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S.V. Domanskyi [a], E.N. Shved [b], K.S. Yutilova [c], G.M. Rozantsev [a]

KINETIC ASPECTS OF CATALYTIC PHENOLYSIS OF EPICHLOROHYDRIN, SELECTIVITY AND REACTION MECHANISM

[a] Vasyl' Stus Donetsk National University, Vinnytsia, Ukraine
[b] L.M. Litvinenko Institute of Physical Organic and Coal Chemistry of the NAS of Ukraine, Kyiv, Ukraine
[c] Institute of Organic Chemistry of the NAS of Ukraine, Kyiv, Ukraine

The catalytic phenolysis of epichlorohydrin (ECH) was studied in terms of regioselectivity and reaction kinetics. The influence of solvent polarity was examined, and the mechanism of nucleophilic oxirane ring opening was detailed. 4-Nitrophenol (pK_a=7.15) was chosen as the nucleophilic reagent, and tetrabutylammonium iodide was used as the catalyst. The kinetic scheme of the reaction was confirmed by studying the structure of the product using ^{1}H NMR spectroscopy and gas chromatography–mass spectrometry. Conclusions were drawn regarding the regioselectivity of the process. The reaction kinetics was studied using excess ECH, which acted simultaneously as both substrate and solvent, as well as in its binary mixture with tetrahydrofuran. A zero-order reaction with respect to the nucleophilic reagent was established. The kinetic law of the reaction is identical to that for the catalytic acidolysis of epichlorohydrin. The sensitivity of the reaction to changes in solvent polarity was assessed. The kinetic features of the phenolysis and acidolysis of epichlorohydrin at varying solvent polarity were analyzed. The mechanism of nucleophilic oxirane ring opening by phenols and carboxylic acids is described as a mechanism involving transfer of the nucleophilic reagent anion by an ion pair.

Keywords: epoxide ring opening, phenolysis, acidolysis, tetraalkylammonium salt, solvent polarity, regioselectivity, catalysis, mechanism.

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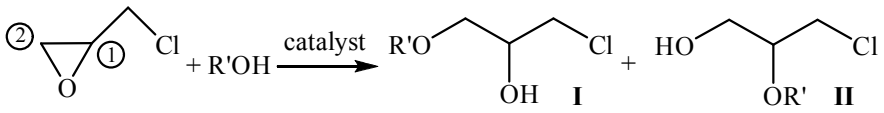
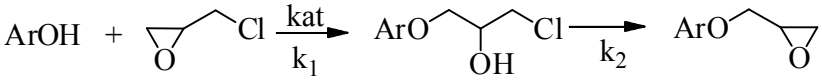
Introduction

Epichlorohydrin (ECH) is a common synthon in organic synthesis [1]. The ability of oxiranes to oxyalkylate proton-donating nucleophiles of different acidity enables the synthesis of structurally diverse substances with a wide range of applications, including pharmaceuticals, epoxy compounds for adhesives, coatings, and furniture materials [2]. The use of phenols as acidic reagents provides the synthesis of epoxides that impart thermal, heat, chemical resistance, and optical transparency to the resulting materials [2]. Organic bases such as tertiary amines and tetraalkylammonium salts effectively catalyze the reaction of ECH with proton-donating nucleophiles [3–5]. The oxirane ring opening reaction by proton-donating nucleophiles in the presence of bases proceeds regioselectively (Reaction (1)) with the formation of chlorohydrin ethers (CHE) **I** («normal» product) and **II** («abnormal» product) [5–7].

A feature of the phenololysis of ECH is its regiospecificity [6,8], when only the product of the «normal» opening of the oxirane ring is formed – chlorohydrin ether **I**, which in the second, slower stage is converted into the corresponding glycidyl ether (Reaction 2).



