

Досліджено дві гетерогенні каталітичні реакції відновлення за механізмом Меєрвейна-Понндорфа-Верлея – відновлення анісового альдегіду з подальшою етерифікацією та циклогексанону. Побудовано математичні моделі досліджених процесів. Проаналізовано активність трьох каталізаторів, за участі яких відбувалась реакція відновлення циклогексанону, та обрано для подальших розрахунків найактивніший. Розраховано константи швидкості досліджених реакцій відновлення альдегідів та кетонів

Ключові слова: механізм Меєрвейна-Понндорфа-Верлея, зворотна задача кінетики, константа швидкості, гетерогенний каталіз, цеоліти

Исследованы две гетерогенные каталитические реакции восстановления по механизму Меєрвейна-Понндорфа-Верлея – восстановление анисового альдегида с последующей этерификацией и циклогексанона. Построены математические модели исследованных процессов. Проанализирована активность трех катализаторов, при участии которых происходила реакция восстановления циклогексанона, и выбран для дальнейших расчетов наиболее активный. Рассчитаны константы скорости исследованных реакций восстановления альдегидов и кетонов

Ключевые слова: механизм Меєрвейна-Понндорфа-Верлея, обратная задача кинетики, константа скорости, гетерогенный катализ, цеолиты

UDC 544.4
DOI: 10.15587/1729-4061.2017.99755

MODELING THE HETEROGENEOUS CATALYTIC RECOVERY PROCESSES OF ALDEHYDES AND KETONES

I. Skoretska

Postgraduate student*

E-mail: ninyovska@mail.ua

Y. Beznosyk

PhD, Associate Professor*

E-mail: yu_beznosyk@ukr.net

*Department of Cybernetics of

Chemical Technology Processes

National Technical University of Ukraine

“Igor Sikorskyi Kyiv Polytechnic Institute”

Peremohy ave., 37, Kyiv, Ukraine, 03056

1. Introduction

In the catalysis and green chemistry, there is a need for environmentally friendly technologies in order to obtain substances using the heterogeneous catalysts. In the synthesis of esters out of a homogeneous catalyst, it is often necessary to use additional solvent, and to recover the catalyst through its deactivation. These problems significantly complicate the process of receiving organic compounds. In contrast to a homogeneous catalyst, a heterogeneous catalyst can be used repeatedly, and it is much easier to separate this catalyst from the products of reaction (employing the mechanical methods).

Promising catalysts of several processes of fine organic synthesis are zeolites, which have a dual structure of porosity – containing micropores and mesopores. Therefore, the development of new catalysts and exploring catalytic properties is a relevant task.

The application of computational technologies and software packages allows calculating, with accuracy acceptable for practice, the required parameters of the examined processes, in particular velocity constants of recovery reactions of cyclohexanone and anise aldehyde.

The aforementioned defines the relevance of the chosen research subject aimed at solving an important applied problem – mathematical modeling of heterogeneous catalytic recovery processes of aldehydes and ketones by the mechanism of Meerwein-Ponndorf-Verley (MPV). Thus, the implementation of organic synthesis in the pres-

ence of a heterogeneous catalyst is an important scientific task [1].

2. Literature review and problem statement

Selective recovery of carbonyl compounds to alcohols in the presence of alcoholates is commonly called the restoration of ketones by the MPV mechanism.

At present, the mechanisms of reactions of ketone and aldehyde recovery by MPV are extensively described in the scientific literature. Some authors [2] described special features of these processes. But no papers have been found up to now, which would have included the results of mathematical modeling and parametric identification of kinetic parameters of mathematical models.

Zeolite is a crystalline form of oxides of metals, which have considerable potential to be applied as heterogeneous catalysts in many chemical reactions [3]. In addition, due to the unique microporous structure, they display different selectivity. A few examples of zeolites are known that are employed in the reaction which proceeds by MPV. For example, in articles [4–6], the reaction occurs in a gas phase on zeolites. There are as well publications about variants of using the zeolite systems for asymmetric aldol process of aldehyde recovery with subsequent esterification [7].

Article [8] presents results of research into selectivity of the recovery reaction of 4-tetra-butyl cyclohexanone

to cis-4-tetra-butyl cyclohexanol on the zeolite catalysts of structural group BEA. This reaction has a commercial application – cis-isomers are widely used in the perfume industry.

