

Isopropyl Lactate Obtaining by Esterification in a Reactive Distillation System

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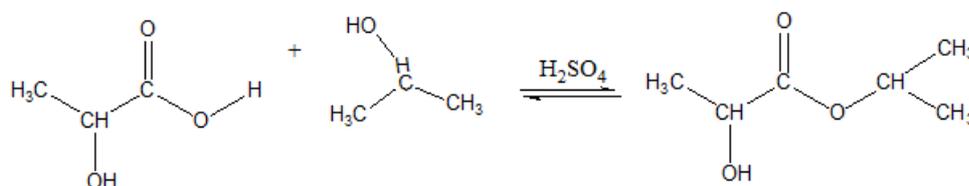
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The reactive distillation is a way for the intensification of chemical processes by thermal integration into a single process of chemical reactions with products separation. Isopropyl lactate is an important intermediate for drug synthesis what can be synthesized through reactive distillation. Based on scientific studies in literature, a preliminary study was performed in a reactive distillation laboratory system, in order to obtain isopropyl lactate by esterification of lactic acid with isopropyl alcohol. The independent variables studied are: the alcohol/lactic acid molar ratio (R), the catalyst concentration (C_A) and the number of theoretical trays in the fractionation zone (NTT). The experimental matrix was established for a 2^3 factorial experiment, by considering two levels for each variable: $R=1$ and 3 mole/mole; $C_A=3\%$ wt and 5 %wt; $NTT=1.9$ and 2.9. A linear mathematical model was proposed to correlate the lactic acid conversion with the molar ratio of reactants, catalyst concentration and the number of theoretical plates in the column. The model shows that R and NTT are the important variables of the process while the acid concentration is less important, in the studied range. The correlation coefficient is $R^2=0.9978$ and the statistical analysis ANOVA of the model's coefficients proved they are significant at a confidence level of 95%, so the model is reliable.

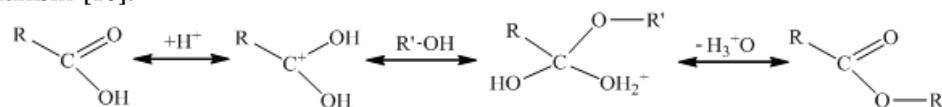
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Organic esters represent an important range of chemical compounds with various uses like perfumes, flavours, pharmaceuticals, plastics, solvents and intermediates in chemical syntheses. The best-known method for obtaining an ester is the reaction between an acid and an alcohol in presence of a catalyst. Usually, esterification in homogenous catalysis rises the problem of compounds separation from the esterification effluent [1]. The esterification of the lactic acid with alcohols can be performed in different ways and the choice of experimental conditions depends on the alcohol used in esterification [2]. During the esterification process, the maximum conversion rate is equilibrium limited. For leading the esterification reaction to the desired products at high yields, large alcohol excess is used and/or one or more products are constantly removed from the reaction mass [3]. An alternative for upgrading the esterification process is the reactive distillation. In recent years, research has been

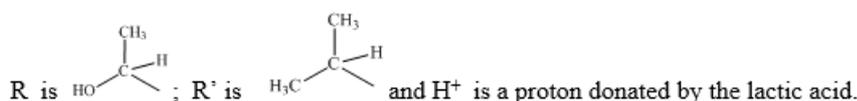
carried out in the reactive distillation process and various approaches to the modeling were adopted [4-7]. Reactive distillation offers some advantages comparing to the conventional process in which the reaction and the purification are separate processes. These are: mitigation of investment and operation costs, high selectivity, low power consumption, reduction or elimination of the solvents [8]. The major advantage is that chemical reaction occurs with important conversion at distillation temperature [9]. The esters are usually obtained by the reaction between an acid and an alcohol with the discharge of water. The esterification rate of different alcohols with acids depends on the molecular structure and the type of functional substitutes of alcohols and acids. Primary alcohols can react fast and complete in the esterification process. In the same reaction conditions, the secondary alcohols are more slowly reactive, and they realize smaller conversion in esters. The reaction for obtaining isopropyl lactate is:



The reaction can be conducted in homogeneous or in heterogeneous acid catalysis. The esterification takes place in a carbo-ionic mechanism [10]:



where:



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In strong acid environment, the alcohol can be dehydrated, resulting propylene highly reactive with the acid, thus forming the corresponding sulfonic acid. This secondary reaction can be mitigated by maintaining the acid concentration at low levels (3-5 %wt).

In homogeneous catalysis, at 363 K with a molar ratio $R=1.4$ *isopropanol:lactic acid* and catalyst concentration $C_c=0.422$ kmol/m³, Rathod et al [11], found the equilibrium conversion of lactic acid to be 51%.

The direct esterification was also performed in heterogeneous catalysis (with cation exchange resins, Amberlyst 15) in liquid phase by Toor et al [12]. The experiments were performed in a stirred batch reactor, and the effect of the following parameters was studied: the temperature (323.15 K to 373.15 K), the molar ratio of *alcohol:lactic acid* (1:1 to 3:1) and the catalyst loading (4.73 kg m⁻³÷11.84 kg m⁻³). The tendency goes to the increasing of conversion with temperature, reactant molar ratio and catalyst loading 42% conversion of lactic acid was obtained at 373 K, catalyst loading 11.84 kg m⁻³ and molar ratio *alcohol:lactic acid* 3:1.