(1)



(2)

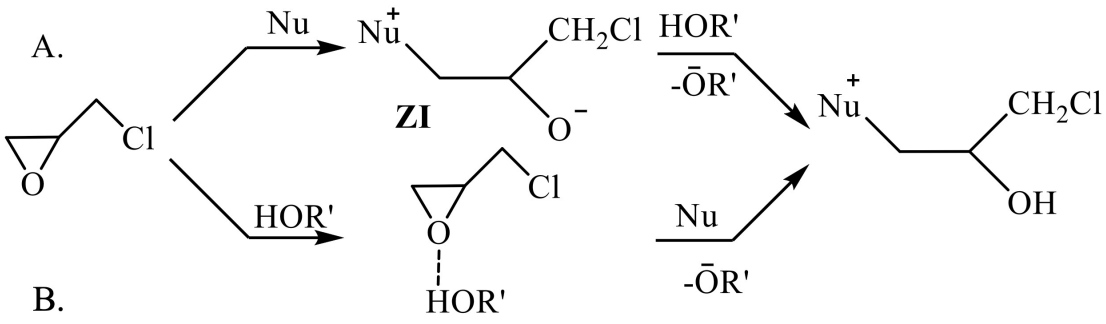
Increasing the temperature, the acidity of phenol, the catalyst content, and the basicity of anions of tetraalkylammonium salts reduces the time to reach the maximum concentration of CHE, which is typical for sequential reactions when $k_2<k_1$ [8].

The absence of product **II** and the significant practical significance of Reaction 2 make this process attractive for establishing conditions for the controlled, regiospecific synthesis of polyfunctional substances and epoxides based on phenols by developing a predictive kinetic model of the process and studying its mechanism.

One of the important kinetic characteristics related to the mechanism of the process is the order of the reaction. Analysis of literature data [3–7] shows that for most reaction series the order of reaction is first for oxirane, 0÷1st for proton-donating nucleophile depending on the reaction series and reagent acidity, and first order for catalyst. It was previously established [6] that, in a significant excess of oxirane, the reaction order for phenols depends on their acidity ($pK_a>8$ – first, $pK_a<8$ – zero), for carboxylic acids on their concentration ($C>0.07$ mol/L – zero, $C<0.07$ mol/L – increasing up to 0.5). Therefore, to create a predictive model of Reaction 2 with the possibility of comparing it to the features of oxirane acidolysis, the reaction system «epichlorohydrin–4-nitrophenol–*n*-Bu_4NI» was chosen as the object of study, where the proton-donating nucleophile has a pK_a of 7.15 [9]). This provides a comparison of the kinetic characteristics of phenololysis and acidolysis of ECH under comparable reaction series conditions (the proton-donating nucleophiles are benzoic and acetic acids with pK_a of 4.18 and 4.75 [9], respectively). Varying the pK_a values of the reagent makes it possible to assess not only the effect of the acidity of the reagent on the regularities of the process, but also to investigate individual stages of the catalysis mechanism.

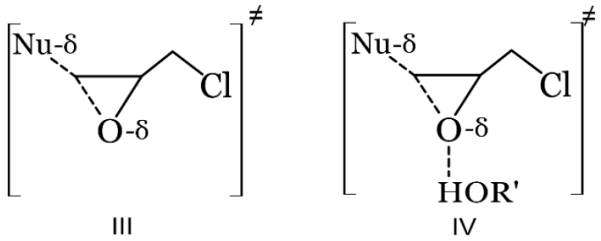
The pathways of nucleophilic oxirane ring opening in the presence of proton donors, consistent with kinetic and stereochemical data [3–6], can be represented (Scheme 1) as reaction 3: A) nucleophilic attack (Nu) on carbon in the ring (limiting step), followed by proton transfer; B) formation of a hydrogen bond between oxirane and proton donor (electrophilic interaction with acid), followed by nucleophilic attack.

As noted earlier [3,5,9,11], the oxirane ring-opening step in type 3 reactions is described as a nucleophilic attack *via* the S_N2 mechanism with some contribution of «borderline» S_N2-like mechanism [5,7,11], where the nucleophile can be either the salt anion of *n*-Bu_4NI or $Bu_4N^{+\cdots}OR$, the formation of which *in situ* in the reaction system is predicted by the proposed catalytic mechanisms [4–6] and has been experimentally confirmed by UV spectroscopy [12]. Thus, the oxirane ring opening can occur through the formation of transition states **III** and **IV**, which