A theoretical possibility of heterogeneous catalytic process for obtaining the alcohol by the MPV mechanism is shown in [9, 10]. Zeolites, mesoporous and micro-mesoporous silicates and aluminum oxide materials may prove to be promising catalysts for this process. The given work describes the synthesis of alcohol on zeolites.

Of particular interest are the Sn-containing zeolites of various structural types, for example, Sn-MFI [2, 11] and Sn-BEA [6, 12], which are effective catalysts for organic reactions. Such as the reaction of Baeyer-Villiger [7, 11, 12]; Meerwein-Ponndorf-Verley [13]; isomerization of hydrocarbons, obtained from biomass [9]. Such reactions involve molecules with a diameter of up to 10 Å.

Sn-containing zeolites containing acidic centers of Lewis and Brønsted may become promising catalysts for cascade (multistage) reactions [1, 10].

As far as the mathematical modeling of the recovery processes of aldehydes and ketones in the presence of heterogeneous catalysts is concerned, the scientific literature (in particular, the above mentioned sources) lacks the description of models of such systems. There are only theoretical provisions and features of modeling the heterogeneous catalytic processes. Thus, [14] describes basic assumptions put forward when compiling a mathematical model for the aforementioned processes, and considers the patterns that are applied to construct mathematical models of heterogeneous catalytic processes. At present, there are no developed algorithms for solving the inverse problem of chemical kinetics (calculation of velocity constants) for the recovery process of aldehydes and ketones by MPV.

Therefore, with regard to the above status of research into the chosen subject, it is expedient to develop an adequate mathematical model of the heterogeneous catalytic recovery process of aldehydes and ketones. The mathematical model to be developed might be used for solving the inverse problems of chemical kinetics.

3. The aim and tasks of research

The aim of present work is to calculate the rate constants of the examined reactions in the presence of heterogeneous catalysts based on the obtained experimental data.

To accomplish the set aim, the following tasks were formulated:

- to conduct experimental study of the recovery reaction of cyclohexanone to cyclohexanol in the presence of various zeolite catalysts;
- to conduct experimental study of the recovery reaction of anise aldehyde to anise alcohol with its subsequent esterification;
- to construct a mathematical model of the heterogeneous catalytic recovery processes of aldehydes and ketones;
- to process the obtained experimental data and to calculate the rate constants of the examined reactions, using the developed mathematical model in the automated

mathematical software package MathCad 15.0 (USA); to analyze the received results of calculations and to choose the most efficient catalyst.

4. Materials and methods for examining the heterogeneous catalytic recovery processes of aldehydes and ketones

At the Institute of Physical Chemistry of the Ukrainian NAN (Kyiv, Ukraine), the zeolite systems of structural group beta (β), which incorporated ions of metals, were investigated: Sn and Al. The main difference between the given zeolites from those already known is the dual structure of porosity (they have micro- and meso-pores).

4.1. The examined materials and equipment used in the experiment

Studies were carried out by using the extra wide porous zeolites of the type BEA (beta or β) in the process. These are complex oxides based on magnesium and aluminum prepared by the decomposition of hydrotalcite ($\text{Mg}_6\text{Al}_2(\text{OH})_{16}\text{CO}_3 \cdot 4\text{H}_2\text{O}$). The crystal lattice of such zeolites is incorporated with ions of tin (Sn) whose specific surface is about 100–120 mm^2/g . The content of built-in metal is around 2 %. To activate the catalyst, it needs to be calcinated for 2 hours at a temperature of 600 °C in an autoclave.

The experiment is carried out in the following way. Starting reagents and a catalyst (powdered) are loaded in a laboratory reactor. The reactor is equipped with the magnetic agitator with heating “WiseStir® MSH-20D DAIHAN” (South Korea). Intensity of stirring is 100 rotations of the agitator per minute [15].

The stirring reactor is warmed to 95 °C in advance.

The installation contains a rotation control unit of the agitator (this experiment is carried out at 100 revolutions per minute).

As a stirrer we used a “tablet”, which consists of a magnet covered with inert teflon coating [16]. It can be used several times. A needle for selecting the samples is connected to the reactor through a special plug. After the installation is enabled, the samples are selected for examination in certain range of time (15 min, 30 min, 1 h, 2 h, 4 h, 6 h, 10 h, etc.).

When the reaction is completed, the catalyst is removed by centrifugation. Zeolite heterogeneous catalyst can be reused.

