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**NUCLEOPHILIC EPOXIDE RING OPENING IN THE SYSTEM  
«EPICHLOROHYDRIN–CARBOXYLIC ACIDS–TETRABUTYLAMMONIUM IODIDE–  
SOLVENT ( $\epsilon=15.1–28.7$ )»**

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The mechanism of the oxirane ring opening by carboxylic acids with different volume of substituents in the system «epichlorohydrin(ECH)–RCOOH–tetrabutylammonium iodide–solvent ( $\epsilon=15.1–28.7$ )» was studied in the excess of ECH at the temperatures of 40–80°C by methods of chemical kinetics and correlation analysis. The effects of solvent polarity (ECH and its mixtures with THF and nitrobenzene), temperature, and spatial structure (topological steric effect index TSEI) of carboxylic acids on the proceeding of the reaction were investigated. The structure of the reaction products was determined by gas chromatography–mass and <sup>1</sup>H NMR spectroscopy. It was found that the reaction accelerates with a decrease in the solvent polarity, an increase in temperature and steric effect in the structure of the reagent. It was shown that the tetraalkylammonium carboxylate ( $R'_4N^+OOCR$ ) which formed in situ causes the final product formation in the rate-determining step of the reaction mechanism.

**Keywords:** epoxide, ring opening, system, acid, tetraalkylammonium salt, solvent polarity, temperature, reaction mechanism.

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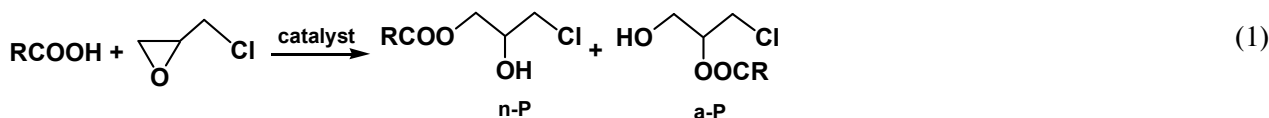
**Introduction**

The epoxide ring opening by proton-donor nucleophiles is one of the fundamental reactions in organic chemistry. Due to the unique ring structure epoxides show high reactivity, which provides for their wide use as synthons in the synthesis of medicines, epoxy resins for high-quality adhesives, sealants, plasticizers [1,2]. The reaction of oxiranes with carboxylic acids is a model for studying the processes of metabolic detoxification of substances of an exogenous nature under the action of epoxide hydrolase enzymes [1,3]. The epichlorohydrin ring opening, one of the most significantly used epoxides, under the action of carboxylic acids leads to a parallel formation of two products: «normal» (n-P) and «abnormal» (a-P) (1), which are versatile intermediates in organic synthesis [3–5].

Effective catalysts for the reaction are organic

bases such as tertiary amines and tetraalkylammonium halides [3,6,7]. To explain the behavior of the reaction path, the following mechanisms of catalytic oxirane ring opening were proposed: general basic, nucleophilic, and transferring the anion of a nucleophilic reagent by an ion pair [3,5–7], that have in common the formation in situ of an intermediate, tetraalkylammonium carboxylate ( $R'_4N^+OOCR$ ) during the reaction, which is a true catalyst that causes the nucleophilic epichlorohydrin ring opening with the formation of the product P. According to the Krasusky rule [4], the formation of the n-P product is favored (2). This is in good agreement with the nucleophilic attack via the  $S_N2$  mechanism with some contribution of «borderline»  $S_N2$ -like mechanism [3,4].

Analysis of possible ways of the oxirane ring opening by such nucleophiles as carboxylate anions

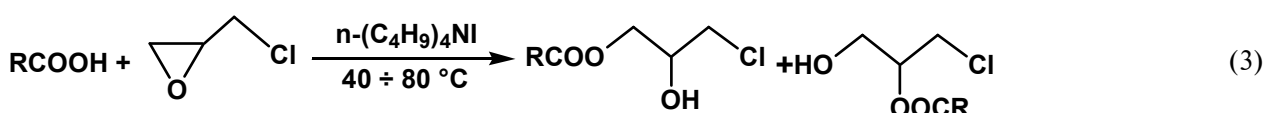
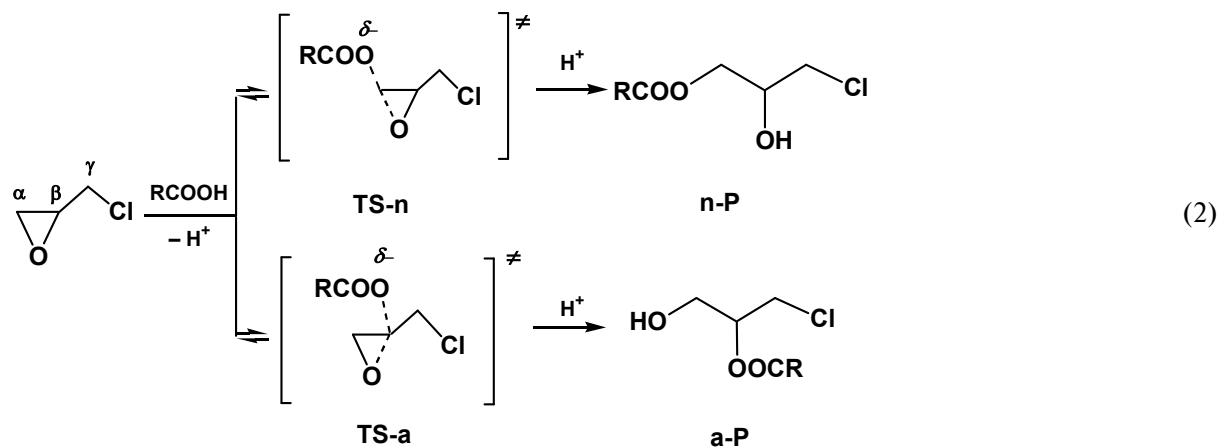