Scheme. Possible pathways for nucleophilic (Nu) oxirane ring opening by an acidic reagent R'OH with the intermediate formation of either a zwitterion (pathway **A**) or an H-complex (pathway **B**) of oxirane with the acidic reagent (electrophilic activation)

differ in electrophilic activation by the reagent R'OH and exhibit a similar nature of the redistribution of electron density from the charged nucleophile to oxygen:



Taking into account the S_N2 character of the oxirane ring-opening stage and the structure of transition states **III** and **IV**, whose rate of formation depends on the solvent polarity, it becomes possible to establish which nucleophile (I^- or $R'O^-$) reacts in the limiting stage of the reaction since in both the studied and comparative reaction series the nucleophile – the I^- anion – is the same, whereas the $R'O^-$ anions formed in the reaction have different nucleophilicity. In order to develop the kinetic model of the catalytic phenololysis of epichlorohydrin and to detail its mechanism, this work studies the reaction system «epichlorohydrin–4-nitrophenol (benzoic and acetic acid as comparative proton-donating nucleophiles)–*n*-Bu_4NI» in solvents of different polarity: ECH (ε=22.6 [9]) and its mixture with less polar tetrahydrofuran (THF, ε=7.6 [9]). To avoid complicating the kinetic picture of the reaction through the presence of various associates of acidic reagents, the studies were carried out in diluted solutions with a significant excess of ECH.

Experimental

Purification of substances

ECH was dried by double distillation over sodium sulfate for 20 hours, and the fraction with b.p. 116–116.5^{0}C was collected (lit. b.p. 116^{0}C [13]).

4-Nitrophenol was recrystallized from an aqueous ethanol solution (m.p. 114–115^{0}C (lit. 114^{0}C [13]).

Tetrabutylammonium iodide (n-$C_4H_9)_4NI$ was recrystallized from benzene (m.p. 144–145^{0}C, lit. m.p. 144.5^{0}C [13]).

Tetrahydrofuran was first purified from peroxides as follows: a 10% aqueous solution of sodium sulfite was added, shaken, and left for 20–30 minutes. The inorganic layer was separated using a separatory funnel, dry sodium hydroxide 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^{0}C (lit. b.p. 66^{0}C [13]).

Kinetic measurements

To study the reaction kinetics, 4-nitrophenol and catalyst solutions were prepared in ECH or in a mixture of ECH:THF, by the accurate weights. Then, 2 mL of the 4-nitrophenol solution and 1 mL of the catalyst solution were taken and placed in a flask with two compartments. The flask was introduced into a water-heating bath for 10 min at the desired temperature. The two solutions were then quickly mixed inside the flask and put in the bath again 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^{0}C) isopropanol:water mixture (1:1 vol.). The contents of the flask were quantitatively transferred to the titration cell 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 temperature 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, δ, ppm: 7.56 d/d (4H, C_6H_4), 3.50 d/tr (2H, CH_2Cl), 4.15 m (1H, CH), 3.95 d/tr (2H, CH_2).

Gas chromatography mass spectrometry (GS-MS) of product system «epichlorohydrin–4-nitrophenol–*n*-Bu_4NI» was recorded using an Agilent 5809 Series II 5972 instrument (electron impact ionization); methylene chloride as an eluent. 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) $[CH_2{}^{35}Cl]^+$.

Results and discussion

As noted earlier, an important characteristic of a kinetic model that depends on its mechanism is the order of the reaction. For the phenololysis of epichlorohydrin, the reaction order depends on the acidity of the reagent when catalyzed by both tetraalkylammonium salts and tertiary amines, pyridines (Table 1).

Therefore, the primary task of the kinetic studies of the reaction between 4-nitrophenol and epichlorohydrin under catalysis by tetrabutylammonium iodide is to determine the order of the reaction with respect to the reagent in solvents

of different polarity: ECH and ECH:THF. Since the order of the reaction of oxiranes with acidic reagents depends on the ratio of the components of the reaction mixture [3,6], a significant excess of ECH (20–60-fold) was maintained in all series, which allowed the studies to be conducted under pseudo-order conditions with respect to oxirane, avoiding complications from association processes.