Water or condensate formed in the course of reaction as a result of esterification of alcohol (applicable only for the recovery reactions of anise aldehyde) is discharged to the refrigerator.

In order to analyze selected samples, we use the automated gas chromatograph of the 4th generation “Kristallux-4000M” (Russia) with a proportional-integral differential detector and a capillary column employing mesitylene as internal standard. Analysis of a sample takes about 15 minutes (depending on the size and complexity of the examined molecule). Next is the preparation for taking the next sample (lasting for 3 minutes on average).

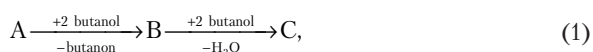
The chromatograph “Kristallux-4000M” processes chromatographic information in automated mode using the compatible software NetChrom (Russia). The software application receives and processes data on the sample. It also has the implemented functions of automatic thermostat temperature control, consumption of the gas-carrier and auxiliary gases, automatic

control of the flame combustion in the process. Measuring the signals from detectors is conducted by using the 24-bit analog-to-digital converter (ADC) “E-24 L” (Russia) [17].

5. Results of examining the heterogeneous catalytic recovery processes of aldehydes and ketones

5.1. The recovery reaction of anise aldehyde to anise alcohol with subsequent esterification

We studied experimentally the recovery process of anise aldehyde and subsequent esterification of the resulting anise alcohol by the MPV mechanism. As a result of the experiment, we obtained dependences of the concentrations of these substances on the time (Table 1). SnAl zeolites were employed as the catalysts. We processed mathematically results of the experiment and obtained a mathematic model of this process. The examined reaction is:



where A is the anise aldehyde; B is the anise alcohol; C is the 4-methoxybenzyl-1-methylpropyl ester.

Table 1

Concentrations of the reaction components*

t, hours	C _A , kmol/m ³	C _B , kmol/m ³	C _C , kmol/m ³
0	0.234	0	0
0.33	0.225	0.00424	0.00487
1	0.214	0.00653	0.01300
2	0.210	0.00617	0.01800
4	0.200	0.00566	0.02800

Note: * – Table 1 gives preliminary processed experimental results

Data given in Table 1 were used to calculate the rate constants in the MathCad 15.0 programming environment.

5.2. The recovery reaction of cyclohexanone to cyclohexanol

In the course of the experiment we obtained the values of conversion degrees (Table 2) of component A in reaction (2) at different time for three different zeolite catalysts. The main difference of zeolites is the type of zeolite mineralizing agent (indicated in brackets next to the type of a catalyst) that defines the type and content of acidic centers and the magnitude of external surface of a zeolite:

- Sn-MgAl(C₄H₁₀O);
- Sn-MgAl(SiO₄);
- Sn-MgAl(CO₃).

Mechanism of the recovery reaction of cyclohexanone is as follows:



where A is cyclohexanone, B is cyclohexanol.

Data given in Table 2 were recalculated to concentrations (in kmol/m³) and used to calculate the rate constants in the MathCad 15.0 programming environment.

Table 2

Conversion degree of cyclohexanone

Sn-MgAl(C ₄ H ₁₀ O)		Sn-MgAl(SiO ₄)		Sn-MgAl(CO ₃)	
t, hours	Conversion A, %	t, hours	Conversion A, %	t, hours	Conversion A, %
0	0	0	0	0	0
0.5	10.75	1	10.09	4	65.46
1.17	20.12	2	16.68	10	89.20
2.25	34.43	4	30.99	–	–
4	44.91	6	38.73	–	–
6	53.54	8	57.55	–	–
8	63.03	10	62.2	–	–
10	67.16	–	–	–	–

Note: * – Table 2 gives preliminary processed experimental results

6. Mathematical modeling of the recovery processes by Meerwein-Ponndorf-Verley

6.1. Mathematical modeling of the recovery process of anise aldehyde

The assumptions that were accepted for modeling the kinetics of recovery process of anise aldehyde:

- a layer of catalyst is the quasi-homogeneous medium;
- since 2-butanol is fed to the reactor in excess, then the change in its concentration can be considered negligible and it can be neglected;
- a layer of catalyst is isothermal;
- the displacement of substance occurs under an ideal agitation mode;
- the transfer of substance along the axial direction is not considered.