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*Nucleophilic epoxide ring opening in the system «epichlorohydrin–carboxylic acids–tetrabutylammonium iodide–solvent ( $\epsilon=15.1–28.7$ )»*



R = CH<sub>3</sub>; C<sub>2</sub>H<sub>5</sub>; C<sub>6</sub>H<sub>5</sub>; *o*-CH<sub>3</sub>-C<sub>6</sub>H<sub>4</sub>

Solvents: ECH; ECH:THF; ECH:NB

$\epsilon = 15.1 \div 28.7$

by quantum-chemical methods [3,8] showed that the most energetically advantageous are transition states (TS) of the backside attack on the  $\alpha$ -carbon for the E-configuration (Fig. 1).

One of the experimental methods of research of the reactions proceeding via the S<sub>N</sub>2 mechanism or the limiting stage of which has an S<sub>N</sub>2 character is the study of the influence of the solvent polarity on the reaction rate. According to the Hughes-Ingold

theory [9], a polar solvent better solvates particles with a more localized charge. Carboxylate anions with a shorter radical possess more localized charge. Thus, they are better solvated in a polar solvent, which results in reducing their nucleophilic reactivity.

The purpose of the present work was to study the mechanism of oxirane ring opening of epichlorohydrin by carboxylic acids with substituents of different volume in solvents of different polarity under the catalysis with tetrabutylammonium iodide (3).

The evaluation of the spatial structure of carboxylic acids was performed by the topological steric effect index, TSEI, which shows the probability decrement for the attacking group relative to the reaction center<sup>1</sup>. The study was conducted in an excess of epichlorohydrin, which is both a substrate and a solvent, in the temperature range of 40–80°C. The relative permittivity of the medium ( $\epsilon$ ) varied from 15.1 to 28.7 due to the use of not only ECH ( $\epsilon=22.6$  [10]), but also its mixtures with THF ( $\epsilon=7.6$  [10]) and nitrobenzene NB ( $\epsilon=34.8$  [10]) as a solvent, where the condition of the significant excess of epichlorohydrin (*s*, mol/L) in compare to carboxylic acid (*a*, mol/L) was preserved: *s/a*=21÷64. The initial catalyst was tetrabutylammonium iodide, which consists of bulky ions contributing to the delocalization of the charge on them and reducing the effect of the solvent polarity. The structure of

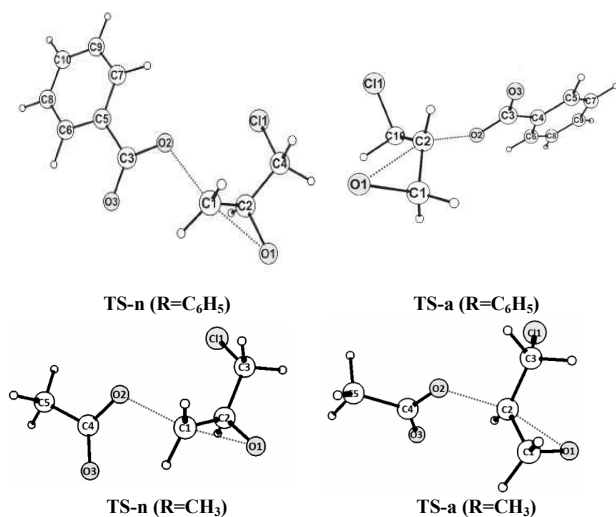


Fig. 1. Transition states of «normal» (TS-n) and «abnormal» (TS-a) epichlorohydrin ring opening with benzoic and acetic acids, E-configuration

<sup>1</sup> «MarvinSketch v. 16.2.8» ChemAxon, 2022. Available from: <https://chemaxon.com/products/marvin>.

the chlorohydrin esters as the reaction products and the ratio of n-P and a-P products were determined by the methods of gas chromatography mass and  $^1\text{H}$  NMR spectroscopy. The reactivity of carboxylic acids in the studied system was estimated by kinetic methods. Control over the depth of the reaction was performed by changing the carboxylic acid concentration by the potentiometric acid-base titration.