They found a kinetic model based on the Eley-Rideal reaction mechanism which fairly corresponds to the experimental data and had shown that esterification is endothermic because the value of the equilibrium constant increases with temperature increasing. Previously, Yadav and Kulkarni [3] have performed a similar experiment of heterogeneous catalysis but in different conditions: temperature 353 K, catalyst loading 27.27 kg m⁻³ and molar ratios 10, 21 and 44. In these conditions, conversion rose to 63-95%; the use of large excess of isopropanol has also drawbacks, especially concerning the production costs.

The catalytic esterification of alcohols and acids in vapor phase is advantageous because the conversion is in general higher than the correspondent reactions in the liquid phase. This synthesis method is most effective in obtaining the lactic esters from light alcohols (methanol and ethanol) [10, 13].

Literature data [14] show that isopropyl lactate can be also obtained by direct esterification of the lactic acid with isopropyl alcohol in the presence of acid catalyst (sulphuric acid) and azeotrope distillation system using benzene as entrainer; yields of 60-68% of the theoretical amount were obtained, with up to 20% higher than in absence of benzene.

Other method for improving the isopropyl lactate yield is the synthesis coupled with pervaporation. A polyvinyl alcohol-polyether sulfone (PVA-PES) composite membrane was used for the separation of water from the reaction mixture during the synthesis [11]; the use of this membrane even allowed to use reactants with high moisture content (lactic acid technical grade containing 8-12 %wt. water), which usually is avoided. Comparing with a maximum 51% conversion of lactic acid in simple direct esterification, the conversion increased at 86% by using the PVA-PES membrane.

In the present study, the reactive distillation was applied in order to increase the conversion of lactic acid in direct esterification with isopropanol.

The experimental study was conducted in order to propose a mathematical model for to predict the lactic acid conversion in correlation with process variables.

Experimental part

The experimental installation is a laboratory batch distillation column equipped with Raschig glass rings, as shown in previous work [15]; the temperature in the bottom can be controlled by progressive heating with the aid of a rheostat; condensation and cooling are performed with running water (20°C). The internal diameter of the column is 20 mm, and its height is 500 mm. The column acts as a rectification zone, removing water and isopropanol. The height of packing in the column was 400 mm then 100 mm, corresponding to 2.9 theoretical plates and 1.9, respectively or the height equivalent to one theoretical plate (HETP) of 138 mm and 52 mm, respectively. The number of theoretical plates was determined experimentally for the system isopropanol-water in concentration range of $x=0 \div 0.5$ mole fraction. The lactic acid conversion was determined by titration with NaOH of samples collected from the bottom all along the reaction and double checked with the material balance for isopropanol, assuming that the only equation taking place in the system is the esterification.

The column was charged from the beginning with reactants and catalyst in the bottom flask, and the heating was progressive; the column was operated at reflux ratio $R=2$. The temperature in the bottom at the beginning of the distillation process varied with the molar ratio of reactants between 85-90°C, and then slightly increased during the experiment to max. 128°C, as the isopropanol and the water were removed at the top. Because the reactive distillation implies the combined effects of the reaction and separation by distillation, it is important to know the operating zones of a reactive distillation column (the zone controlled by reaction and the fractioning zone) and to understand how the column behaves under the influence of the process variables. In literature, a large variety of data is presented for the analysis, design and optimization of models in reactive distillation systems [16]. In esterification with distillation, the design and operation variables (the factors) relevant for replication, are:

- the molar ratio of the reactants;
- the number of theoretical plates;
- the concentration of catalyst in the reaction mass.

In order to establish the optimal conditions of the process, a factorial experiment 2³ was conceived, where these three factors vary on two levels (inferior and superior). The factors, the range and the units of variability for each factor are shown in table 1.

In table 2, the experimental conditions are shown for each of the 8 programmed observations.

Factor	U.M.	Factor code	Central point x_{j0}	Variability unit Δx_j	Factor values at two levels	
					Inferior -	Superior +
Molar ratio <i>Isopropanol:Lactic acid</i>	-	x_1	2:1	1	1:1	3:1
Number of theoretical plate	-	x_2	2.4	0.5	1.9	2.9
Catalyst concentration	%wt	x_3	4	1	3	5

Table 1
THE FACTORS AND THEIR LEVELS IN THE EXPERIMENT OF ESTERIFICATION

Table 2
EXPERIMENTAL ARRAY

Experiment code	Coded value of x_1 factor	Coded value of x_2 factor	Coded value of x_3 factor
0.	-	-	-
1.	+	-	-
2.	-	+	-
1.2.	+	+	-
3.	-	-	+
1.3.	+	-	+
2.3.	-	+	+
1.2.3.	+	+	+

Results and discussions

The experimental results presented in table 3 show that all three factors (*the molar ratio of the reactants, the number of theoretical plates and the concentration of catalyst in the reaction mass*) exert an influence on the conversion of lactic acid. The tendency is the increasing of conversion with the increase of each factor values. Also, it was observed that the coupling of the reaction with distillation can lead to conversions up to 63.6%, superior to those obtained in the simple chemical process: max. 51% reported in [16], or max. 42%, reported in [12].