Mathematical model of the process with regard to the assumptions takes the following form:

$$\begin{cases} \frac{dC_A}{dt} = -k_1 \cdot C_A, \\ \frac{dC_B}{dt} = k_1 \cdot C_A - k_2 \cdot C_B, \\ \frac{dC_C}{dt} = k_2 \cdot C_B. \end{cases} \tag{3}$$

Initial conditions:

- C_A(0)=0.234 kmol/m³ is the starting concentration of component A in reaction (1);
- C_B(0)=C_C(0)=0 kmol/m³ is the starting concentration of components B and C in reaction (1).

6.2. Mathematical modeling of the recovery process of cyclohexanone

The assumptions that were accepted in the construction of a mathematical model of the recovery process of cyclohexanol [18]:

– a layer of catalyst is the quasi-homogeneous medium, which is why in a mathematical model the catalyst surface area can be ignored;

– since isopropanol is fed to the reactor in excess, then the change in its concentration can be considered negligible and it can be neglected;

– a layer of catalyst is isothermal;

– the displacement of substance occurs under an ideal agitation mode;

– the transfer of substance along the axial direction is not considered.

Mathematical model of the recovery process of cyclohexanone to cyclohexanol takes the following form:

$$\begin{cases} \frac{dC_A}{dt} = -k_1 \cdot C_A, \\ \frac{dC_B}{dt} = k_1 \cdot C_A. \end{cases} \quad (4)$$

Initial conditions for mathematical model (2):

– $C_A(0)=0.3 \text{ kmol/m}^3$ is the starting concentration of component A in reaction (2);

– $C_B(0)=0 \text{ kmol/m}^3$ is the starting concentration of component B in reaction (2).

It is worth noting that when computing the rate constants of reaction (2) using model (4), different rate constants will be received for different catalysts. This is explained by the fact that the more effective a catalyst is, the larger is the value of the rate constant.

By using the above mathematical model in the MathCad 15.0 programming environment we calculated the rate constants of recovery reaction of anise aldehyde.

7. Recalculation of the component concentrations in the recovery reaction of cyclohexanone

In order to calculate the rate constants, it is required to recalculate the degree of conversion of the reaction components to the molar concentration.

Fragments of calculation of cyclohexanol and cyclohexanone concentrations in the MathCad 15.0 programming environment for three catalysts are shown in Fig. 1–3.

Conversion degree, % (Sn-MgAl(CO ₃))	Time, hours	Cyclohexanol concentrations, kmol/m ³ (Sn-MgAl(CO ₃))
$x3 := \begin{pmatrix} 0 \\ 65.46 \\ 89.20 \end{pmatrix}$	$t3 := \begin{pmatrix} 0 \\ 4 \\ 10 \end{pmatrix}$	$cb3 := \frac{x3}{100} \cdot Ca0 \quad cb3 = \begin{pmatrix} 0 \\ 0.196 \\ 0.268 \end{pmatrix}$
Cyclohexanone concentrations, kmol /m ³ (Sn-MgAl(CO ₃))		
$ca3 := Ca0 \cdot \left(1 - \frac{x3}{100}\right) \quad ca3 = \begin{pmatrix} 0.3 \\ 0.104 \\ 0.032 \end{pmatrix}$		

Fig. 1. Calculation in the MathCad 15.0 programming environment of the component concentrations for catalyst Sn-MgAl(CO₃)

By using the calculated concentrations, we constructed dependences of the concentrations of different components of the recovery reaction of cyclohexanone to cyclohexanol by

the Meerwein-Ponndorf-Verley mechanism on the duration of the reaction (Fig. 4).

Initial conditions, kmol/m ³	Time, hours	Cyclohexanol concentrations, kmol/m ³ (Sn-MgAl(C ₄ H ₁₀ O))
$x1 := \begin{pmatrix} 0 \\ 10.75 \\ 20.12 \\ 34.43 \\ 44.91 \\ 53.54 \\ 63.03 \\ 67.16 \end{pmatrix}$	$t1 := \begin{pmatrix} 0 \\ 0.5 \\ 1.17 \\ 2.25 \\ 4 \\ 6 \\ 8 \\ 10 \end{pmatrix}$	$cb1 := \frac{x1}{100} \cdot Ca0 \quad cb1 = \begin{pmatrix} 0 \\ 0.032 \\ 0.06 \\ 0.103 \\ 0.135 \\ 0.161 \\ 0.189 \\ 0.201 \end{pmatrix}$
Cyclohexanone concentrations, kmol/m ³ (Sn-MgAl(C ₄ H ₁₀ O))		
$ca1 := Ca0 \cdot \left(1 - \frac{x1}{100}\right) \quad ca1 = \begin{pmatrix} 0.3 \\ 0.268 \\ 0.24 \\ 0.197 \\ 0.165 \\ 0.139 \\ 0.111 \\ 0.099 \end{pmatrix}$		