### **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°C was collected (lit. b.p. 116°C [11]). Residues of water from glacial acetic acid were removed by boiling over anhydrous copper (II) sulfate [11] and subsequent distillation with collecting the fraction with b.p. 117–119°C (lit. b.p. 118°C [11]). To remove residual water and carbonyl compounds from propionic acid, it was dried for 16 hours over  $\text{Na}_2\text{SO}_4$ , distilled under atmospheric pressure and boiled for 2 hours under reflux, and then distilled again with collecting the fraction with b.p. 141–142°C (lit. b.p. 141°C [11]). Benzoic and 3-methylbenzoic acids were recrystallized from water in the presence of activated carbon (benzoic acid m.p. 121–122.5°C, lit. m.p. 123°C [12], 3-methylbenzoic acid m.p. 110–112°C, lit. m.p. 112°C [11]). Tetrabutylammonium iodide ( $n\text{-C}_4\text{H}_9$ ) $_4\text{NI}$  was recrystallized from benzene (m.p. 144–145°C, lit. m.p. 144.5°C [11]).

#### *Kinetic measurements*

To study the reaction kinetics, carboxylic acid and catalyst solutions were prepared in ECH or a mixture of ECH:THF, ECH:NB by the accurate weights. Then 2 mL of the acid 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 a required time. The initial time of reaction was pointed as the time of solution mixing. After the ending of the required exact time, the reaction was stopped by addition of 10 mL of cold (0–5°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 acid was determined by pH-potentiometric acid-base titration with a 0.1 mol/L NaOH solution.

#### *Analysis of reaction products*

$^1\text{H}$  NMR spectra were recorded at temperature 25°C on a Bruker 400 MHz device in deaerated chloroform. Chemical shifts were determined on a  $\delta$

scale from tetramethylsilane as an internal standard. The authenticity of the obtained spectra of corresponding reaction products was confirmed by the chemical shift calculations in the ACD/ChemSketch software package.

Product n-P, system ECH+AcOH+ $\text{Bu}_4\text{NI}$ .  $^1\text{H}$  NMR spectra,  $\delta$ , ppm: 2.07 s (3H,  $\text{CH}_3$ ), 4.06 d (2H,  $\text{CH}_2\text{Cl}$ ), 3.59 m (1H, CH), 4.19 d (2H,  $\text{CH}_2$ ).

Product a-P, system ECH+AcOH+ $\text{Bu}_4\text{NI}$ .  $^1\text{H}$  NMR spectra,  $\delta$ , ppm: 2.07 s (3H,  $\text{CH}_3$ ), 3.69 d (2H,  $\text{CH}_2\text{Cl}$ ), 5.05 m (1H, CH), 3.79 d (2H,  $\text{CH}_2$ ). Product yield a-P, % (solvent): 11.1 (ECH:THF=1:1 vol.); 11.3 (ECH); 14.7 (ECH:NB=1:1 vol.).

Product n-P, system ECH+ $\text{C}_6\text{H}_5\text{COOH}$ + $\text{Bu}_4\text{NI}$ .  $^1\text{H}$  NMR spectra,  $\delta$ , ppm: 7.73 m (5H,  $\text{C}_6\text{H}_5$ ), 3.70 d (2H,  $\text{CH}_2\text{Cl}$ ), 4.24 m (1H, CH), 4.38 d (2H,  $\text{CH}_2$ ).

Product a-P, system ECH+ $\text{C}_6\text{H}_5\text{COOH}$ + $\text{Bu}_4\text{NI}$ .  $^1\text{H}$  NMR spectra,  $\delta$ , ppm: 7.73 m (5H,  $\text{C}_6\text{H}_5$ ), 3.73 d (2H,  $\text{CH}_2\text{Cl}$ ), 4.83 m (1H, CH), 3.91 d (2H,  $\text{CH}_2$ ). Product yield a-P, % 11.2 (solvent ECH).

Gas chromatography mass spectra of product mixtures were recorded using the Combiflash Companion system (Isco Inc.), column: silica gel, eluent – ethyl acetate/hexane. m/e (I, %): 81 (23.2) [ $\text{CH}(\text{OH})\text{CH}_2^{37}\text{Cl}^+$ ]; 79 (71.0) [ $\text{CH}(\text{OH})\text{CH}_2^{35}\text{Cl}^+$ ]; 61 (77.6) [ $\text{CH}=\text{CH}^{35}\text{Cl}^+$ ]; 44 (68.6) [ $\text{CO}_2^+$ ]; 43 (92.7) [ $\text{CH}_3\text{CO}^+$ ].