The kinetics of the reaction of 4-nitrophenol with ECH was investigated at four different concentrations of tetrabutylammonium iodide in ECH and its binary mixture with THF. The progress of the reaction was monitored by measuring the change in reagent concentration over time according to the method described in the experimental part. Kinetic curves describing the effect of varying the catalyst concentration, temperature, and solvent polarity are shown in Figure. The linear relationship observed in the plot of «current reagent concentration vs. conversion time» indicates a zero-order reaction with respect to 4-nitrophenol.

Taking into account the significant excess of ECH and the zero order of the reaction on the reagent, the observed rate constants were calculated using the formula:

$$k_{obs} = \frac{a-(a-x)}{st} . \quad (4)$$

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

$$k_{obs} = k_{non} + k_{cat} b . \quad (5)$$

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

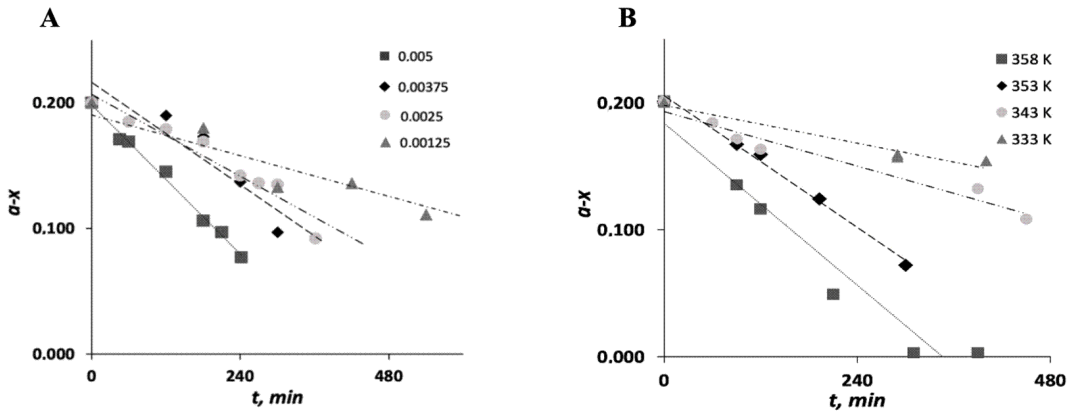
Calculations according to equation (5) allowed the determination of the catalytic and non-catalytic reaction rate constants:

$$k_{obs} = (0.4 \pm 5.4)\cdot 10^{-8} + (1.44 \pm 0.16)\cdot 10^{-4} b , \quad (6)$$

Table 1

The observed rate constants (k_{obs}) of the reaction of phenols (RPhOH, a=0.2 mol/L) with ECH (s=12.8 mol/L) in the presence of R'$_4$NBr ($b\cdot 10^3$=5.00 mol/L) in ECH, 353 K

R in RPhOH	pK_a	(n-Pr)$_4$NBr	Et$_4$NBr	[PyCH$_3$]Br	PhNMe$_2$	Py
$k_{obs}\cdot 10^5$, L/(mol·s), reaction order for phenol is 1						
3-CH$_3$	10.09	3.73±0.04 [6]				
H	10.0	2.75±0.01 [6]				
4-Cl	9.38	2.21±0.09 [6]				
3-Cl	9.02	1.57±0.04 [6]	1.41±0.08 [6]		0.361±0.002 [6]	1.27±0.02 [6]
$k_{obs}\cdot 10^6$, s^{-1}, reaction order for phenol is 0						
3-NO$_2$	8.40	1.22±0.07 [6]				
4-NO$_2$	7.15	0.646±0.038 [6]	0.730±0.020	0.825±0.025	0.650±0.030	0.660±0.025 [6]



Plots of the residual concentration ($a-x$) *vs.* time (t) for the reaction of 4-nitrophenol (a=0.2 mol/L) with ECH [s=12.75 mol/L (**A**), 6.36 mol/L (**B**)] in the presence of n-Bu$_4$NI [b=1.25·10^{-3}÷5.00·10^{-3} mol/L (**A**), 5.00·10^{-3} mol/L (**B**)] in ECH (**A**) and ECH:THF (1:1) (**B**) as solvent; 353 K (**A**) and 343–353 K (**B**)

r=0.988; SD=0.0305; N=4.