Fig. 2. Calculation in the MathCad 15.0 programming environment of the component concentrations for catalyst Sn-MgAl(C₄H₁₀O)

Conversion degree, % (Sn-MgAl(SiO ₄))	Time, hours	Cyclohexanol concentrations, kmol/m ³ (Sn-MgAl(SiO ₄))
$x2 := \begin{pmatrix} 0 \\ 10.09 \\ 16.68 \\ 30.99 \\ 38.73 \\ 57.55 \\ 62.20 \end{pmatrix}$	$t2 := \begin{pmatrix} 0 \\ 1 \\ 2 \\ 4 \\ 6 \\ 8 \\ 10 \end{pmatrix}$	$cb2 := \frac{x2}{100} \cdot Ca0 \quad cb2 = \begin{pmatrix} 0 \\ 0.03 \\ 0.05 \\ 0.093 \\ 0.116 \\ 0.173 \\ 0.187 \end{pmatrix}$
Cyclohexanone concentrations, kmol/m ³ (Sn-MgAl(SiO ₄))		
$ca2 := Ca0 \cdot \left(1 - \frac{x2}{100}\right) \quad ca2 = \begin{pmatrix} 0.3 \\ 0.27 \\ 0.25 \\ 0.207 \\ 0.184 \\ 0.127 \\ 0.113 \end{pmatrix}$		

Fig. 3. Calculation in the MathCad 15.0 programming environment of the component concentrations for catalyst Sn-MgAl(SiO₄)

We also built a dependence of the degree of conversion on the duration for different catalysts (Fig. 5).

Table 3 gives the calculated values of cyclohexanone and cyclohexanol concentrations.

Data given in Table 3 were used to calculate the rate constants in the MathCad 15.0 programming environment.

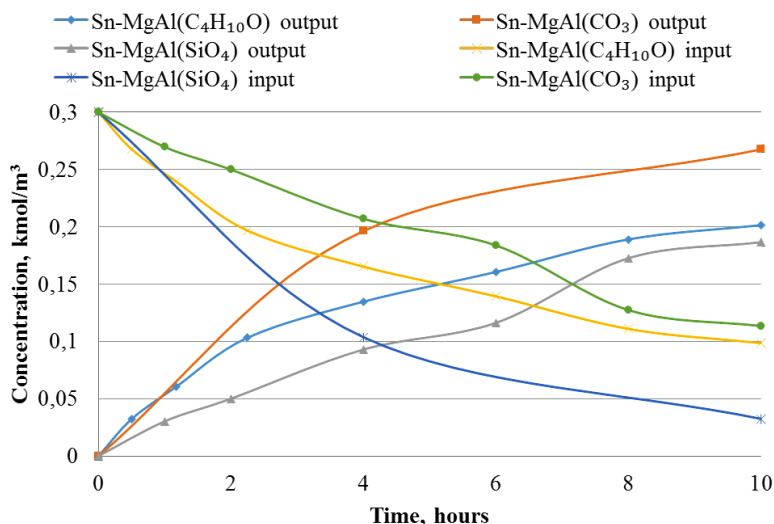


Fig. 4. Dependence of cyclohexanone (input) and cyclohexanol (output) concentrations on the duration for different catalysts

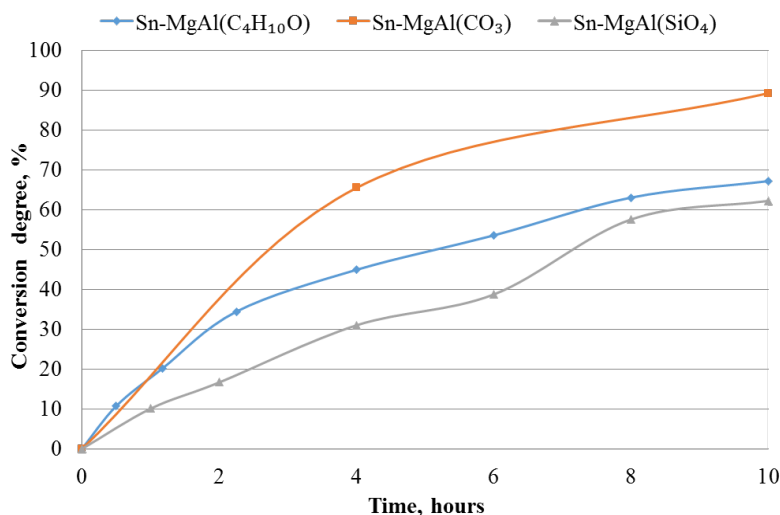


Fig. 5. Dependence of the degree of conversion on the duration for different catalysts