### **Results and discussion**

A key question for understanding the reaction mechanism is the order of the reaction. For most of the studied reaction series, the reaction order is the first for the oxirane and the catalyst of the basic nature, regardless of their structure [3,5,7,12]. The reaction order by the acidic reagent varies between 0 and 1 depending on its acidity, the ratio of reagent and substrate, and the degree of association of reacting particles in the system [4,5,12,13]. The reaction has mainly zeroth order of reaction with respect to carboxylic acids in the conditions of an excess of ECH in the presence of tetraalkylammonium salts [3,7,12,13]. One of the factors that affects the degree of association of particles in the system is the polarity and nature of the solvent, therefore the task of determination of the reaction order for carboxylic acids of different structures in solvents of different polarity became a priority. The kinetics of the carboxylic acid reaction with epichlorohydrin in the presence of tetrabutylammonium iodide was studied with four concentrations of the catalyst (Table 1). The stable values were obtained for the observed rate constants  $k_{\text{obs}}$  of the first general order of the reaction and the zeroth order of the reaction with respect to acid, which were calculated by formula (4):

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

where  $a$  and  $(a-x)$  are the initial and the final concentrations of acid (mol/L), respectively;  $s$  is the concentration of ECH (mol/L); and  $t$  is the reaction time (s).

A comparison of the observed rate constants (Table 1) with rate constants of the catalyzed reactions shows (Fig. 2) the presence of a linear dependence (correlation coefficient  $r > 0.99$ ), which corresponds to the first order with respect to tetrabutylammonium iodide. According to the equation (5), the rate constants of the catalytic flow

of the reaction were calculated (Table 2). Their comparison with the polarity of the solvent shows a decrease of  $k_{\text{cat}}$  with an increase of  $\epsilon$  and the Kirkwood function (KF), which is typical for  $S_N2$  processes [3,4].

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

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

Treating the data from Table 2 by the Leidler-Eyring equation (6) shows the linear relationship between  $\log k_{\text{cat}}$  and KF. The parameter  $U$ , which has a negative value, shows a high sensitivity of the

Table 1  
The observed rate constants ( $k_{\text{obs}}$ ) of the reaction of carboxylic acids ( $a=0.2 \div 0.3$  mol/L) with ECH ( $s=6.36 \div 12.77$  mol/L) in the presence of  $n\text{-}(\text{C}_4\text{H}_9)_4\text{NI}$  ( $b \cdot 10^3 = 1.25 \div 5.00$  mol/L) in ECH and binary solvents ECH:THF and ECH:NB 1:1 vol., 60°C

R in RCOOH	$k_{\text{obs}} \cdot 10^6, s^{-1}$			
	$b \cdot 10^3 = 1.25$	$b \cdot 10^3 = 2.50$	$b \cdot 10^3 = 3.75$	$b \cdot 10^3 = 5.00$
Solvent – ECH:THF 1:1 vol., $\epsilon=15.1$				
$\text{C}_6\text{H}_5$ [13]	$0.997 \pm 0.003$	$2.09 \pm 0.01$	$2.98 \pm 0.01$	$4.53 \pm 0.05$
3- $\text{CH}_3\text{-C}_6\text{H}_4$	$1.10 \pm 0.02$	$1.93 \pm 0.05$	$2.82 \pm 0.07$	$3.92 \pm 0.33$
$\text{CH}_3$ [13]	$0.403 \pm 0.006$	$0.820 \pm 0.019$	$1.19 \pm 0.07$	$1.64 \pm 0.08$
$\text{C}_2\text{H}_5$ [13]	$0.437 \pm 0.051$	$0.943 \pm 0.084$	$1.51 \pm 0.27$	$1.95 \pm 0.16$
Solvent – ECH:THF 7:3 vol., $\epsilon=18.1$				
$\text{C}_6\text{H}_5$	$1.14 \pm 0.03$	$2.13 \pm 0.07$	$3.36 \pm 0.26$	$4.15 \pm 0.21$
Solvent – ECH, $\epsilon=22.6$				
$\text{C}_6\text{H}_5$	$0.900 \pm 0.030$	$1.80 \pm 0.07$	$2.80 \pm 0.13$	$3.37 \pm 0.07$
3- $\text{CH}_3\text{-C}_6\text{H}_4$	$0.925 \pm 0.011$	$2.23 \pm 0.21$	$2.41 \pm 0.10$	$3.75 \pm 0.05$
$\text{CH}_3$	$0.270 \pm 0.004$	$0.556 \pm 0.037$	$0.886 \pm 0.024$	$1.09 \pm 0.03$
$\text{C}_2\text{H}_5$	$0.599 \pm 0.041$	$0.814 \pm 0.033$	$1.31 \pm 0.21$	$1.59 \pm 0.11$
Solvent – ECH:NB 1:1 vol., $\epsilon=28.7$				
$\text{C}_2\text{H}_5$	$0.455 \pm 0.038$	$0.781 \pm 0.032$	$1.05 \pm 0.07$	$1.40 \pm 0.11$