The correlation coefficient (r) is close to unity, i.e., equation (5) describes the dependence of the observed rate constants on the catalyst concentration in the first degree, which corresponds to the first order of the reaction behind the catalyst. The correlation of the values of k_{non} and k_{cat} shows that the catalytic process occurs approximately 4 orders of magnitude faster than the non-catalytic one. This allows us to calculate k_{cat} using a simpler formula, namely:

$$k_{obs} = k_{cat} b \,. \quad (7)$$

The rate constants of catalytic phenololysis of ECH, calculated by equations (5) and (7), are given in Table 2 and compared with the corresponding constants for carboxylic acids with higher acidity.

Comparison of catalytic rate constants with pK_a values (Brønsted equation) for the three R'OH reagents in the solvent ECH:THF (1:1) at the temperature of 333 K shows a satisfactory correlation:

$$\lg k_{cat} = (-1.7 \pm 0.4) - (0.35 \pm 0.08)\mathrm{p}K_a \,, \quad (8)$$

r=0.975; SD=0.178.

Thus, more acidic reagents accelerate the reaction. Considering the relationship «acidity R'OH vs. nucleophilicity R'O$^-$», it should be noted that that the more favorable way to open the oxirane ring, which is represented by equation (3), is path **B** with electrophilic interaction with an acidic reagent through the realization of transition state **IV**.

The effect of solvent polarity on the reaction rate was estimated using the Leidler–Eyring equation:

$$\lg k_{cat} = \lg k_{st} + \frac{U(\varepsilon - 1)}{2\varepsilon + 1} \,, \quad (9)$$

where k_{cat} and k_{st} are the reaction rate constants in the studied and standard solvents, respectively; U is the sensitivity coefficient of the reaction series to the change of solvent polarity; $\frac{(\varepsilon - 1)}{2\varepsilon + 1}$ is the Kirkwood function (KF) characterizing the polarity of the solvent.

The value of U is negative for all three series, indicating that increasing the polarity of the solvent reduces the reaction rate. This behavior is consistent with the laws of bimolecular substitution reactions, when the attacking nucleophile is an anion.

Determining the nature of the nucleophile that leads to the formation of the reaction product is a key task in establishing the reaction mechanism. Analysis of the data in Table 2 shows that the catalytic activity of n-Bu_4NI is higher in reaction systems with a more acidic reagent R'OH and in a less polar solvent. The effect of the latter factor is consistent with the laws of reactions occurring according to the S_N2 mechanism involving a charged nucleophile, as well as for complex reactions whose limiting stage follows the same mechanism. Reducing the solvent polarity decreases the solvation of the nucleophilic anion [15] and promotes charge delocalization in transition states **III** and **IV**. If in the three systems under consideration the product is formed solely upon attack by the same nucleophile (I^-), then the sensitivity of the process to a change in the solvent polarity should be identical. Taking into account the more complex mechanism of opening of the oxirane ring (3), at the beginning of the reaction, when attacked by the initial nucleophile, the R'O$^-$ anion is formed *in situ* from the acidic reagent, the nucleophilicity of which is determined by the nature of the acid, i.e., the higher

Table 2

The catalytic rate constants (k_{cat}, L/(mol·s)) for the reaction of acids R'OH (a=0.2–0.3 mol/L) with ECH (s=6.36–12.77 mol/L) in the presence of n-Bu_4NI ($b\cdot10^3$=1.25–5.00 mol/L) and the sensitivity of the process (U) to variations in solvent polarity (KF)