8. Calculation of the rate constants of the examined reactions

8. 1. Rate constants of the recovery reaction of cyclohexanone

By using the calculated values of cyclohexanone and cyclohexanol concentrations, given in Table 3, in the MathCad 15.0 programming environment we calculated the rate constants of reaction (2) for three zeolite catalysts. We employed the listing given in [19] for the calculation.

Fragment of the code in the MathCad 15.0 programming environment to calculate the rate constants is shown in Fig. 6 [20].

Using the algorithm shown in Fig. 6, we calculated the rate constants for all examined catalysts. The obtained results of calculation are given in Table 4.

Analysis of the received values of constants is given in chapter 9.

Table 3

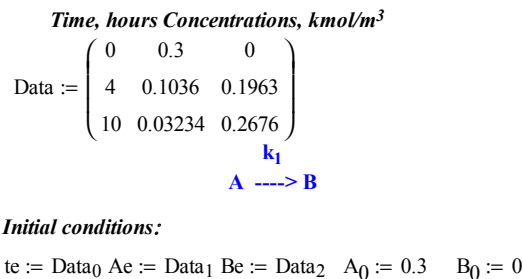
Results of calculation of the reaction components concentrations

Sn-MgAl(CO ₃)		
t, hours	C _A , kmol/m ³	C _B , kmol/m ³
0	0.3	0.0000
4	0.10363	0.1964
10	0.03240	0.2676
Sn-MgAl(SiO ₄)		
t, hours	C _A , kmol/m ³	C _B , kmol/m ³
0	0.3	0.0000
1	0.2697	0.0303
2	0.2500	0.0500
4	0.2070	0.0930
6	0.1838	0.1162
8	0.1274	0.1726
10	0.1134	0.1866
Sn-MgAl(C ₄ H ₁₀ O)		
t, hours	C _A , kmol/m ³	C _B , kmol/m ³
0	0.3	0.0000
0.5	0.2677	0.0323
1.17	0.2396	0.0604
2.25	0.1967	0.1033
4	0.1653	0.1347
6	0.1394	0.1606
8	0.1109	0.1891
10	0.0985	0.2015

Table 4

Calculated values of the reaction rate constants

Catalyst	Calculated values of the rate constant, s ⁻¹
Sn-MgAl(C ₄ H ₁₀ O)	0.1340
Sn-MgAl(CO ₃)	0.2544
Sn-MgAl(SiO ₄)	0.0953



Initial approximations:

$$\text{value}(f, t) := \vec{f}(t) \quad k_1 := 1$$

Mathematical model:

Given

$$A'(t) = -k_1 \cdot A(t)$$

$$B'(t) = k_1 \cdot A(t)$$

$$A(0) = A_0 \quad B(0) = B_0$$

$$S(k_1) := \text{Odesolve} \left(\begin{pmatrix} A \\ B \end{pmatrix}, t, \max(te), 1000 \right)$$

Given

$$\begin{pmatrix} A \\ B \end{pmatrix} \leftarrow S(k_1) \quad = \text{augment}(Ae, Be)$$

$$\text{augment}(\text{value}(A, te), \text{value}(B, te))$$

$$k_1 := \text{Minerr}(k_1) \quad \begin{pmatrix} A \\ B \end{pmatrix} := S(k_1) \quad k_1 = 0.25444$$

Fig. 6. Calculation of the rate constant of the recovery reaction of cyclohexanone that proceeds on zeolite Sn-MgAl(CO₃)

8. 2. Rate constants of the recovery reaction of anise aldehyde

Using the values of concentrations of anise aldehyde, anise alcohol and the resulting ester, given in Table 1, in the MathCad 15.0 programming environment we calculated the rate constants of reaction (1) for the zeolite catalyst. We employed the listing given in [19] for the calculation.

Fragment of the code in the MathCad 15.0 programming environment to calculate the rate constants is shown in Fig. 7 [20].