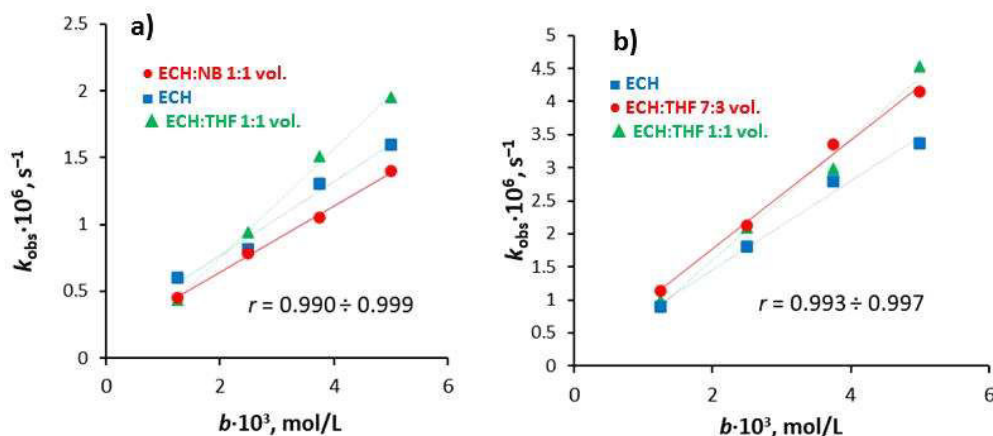


Fig. 2. Dependence of the observed rate constants on the concentration of the catalyst for the reaction of (a) propionic acid ( $a=0.2$  mol/L); (b) benzoic acid ( $a=0.3$  mol/L) with ECH ( $s=6.36 \div 12.77$  mol/L) in the presence of  $n\text{-}(\text{C}_4\text{H}_9)_4\text{NI}$  in ECH and binary solvents ECH:THF and ECH:NB=1:1 vol., 60°C

Table 2

The catalytic rate constants ( $k_{\text{cat}}$ ), topological steric effect indices TSEI of RCOOH for the reaction of carboxylic acids ( $a=0.2\pm 0.3$  mol/L) with ECH ( $s=6.36\pm 12.77$  mol/L) in the presence of  $\gamma$ -n-(C<sub>4</sub>H<sub>9</sub>)<sub>4</sub>NI ( $b\cdot 10^3=1.25\pm 5.00$  mol/L) in ECH, ECH:THF and ECH:NB, 60°C

R in RCOOH (TSEI)	$k_{\text{cat}}\cdot 10^4$ , L/(mol·s)						-U
	ECH:THF				ECH, $\epsilon=22.6$ , KF 0.468	ECH:NB, 1:1 vol., $\epsilon=28.7$ , KF 0.474	
	1:1 vol., $\epsilon=15.1$ , KF 0.452	7:3 vol., $\epsilon=18.1$ , KF 0.460	3:1 vol., $\epsilon=18.8$ , KF 0.461	9:1 vol., $\epsilon=21.1$ , KF 0.465			
C <sub>6</sub> H <sub>5</sub> (1.31)	9.2±0.4	8.4±0.9	–	–	6.7±0.5	–	10.5±0.9
3-CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub> (1.32)	7.5±0.4	5.2±0.5	–	–	7.1±0.9	–	
CH <sub>3</sub> (1.20)	3.3±0.1	–	2.8±0.1	2.6±0.1	2.2±0.2	–	10±2
C <sub>2</sub> H <sub>5</sub> (1.24)	4.1±0.2	–	–	–	2.8±0.3	2.5±0.1	9.6±0.9

reaction series to the polarity of the solvent and a decrease in the rate of the process with increasing of KF.

$$\lg k_{\text{cat}} = \lg k_{\text{st}} + \frac{U(\epsilon-1)}{2\epsilon+1}, \quad (6)$$

where  $k_{\text{cat}}$  and  $k_{\text{st}}$  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 substituent; and  $\frac{(\epsilon-1)}{2\epsilon+1}$  is the

Kirkwood function characterizing the polarity of the solvent.

The highest values of  $k_{\text{cat}}$  are observed for aromatic acids: benzoic and 3-methylbenzoic, which have the highest topological steric effect indices TSEI:

$$\lg k_{\text{cat}} = -(8.6\pm 0.7) + (4.1\pm 0.6) \cdot \text{TSEI} \quad (7)$$

$r=0.914$ ,  $SD=0.0966$ ,  $N=12$  (not taken into account  $k_{\text{cat}}$  for CH<sub>3</sub>COOH, ECH)

Furthermore, the sensitivity of the reaction to a change of the substituent volume in the reagent increases with growth of the solvent polarity. Dependence of  $\lg k_{\text{cat}}$  on the TSEI parameter in the ECH:THF solvent (1:1 vol.) is as follows:

$$\lg k_{\text{cat}} = -(7.8\pm 0.9) + (3.6\pm 0.7) \cdot \text{TSEI} \quad (8)$$

$r=0.965$ ,  $SD=0.0685$ ,  $N=4$

and the dependence in ECH solvent is as follows:

$$\lg k_{\text{cat}} = -(9.1\pm 0.6) + (4.5\pm 0.4) \cdot \text{TSEI} \quad (9)$$

$r=0.991$ ,  $SD=0.0432$ ,  $N=4$

This is consistent with the ideas of the Hughes-Ingold theory regarding the effect of solvent polarity

on processes that proceed via the S<sub>N</sub>2 mechanism and proves that the true catalyst for the reaction of nucleophilic epichlorohydrin ring opening is tetraalkylammonium carboxylate R'<sub>4</sub>N<sup>+</sup>OOCR [3,5,13], which is formed *in situ* in the fast stage and consumed in the rate-determining step with the formation of chlorohydrin esters.