R'OH	pK_a	T, K	Solvent	KF	$k_{cat}\cdot10^4$, L/(mol·s)	U
4-$NO_2C_6H_4OH$	7.15	353	ECH	0.468	1.4±0.2	–9.4
			ECH:THF (1:1)	0.452	2.0±0.2	
		333	ECH:THF (1:1)	0.452	0.706±0.001	–
CH_3COOH	4.75	333	ECH	0.468	2.2±0.2	–10 [14]
			ECH:THF (9:1)	0.465	2.6±0.1	
			ECH:THF (3:1)	0.461	2.8±0.1	
			ECH:THF (1:1)	0.452	3.3±0.1	
PhCOOH	4.18	333	ECH	0.468	6.7±0.5	–10.5 [14]
			ECH:THF (7:3)	0.460	8.4±0.9	
			ECH:THF (1:1)	0.452	9.2±0.4	

the pK_a value of the reagent, the higher the nucleophilicity of the anion. In this case, the degree of solvation of R'O$^-$ also depends on the nucleophilicity of the anion, so the sensitivity to a change in solvent polarity should be different. This pattern is precisely observed in the experiment under discussion. Comparison of the reaction sensitivity parameters with the reagent pK_a shows the satisfactory correlation relationship (equation (10)):

$$U=(-11.8\pm0.5)+(0.3350.0997)\mathrm{p}K_a, \quad (10)$$

r=0.958; SD=0.222; N=3.

This conclusion is consistent with the fundamental principle of the mechanism of transfer of the anion of a nucleophilic reagent by an ion pair [5,6,11,12].

Since the rate of the oxirane ring opening depends not only on the nucleophilicity of the anion but also on its concentration, it was important to estimate the concentrations of R'O$^-$ for each acid. For this purpose, the pK_a values of acids were used. Although the degree of dissociation depends on the solvent, the ratio of the concentrations of ions formed during dissociation depends primarily on the nature of the acids, and not on the solvent. The calculation of the concentration of R'O$^-$ was carried out according to the following scheme:

$$\mathrm{R'OH} \leftrightarrow \mathrm{R'O^-} + \mathrm{H^+}$$

C, mol/L	$a-x$	x	x

$$K_a=x^2/(a-x)$$

The calculated values of the concentration of R'O$^-$ anions (Table 3) are compared with the U values from Table 2.

According to equation (11), benzoic acid has the greatest sensitivity to changes in solvent polarity, and 4-nitrophenol has the least sensitivity.

$$U=-(9.38\pm0.033)+(0.2560.011)\cdot10^{-3}C(\mathrm{RO^-}), \quad (11)$$

r=0.999; SD=0.0345; N=3.

Indeed, the higher the acidity of the reagent, the greater the amount of carboxylate/phenolate ions formed, the higher the amount of solvated anions and the more significant the influence of the solvent on the reaction rate.

This experimentally confirms the mechanism of oxirane ring opening as a mechanism of transfer of the anion of a nucleophilic reagent by an ion pair, where the initial nucleophilic catalyst in the first stage generates a new nucleophile – the anion of the initial reagent – which in the next cycle leads to the formation of the ring opening product – chlorohydrin ethers I. Path **B**, involving electrophilic activation of oxirane (3), should be considered the more preferable route for ring opening.

Conclusions

The study of the catalytic phenolisys of the unsymmetrical oxirane, epichlorohydrin, showed that the process is regiospecific, yielding exclusively the product of «normal» ring opening – 1-chloro-3-phenoxy-2-hydroxypropane. The zero order of the reaction for 4-nitrophenol was established, that is, for phenols with pK_a<8, the zero order of the reaction is preserved when the polarity of the solvent changes. It was shown that the reactivity of phenols and carboxylic acids is greater, the higher their acidity. This indicates the important role of electrophilic activation by an acidic reagent on the oxirane ring opening process. From the assessment of the reaction sensitivity to a change in the solvent polarity, it was established that the said parameter is higher, the greater the acidity of the reagent, that is, it increases with an increasing the concentration of the anion of the nucleophilic reagent. These findings support the mechanism of the catalytic oxirane ring opening, where the initial nucleophile leads to the *in situ* formation of a carboxylate/phenolate anion of the reagent, which subsequently reacts with oxirane to form the chlorohydrin ether product.