Table 3
EXPERIMENTAL RESULTS

Run	Experiment code	Lactic acid conversion, %
1	0.	27.8
2	1.	50.2
3	2.	39
4	1.2.	62.3
5	3.	29
6	1.3.	54.1
7	2.3.	41.5
8	1.2.3.	63.6

The experimental results suggest that the dependency of the lactic acid conversion on the operation variable can be described by a first order polynomial equation, since the conversion increases monotone with their values. So, the linear mathematical model predicting the lactic acid conversion in esterification with isopropanol is eq.1:

$$y = A_0 + A_1x_1 + A_2x_2 + A_3x_3 \quad (1)$$

where:

y is the conversion of lactic acid, %wt; x_1 - the molar ratio of the reactants, mol/mol; x_2 - the number of theoretical plates; x_3 - the catalyst concentration, %wt; $A_0 \div A_3$ - the regression coefficients.

The coefficients $A_0 \div A_3$ were calculated by linear regression and statistically processed with *Data analysis* facility of Microsoft Excel.

The particular equation resulted from the regression (eq.2):

$$y = 6.024 + 3.653 x_1 + 11.613 x_2 + 1.113 x_3 \quad (2)$$

The magnitude of coefficients in eq. 2 shows the relative influence of each factor controlling the process. $A_0 = 6.024$ indicates a minimum value of the conversion (%wt) in the studied range of parameters. The molar ratio of reactants x_1 and the number of theoretical plates x_2 are the important

variables of the process, because they have high coefficients: $A_1 = 3.653$ and $A_2 = 11.613$. The catalyst concentration x_3 is less important because it has the lowest value of the regression coefficient ($A_3 = 1.113$) corroborated with low concentration of acid (3%wt and 5%wt, respectively). Coefficients taking positive values confirm the experimental observations: increasing of the conversion with each studied factor.

Table 4
REGRESSION STATISTICS

Regression statistics	
Multiple R	0.9989
R ²	0.9978
Adjusted R ²	0.9962
Standard error	0.8581
Experiences	8

As seen in table 4, the regression statistics, calculated in three possible ways, gives correlation coefficients close to +1: multiple R is 0.9989, R² is 0.9978 and adjusted R² is 0.9962, proving that the model is consistent. The R²=0.9978 indicates that experimental points are very close to the regression line, so the model fits them very well. The adjusted R² shows that there are not useless variables added to the model.

The model quality was also assessed through the analysis of variance (ANOVA).

The ANOVA results are shown in table 5, and p-values are smaller than 0.05 for all the coefficients of the model, this demonstrating that all coefficients are significant at a confidence level of 95%, so the model is reliable.

Table 5
THE ANOVA RESULTS

	Coefficients	Standard Error	t Stat	P-value
Intercept	6.024	1.537	3.919	0.017
x_1	3.653	0.196	18.666	4.85E-05
x_2	11.613	0.303	38.279	2.8E-06
x_3	1.113	0.303	3.667	0.021

Comparing the experimental data for the lactic acid conversion with those predicted by the model (eq.2), the differences denoted with *residual outputs* in table 6 demonstrate an acceptable tolerance.

Altogether, the statistical analysis proved the rightness of the proposed model.

Table 6
RESIDUAL OUTPUT

Observation	$y_{predicted}$	$y_{experimental}$	Residuals
1	27.550	27.8	0.250
2	50.775	50.2	-0.575
3	38.875	39.0	0.125
4	62.100	62.3	0.200
5	29.775	29.0	-0.775
6	53.000	54.1	1.100
7	41.100	41.5	0.400
8	64.325	63.6	-0.725

Conclusions

The present study is about obtaining the isopropyl lactate, an important intermediate for drug synthesis, by esterification of the lactic acid with isopropanol in a reactive distillation system. The influence of the process factors on the lactic acid conversion was investigated, in a 2^3 factorial experiment including three factors: reactants ratio, number of theoretical plates and catalyst concentration, and two levels. The conclusions of the study was that all three factors affect the conversion in the sense of increasing conversion with increasing value of each factor. So, the maximum conversion, 63.6%, was obtained at their highest level chosen: for *isopropanol:lactic acid* molar ratio 3:1, 2.9 theoretical plates and catalyst concentration 5 %wt.

A linear mathematical model was proposed for the prediction of conversion as a function of these factors. The model coefficients were calculated by linear regression.

The model is valid for the factors varying within the following limits: *isopropanol:lactic acid* molar ratio (1:1 ÷ 3:1), number of theoretical plates in range (1.9 ÷ 2.9) and catalyst concentration (3 ÷ 5) %wt. Observing the model coefficients, one can conclude that the strongest affecting factor is the number of theoretical plates, so the choice of a reactive distillation system is right.

The model was statistically checked and the conclusion was that it is a good fitting to the experimental data and all its coefficients are significant, so the model is reliable for scaling up.

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