The analysis of the temperature effect on the reaction path was conducted in the temperature range of 40–80°C when varying solvent polarity from 15.1 to 28.7 (Table 3).

An increase in temperature leads to the raising of the catalytic rate constants (Fig. 3) for all the studied acids.

The activation parameters of the reaction ( $\Delta H^\ddagger$  and  $\Delta S^\ddagger$ ) were calculated by the Eyring equation (10) (Table 3) [7].

$$\lg \frac{k_{\text{cat}}}{T} = A + \frac{B_T}{T} \cdot 1000, \quad (10)$$

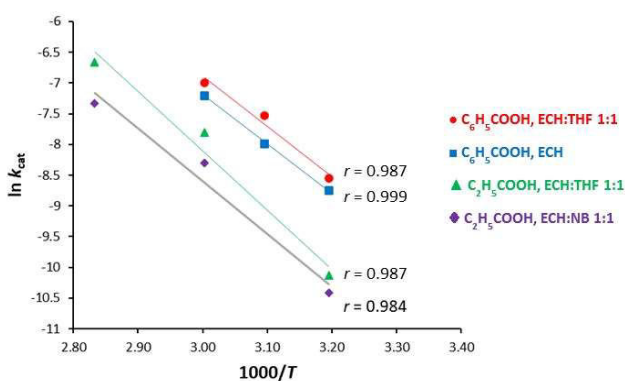


Fig. 3. Plots of the catalytic rate constants ( $\ln k_{\text{cat}}$ ) vs. temperature ( $1000/T$ ,  $T=313\text{--}353$  K) for the reaction of carboxylic acid ( $a=0.2\text{--}0.3$  mol/L) with ECH ( $s=6.36$  mol/L) in the presence of  $n\text{-(C}_4\text{H}_9)_4\text{NI}$  ( $b=5.00\cdot 10^{-3}$  mol/L) in ECH and binary solvents ECH:THF and ECH:NB=1:1 vol.

Table 3

The catalytic rate constants ( $k_{cat}$ ), the activation parameters of the reaction ( $E_a$ ,  $\Delta H_{333}^\ddagger$ ,  $\Delta G_{333}$ ,  $\Delta S_{333}^\ddagger$ ) of the reaction of in the presence of catalyzed by  $n\text{-(C}_4\text{H}_9)_4\text{NI}$  ( $b=5.00 \cdot 10^{-3}$  mol/L) in ECH, ECH:THF and ECH:NB, 40–80°C

R in RCOOH	T, °C	$k_{cat} \cdot 10^4$ , L/(mol·s)	$E_a$ , ‡, kJ/mol	$\Delta H_{333}^\ddagger$ , kJ/mol	$-\Delta S_{333}^\ddagger$ , J/(mol·K)	$\Delta G_{333}^\ddagger$ , kJ/mol
ECH:THF 1:1 vol., $\epsilon=15.1$						
C <sub>6</sub> H <sub>5</sub>	40	1.94±0.12	70±9	65±1	108±4	101±4
	50	5.39±1.12				
	60	9.19±0.41				
3-CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub>	40	1.59±0.06	67±2	64.1±0.3	113±1	102±1
	50	3.38±0.12				
	60	7.45±0.36				
C <sub>2</sub> H <sub>5</sub>	40	0.397±0.069	78±1	77±2	81±5	104±3
	60	4.08±0.15				
	80	12.8±1.6				
ECH:THF 7:3 vol., $\epsilon=18.1$						
C <sub>6</sub> H <sub>5</sub>	40	1.09±0.02	61±14	58.6±0.1	133.0±0.1	102.0±0.1
	50	2.07±0.05				
	60	8.38±0.92				
3-CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub>	40	1.57±0.08	52±4	49.6±0.5	159±2	103±1
	50	3.16±0.11				
	60	5.24±0.50				
ECH, $\epsilon=22.6$						
C <sub>6</sub> H <sub>5</sub>	40	1.14±0.14	67±6	74±2	82±6	102±4
	50	3.88±0.41				
	60	6.72±0.53				
3-CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub>	40	1.38±0.10	71±1	68.2±0.2	101±1	101.8±0.3
	50	3.29±0.17				
	60	7.09±0.99				
CH <sub>3</sub> [7]	30÷60	2.36±0.02 (at 60°C)	80±4	74.1	92.8	105
C <sub>2</sub> H <sub>5</sub>	40	0.449±0.078	70±1	70.5±0.4	103±1	105±1
	60	2.79±0.29				
	80	10.9±1.6				
ECH:NB 1:1 vol., $\epsilon=28.7$						
C <sub>2</sub> H <sub>5</sub>	40	0.298±0.050	70.7±0.8	69±2	112±5	106±3
	60	2.49±0.08				
	80	6.52±1.60				

where  $A=\lg(k_B/h)+\Delta S^\ddagger/2.3R$ ,  $B_T=-\Delta H^\ddagger/2.3R$ ,  $k_B$  is the Boltzmann constant ( $1.38 \cdot 10^{-23}$  J/K);  $h$  is the Planck constant ( $6.62 \cdot 10^{-34}$  J·s); and  $R$  is the universal gas constant ( $8.314$  J·(mol·K)).