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Table 3

The sensitivity of the process (U) to variations in solvent polarity for the reaction of acids R;OH (a=0.2–0.3 mol/L) with ECH (s=6.36–12.77 mol/L) in the presence of n-Bu_4NI ($b\cdot10^3$=1.25–5.00 mol/L) and the concentration of nucleophilic anion R'O$^-$ for acids R'OH

R'OH	K_a	x, mol/L	U
4-$NO_2C_6H_4OH$	$7.08\cdot10^{-8}$	$1.19\cdot10^{-4}$	–9.4
CH_3COOH	$1.78\cdot10^{-5}$	$2.30\cdot10^{-3}$	–10 [14]
PhCOOH	$6.61\cdot10^{-5}$	$4.42\cdot10^{-3}$	–10.5 [14]

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КІНЕТИЧНІ АСПЕКТИ КАТАЛІТИЧНОГО ФЕНОЛІЗУ ЕПІХЛОРГІДРИНУ, СЕЛЕКТИВНІСТЬ І МЕХАНІЗМ РЕАКЦІЇ

С.В. Доманський, О.М. Швед, К.С. Ютілова, Г.М. Розанцев

Вивчено каталітичний феноліз епіхлоргідрину (ЕХГ): регіоселективність та кінетику реакції, вплив полярності розчинника, деталізований механізм нуклеофільного розкриття циклу оксирану. Як нуклеофільний реагент обраний 4-нітрофенол (pK_a=7.15), тетрабутиламоній йодид – як каталізатор. Кінетична схема реакції підтверджена вивченням структури продукту методами ^{1}H ЯМР та хромато-масспектроскопії. Зроблено висновки про регіоселективність реакції. Кінетика реакції вивчена в надлишку ЕХГ, що виступає як субстрат і розчинник одночасно, а також у його бінарній суміші з тетрагідрофураном. Встановлено нульовий порядок реакції за нуклеофільним реагентом. Кінетичний закон реакції такий же як і для каталітичного ацидолізу епіхлоргідрину. Оцінено чутливість реакції до зміни полярності розчинника. Проаналізовано кінетичні особливості фенолізу та ацидолізу епіхлоргідрину при варіюванні полярності розчинника. Деталізовано механізм нуклеофільного розкриття оксиранового циклу фенолами та карбоновими кислотами, який описується як механізм переносу аніону нуклеофільного реагенту іонною парою.

Ключові слова: епоксид; розкриття циклу; феноліз і ацидоліз; сіль тетраалкіламонію; полярність розчинника; регіоселективність; каталіз; механізм.

KINETIC ASPECTS OF CATALYTIC PHENOLYSIS OF EPICHLOROHYDRIN, SELECTIVITY AND REACTION MECHANISM

S.V. Domanskyi [a], E.N. Shved [b, *], K.S. Yutilova [c], G.M. Rozantsev [a]

[a] Vasyl' Stus Donetsk National University, Vinnytsia, Ukraine

[b] L.M. Litvinenko Institute of Physical Organic and Coal Chemistry of the NAS of Ukraine, Kyiv, Ukraine

[c] Institute of Organic Chemistry of the NAS of Ukraine, Kyiv, Ukraine

[*] e-mail: shved_e@yahoo.com

The catalytic phenolysis of epichlorohydrin (ECH) was studied in terms of regioselectivity and reaction kinetics. The influence of solvent polarity was examined, and the mechanism of nucleophilic oxirane ring opening was detailed. 4-Nitrophenol (pK_a=7.15) was chosen as the nucleophilic reagent, and tetrabutylammonium iodide was used as the catalyst. The kinetic scheme of the reaction was confirmed by studying the structure of the product using ^{1}H NMR spectroscopy and gas chromatography–mass spectrometry. Conclusions were drawn regarding the regioselectivity of the process. The reaction kinetics was studied using excess ECH, which acted simultaneously as both substrate and solvent, as well as in its binary mixture with tetrahydrofuran. A zero-order reaction with respect to the nucleophilic reagent was established. The kinetic law of the reaction is identical to that for the catalytic acidolysis of epichlorohydrin. The sensitivity of the reaction to changes in solvent polarity was assessed. The kinetic features of the phenolysis and acidolysis of epichlorohydrin at varying solvent polarity were analyzed. The mechanism of nucleophilic oxirane ring opening by phenols and carboxylic acids is described as a mechanism involving transfer of the nucleophilic reagent anion by an ion pair.

Keywords: epoxide ring opening; phenolysis; acidolysis; tetraalkylammonium salt; solvent polarity; regioselectivity; catalysis; mechanism.

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