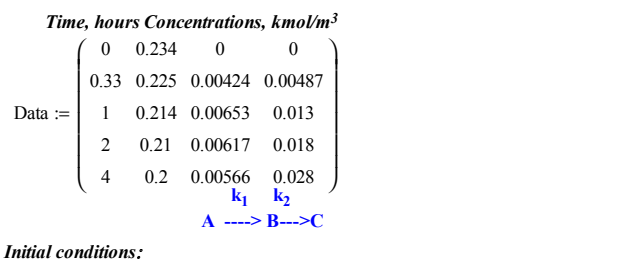
Using the algorithm shown in Fig. 7, we calculated the rate constants for all stages of the examined reaction. The obtained results of calculation are given in Table 5.

Table 5

Calculated rate constants

Rate constants	Calculated value of the rate constant, s ⁻¹
k ₁	0.0323
k ₂	0.4738

Analysis of the received values of constants is given in chapter 9.



Initial conditions:

$$\text{value}(f, t) := \vec{f}(t) \quad \begin{pmatrix} k_1 \\ k_2 \end{pmatrix} := \begin{pmatrix} 1 \\ 1 \end{pmatrix}$$

Mathematical model:

Given

$$A'(t) = -k_1 \cdot A(t)$$

$$B'(t) = k_1 \cdot A(t) - k_2 \cdot B(t)$$

$$C'(t) = k_2 \cdot B(t)$$

$$A(0) = A_0 \quad B(0) = B_0 \quad C(0) = C_0$$

$$S(k_1, k_2) := \text{Odesolve} \left(\begin{pmatrix} A \\ B \\ C \end{pmatrix}, t, \max(te), 1000 \right)$$

Given

$$\begin{pmatrix} A \\ B \\ C \end{pmatrix} \leftarrow S(k_1, k_2) \quad = \text{augment}(Ae, Be, Ce)$$

$$\text{augment}(\text{value}(A, te), \text{value}(B, te), \text{value}(C, te))$$

$$\begin{pmatrix} k_1 \\ k_2 \end{pmatrix} := \text{Minerr}(k_1, k_2) \quad \begin{pmatrix} A \\ B \\ C \end{pmatrix} := S(k_1, k_2) \quad \begin{pmatrix} k_1 \\ k_2 \end{pmatrix} = \begin{pmatrix} 0.0323 \\ 0.4738 \end{pmatrix}$$

Fig. 7. Calculation of the rate constant of the recovery reaction of anise aldehyde that proceeds on zeolite

9. Analysis of results of the experiment and solution of the inverse problem of kinetics

An analysis of Table 1 revealed that the maximum concentration of anise alcohol, which is achieved in the process of converting the anise aldehyde (component B in reaction (1)) by the MPV mechanism, is 0.00653 kmol/m³. Such a value of the concentration is achieved within 1 hour of conducting the experiment. Then the concentration of component B in reaction (1) starts to decrease. This is explained by the fact that in the reactor at this time there starts an esterification reaction of the obtained anise alcohol. The received values of the component concentrations could be also used for the simulation of chemical reactors with different modes of operation – agitation and extrusion.

On analyzing the obtained values of the rate constants of the recovery reaction of anise aldehyde (Table 5), we can state the following. The second stage of the reaction (formation of ester) proceeds much faster than the first stage. Thus, the rate constant of the first stage is 0.0323 s⁻¹, and that of the second is 0.4738 s⁻¹.

As far as the recovery reaction (2) of cyclohexanone to cyclohexanol is concerned, an analysis of the obtained data (Table 3, Fig. 4, 5) revealed the following. The maximum concentration of the product of reaction (cyclohexanol) is achieved when using the zeolite catalyst Sn-MgAl(CO₃). The maximum concentration of cyclohexanol is 0.2676 kmol/m³. Such value is achieved within 10 hours of the reaction

course. The second best in performance is the catalyst Sn-MgAl(C₄H₁₀O) (the maximum value of concentration of the product of reaction is 0.2015 kmol/m³). The worst catalyst for this process is the zeolite Sn-MgAl(SiO₄).

10. Conclusions

1. We examined the recovery reaction of cyclohexanone to cyclohexanol by the MPV mechanism in the presence of three new zeolite catalysts: Sn-MgAl(C₄H₁₀O), Sn-MgAl(SiO₄), Sn-MgAl(CO₃), which have a dual structure of porosity. Experimental data are obtained (conversion degrees of cyclohexanone), which were recalculated into concentrations (kmol/m³) and used to calculate the rate constants in the MathCad 15.0 programming environment.