There is a linear relationship between the activation enthalpy and entropy parameters for all four acids in the studied solvents:

$$\Delta H_{333}^\ddagger = (104 \pm 3) + (343 \pm 25) \cdot \Delta S_{333}^\ddagger \cdot 10^{-3}, \quad (11)$$

$r=0.980$ ,  $SD=1.74$ ,  $N=10$ .

This fact points on the presence of a kinetic

enthalpy-entropy compensation effect [14] for the whole reaction series under study. Consequently, there is a single mechanism for the catalytic reaction of epichlorohydrin with carboxylic acids with different steric indices TSEI in solvents of different polarity. The activation parameters of the reaction (Table 3) correspond to the processes going via the  $S_N2$  and Ad2 mechanisms [3,4]:

Ad2:  $\Delta S^\ddagger \approx -70 \div -150$  J·(mol·K);

$S_N2$ :  $\Delta H^\ddagger \approx 48 \div 72$  kJ/mol;  $\Delta S^\ddagger \approx -100 \div -176$  J·(mol·K).

Therefore, the reaction of the epoxyde ring opening by carboxylic acids in the presence of

tetrabutylammonium iodide in an excess of oxirane accelerates with a decrease in the solvent polarity, an increase in temperature and the steric factor in the structure of the reagent. The application of the method of multivariate correlation analysis made it possible to assess the joint effect of these factors on the reaction rate.

The best correlation is found for  $k_{\text{cat}}$  from the parameters KF and TSEI (Fig. 4):

$$\lg k_{\text{cat}} = -(4 \pm 2) - (8 \pm 3) \cdot \text{KF} + (3.7 \pm 0.5) \cdot \text{TSEI}, \quad (12)$$

$$r = 0.943, \text{SD} = 0.0827, \text{N} = 11.$$

The high slopes show the significant sensitivity of the reaction to the solvent polarity and the steric index of carboxylic acid, which are comparable to the similar parameters in equations (7), (8) and (9), respectively.

Consideration of the joint effect of solvent polarity and temperature (13), temperature and steric factor (14) shows a high sensitivity to these parameters but has correlation coefficients of  $r = 0.8 \div 0.9$ .

$$\lg k_{\text{cat}} = (11 \pm 3) - (10 \pm 7) \cdot \text{KF} - (3.4 \pm 0.5) \cdot 10^3/T \quad (13)$$

$$r = 0.811, \text{P} = 5.41 \cdot 10^{-3}, \text{SD} = 0.292, \text{N} = 29$$

$$\lg k_{\text{cat}} = (2 \pm 1) - (4.1 \pm 0.4) \cdot 10^3/T + (5 \pm 1) \cdot \text{TSEI} \quad (14)$$

$$r = 0.893, \text{P} = 0.111, \text{SD} = 0.224, \text{N} = 29$$

Evaluation of the joint effect of three factors on the reaction rate according to equation (15) shows that an increase of the steric index of the carboxylic acid contributes most to the reaction rate. The

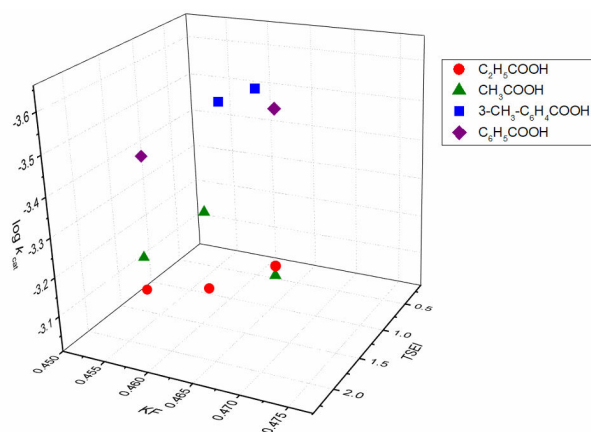


Fig. 4. Two-parameter dependence of the catalytic rate constants ( $\lg k_{\text{cat}}$ ) on the Kirkwood function and the TSEI parameter for the reaction of carboxylic acids ( $a = 0.2 - 0.3$  mol/L) with ECH ( $s$ , mol/L) in the presence of  $n\text{-(C}_4\text{H}_9\text{)}_4\text{NI}$  ( $b = 5 \cdot 10^{-3}$  mol/L) in ECH and binary solvents ECH:THF and ECH:NB = 1:1 vol.

sensitivity of the reaction to a decrease in the solvent polarity and an increase in temperature are equivalent, so these factors accelerate the process to the same extent.

$$\lg k_{\text{cat}} = (4 \pm 3) - (4 \pm 5) \cdot \text{KF} - (4.1 \pm 0.4) \cdot 10^3/T + (5 \pm 1) \cdot \text{TSEI} \quad (15)$$

$$r = 0.895, \text{P} = 0.212, \text{SD} = 0.227, \text{N} = 29$$

Thus, the methods of quantum chemical modeling, kinetic studies, and correlation analysis showed that in the system «epichlorohydrin–RCOOH–tetrabutylammonium iodide–solvent ( $\epsilon = 15.1 - 28.7$ )», the reaction rate rises with a decrease in the solvent polarity and an increase in the reaction temperature and steric hindrances near the reaction center in the reagent.

