucleophilic Epoxide Ring Opening in the System "Epichlorohydrin–Carboxylic Acids–Tetrabutylamonium Iodine–Solvent (ε=15.1–28.7). *Vopr. Khimii i Khimicheskoi Tekhnologii*, *2*, 159–167. doi.org/10.32434/0321-4095-2023-147-2-159-167

[28] Reichardt, C. T., Welton, T. (2011). *Solvents and Solvent Effects in Organic Chemistry*. Fourth. Weinheim: Wiley-VCH.

[29] Armarego, W. L. F., Chai, C. (2013). *Purification of Laboratory Chemicals*. Waltham: Elsevier.