2. We studied the recovery reaction of anise aldehyde to anise alcohol with its subsequent esterification by the MPV mechanism. Experimental data are received (component concentrations of the reaction, kmol/m³) and used to calculate the rate constants in the MathCad 15.0 programming environment.

3. Mathematical models of heterogeneous catalytic processes are constructed. The mathematical model of the recovery process of anise aldehyde is a system of three differential equations and initial conditions (starting concentrations of the reaction components). The mathematical model of the recovery process of cyclohexanone is a system of two differential equations and initial conditions. The equations included in the models describe a change in the reaction components concentrations over time. The developed mathematical models of the processes were employed for solving the inverse problem of chemical kinetics.

4. We calculated rate constants of the examined reactions by using the developed mathematical models in the automated mathematical software package MathCad 15.0. On analyzing the calculated values of rate constants, one may conclude that the most efficient catalyst for the recovery reaction of cyclohexanone is the zeolite Sn-MgAl(CO₃), since when using it in the process the maximum concentration of the product of reaction is achieved – cyclohexanol (0.2676 kmol/m³). An analysis of rate constants of the recovery process of anise aldehyde revealed that the limiting stage in the formation of anise alcohol is the one whose rate constant is 0.0323 s⁻¹.

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Розроблено модель з використанням бутстреп-методу для оцінки функції розподілу вивільнення лікарського препарату в людському організмі. Показаний приклад застосування методу на препараті Трізіпін-Лонг. Розглянуто випадки з використанням різної кількості випробувань (100, 1000 і 10000). Для дослідження впливу методу інтерполяції проведено порівняльне дослідження емпіричних функцій розподілу кількості препарату, який вивільнився в шлунок, 12-палої кишки і повне вивільнення

Ключові слова: бутстреп-моделювання, сплайн, інтерполяція, профіль вивільнення in vivo, Трізіпін-Лонг, функція розподілу

Разработана модель с использованием бутстреп-метода для оценки функции распределения высвобождения лекарственного препарата в человеческом организме. Показан пример применения метода на препарате Тризипин-Лонг. Рассмотрены случаи с использованием разного количества испытаний (100, 1000 и 10000). Для исследования влияния метода интерполяции проведено сравнительное исследование эмпирических функций распределения количества препарата, высвободившегося в желудке, 12-перстной кишке и полное высвобождение

Ключевые слова: бутстреп-моделирование, сплайн, интерполяция, профиль высвобождения in vivo, Тризипин-Лонг, функция распределения

UDC 519.22:615.275.4 : 691.175.5/8
DOI: 10.15587/1729-4061.2017.102182

DEVELOPMENT OF A BOOTSTRAP-MODEL FOR DETERMINING THE RELEASE OF MEDICINAL PREPARATIONS IN THE HUMAN ORGANISM

A. Chorny

Postgraduate student*

E-mail: chorny@microkhim.com

R. Savyak

PhD, Associate Professor*

E-mail: savyak@microkhim.com

S. Kondratov

Doctor of Chemical Sciences, Professor

Department of mathematics and computer technologies

Institute of Chemical Technology

Volodymir Dahl East-Ukrainian National University

Volodymyrs'ka str., 31, Rubizhne, Ukraine, 93009

E-mail: kondratovsa@gmail.com

*Research and Production Company "Microkhim"

Volodymyrs'ka str., 33, Rubizhne, Ukraine, 93009

1. Introduction

One of the intensively developed directions of contemporary pharmacology is the development of compositions of oral medicines with the assigned profile of the release of medicinal substance in the gastrointestinal tract (GIT), which ensures its optimal effect on the organism. A basis for developing these preparations are experimental studies on the kinetics of dissolution in vitro of finished dosage forms under conditions that imitate the work of GIT. In certain cases, results of studying the kinetics of release can be substituted with studies into bioequivalence. In Ukraine,

studies on the kinetics of release are conducted according to the State Pharmacopoeia [1].

A widespread introduction of information technologies contributed to the emergence of a new approach to the creation of preparations with the assigned profile of release, based on the application of mathematical modeling and computer simulation. These models are built based on the results of experimental studies under standard conditions.

Development of models, not linked to particular mechanisms of release and oriented at solving the practical problems of devising medicines is a relevant task.