Since the nucleophilic oxirane ring opening refers to the processes that proceed via  $S_N2$  mechanism, the dependence of the reaction rate on the spatial structure of the carboxylic acid and the polarity of the solvent proves that it is the tetraalkylammonium carboxylate ( $\text{R}'_4\text{N}^+\text{OOCR}$ ) (formed *in situ* during the reaction and is an intermediate) is a true catalyst capable of resulting in the formation of product P (n-P and a-P) in the rate-determining step.

### Conclusions

The study by methods of chemical kinetics, quantum chemical modeling and correlation analysis of the reaction series «epichlorohydrin–RCOOH–tetrabutylammonium iodide–solvent ( $\epsilon = 15.1 - 28.7$ )» in an excess of epichlorohydrin showed that the oxirane ring opening belongs to the processes that proceed via  $S_N2$  mechanism with some contribution of “borderline”  $S_N2$ -like mechanism. The reaction accelerates with a decrease in the polarity of the solvent, an increase in temperature and the steric factor in the structure of the reagent. The growth of the steric index of the carboxylic acid contributes most to the reaction rate. The dependence of the reaction rate on the spatial structure of the carboxylic acid and the polarity of the solvent proves that tetraalkylammonium carboxylate ( $\text{R}'_4\text{N}^+\text{OOCR}$ ) (formed *in situ* during the reaction) is a key intermediate and a true catalyst capable of forming the product P (n-P and a-P) in the rate-determining step of the catalytic process.

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### НУКЛЕОФІЛЬНЕ РОЗКРИТТЯ ЕПОКСИДНОГО ЦИКЛУ В СИСТЕМІ «ЕПІХЛОРОГІДРИН–КАРБОНОВІ КИСЛОТИ–ТЕТРАБУТИЛАМОНІЙ ЙОДИД–РОЗЧИННИК ( $\epsilon=15,1-28,7$ )»

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Вивчено механізм розкриття оксиранового циклу карбоновими кислотами з різним об'ємом замісників у системі «епіхлоргідрин(ЕХГ)–RСООН–тетрабутиламоній йодид–розчинник ( $\epsilon=15,1-28,7$ )» в надлишку ЕХГ за температури 40–80°C із застосуванням методів хімічної кінетики та кореляційного аналізу. Досліджено вплив полярності розчинника (ЕХГ та його суміші з ТГФ і нітробензолом), температури та просторової структури карбонових кислот (індекс топологічного стеричного ефекту *TSEI*) на перебіг реакції. Структуру продуктів реакції визначено методами газової хромато-мас- та <sup>1</sup>H ЯМР-спектроскопій. Встановлено, що швидкість реакції зростає зі зменшенням полярності розчинника, підвищенням температури і стеричного ефекту в структурі реагенту. Показано, що утворений *in situ* карбоксилат тетраалкіламонію (R'<sub>4</sub>N<sup>+</sup>ООСR) спричиняє утворення кінцевого продукту на лімітуючій стадії механізму реакції.

**Ключові слова:** епоксид; розкриття циклу; система; кислоти; сіль тетраалкіламонію; полярність розчинника; температура; механізм реакції.

### NUCLEOPHILIC EPOXIDE RING OPENING IN THE SYSTEM «EPICHLOROHYDRIN–CARBOXYLIC ACIDS–TETRABUTYLAMMONIUM IODIDE–SOLVENT ( $\epsilon=15.1-28.7$ )»

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The mechanism of the oxirane ring opening by carboxylic acids with different volume of substituents in the system «epichlorohydrin(ECH)–RСООН–tetrabutylammonium iodide–solvent ( $\epsilon=15.1-28.7$ )» was studied in the excess of ECH at the temperatures of 40–80°C by methods of chemical kinetics and correlation analysis. The effects of solvent polarity (ECH and its mixtures with THF and nitrobenzene), temperature, and spatial structure (topological steric effect index *TSEI*) of carboxylic acids on the proceeding of the reaction were investigated. The structure of the reaction products was determined by gas chromatography–mass and <sup>1</sup>H NMR spectroscopy. It was found that the reaction accelerates with a decrease in the solvent polarity, an increase in temperature and steric effect in the structure of the reagent. It was shown that the tetraalkylammonium carboxylate (R'<sub>4</sub>N<sup>+</sup>ООСR) which formed *in situ* causes the final product formation in the rate-determining step of the reaction mechanism.

**Keywords:** epoxide; ring opening; system; acid; tetraalkylammonium salt; solvent polarity; temperature; reaction mechanism.



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