

# Isopropyl Lactate Obtaining by Transesterification in Reactive Distillation System

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*Transesterification is a classical organic synthesis reaction with many uses in both laboratory and industrial applications. In this reaction, one ester is converted to another by the radical alkoxy exchange. In some cases, the transesterification process is more advantageous when used in the manufacturing of esters than their synthesis by direct esterification of the carboxylic acids with alcohols. Based on literature studies, a transesterification study coupled with the reactive distillation (RD) was performed in order to obtain isopropyl lactate (IPL) by methyl lactate (ML) with isopropanol (IPA). The independent variables studied were: the alcohol/methyl lactate molar ratio (R), the number of the theoretical stages in the fractionation zone (NTS) and the reactive distillation column reflux ratio (RR). The experimental matrix was set for a 2<sup>3</sup> factorial experiment with three variables at two levels: R = 2 and 4; NTS = 1.7, respectively 2.4 and RR = 2 and 7. A linear mathematical model was proposed to correlate the methyl lactate conversion with all three variables. The model is reliable as the statistical analysis proved.*

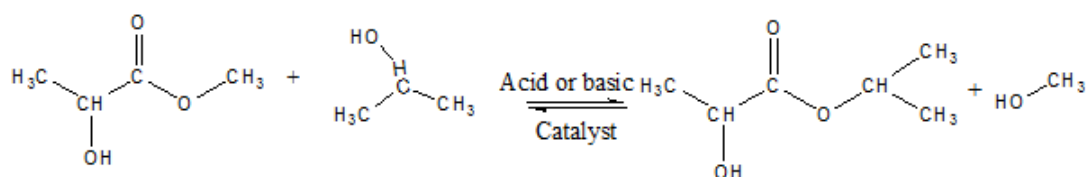
**Keywords:** reactive distillation, transesterification, isopropyl lactate, mathematical modeling

Esterification, one of classical organic syntheses, is a method for obtaining chemicals with multiple uses: solvents, odorizing agents, pharmaceutical products, etc. For example, isopropyl lactate is an ester serving as a solvent or as an intermediate in some pharmaceutical products. It is known that esters are usually obtained by the reaction between a carboxylic acid and an alcohol with removal of water [1-3]. In transesterification reactions, the carboxylic acid ester is converted to another carboxylic acid ester, in acid or base catalysis, with the use of excess alcohol. The most common method of transesterification is the reaction of an ester with an alcohol in the presence of an acid catalyst [4].

In general, lactic acid esters are synthesized by direct esterification of lactic acid with primary and secondary alcohols. For the esters of heavier alcohols, a better method of synthesis is considered the transesterification of methyl or ethyl lactates with the suitable alcohol [5].

The transesterification is a slow, balanced reaction, and therefore RD can also be applied to transesterification to improve the conversion of the reaction [6]. The transesterification has a great advantage over the direct esterification since it doesn't produce water, also being known that water introduces azeotropy in many systems, with implications on the product separation and purification.

The stoichiometry of the transesterification reaction of the methyl lactate with isopropyl alcohol is as follows:

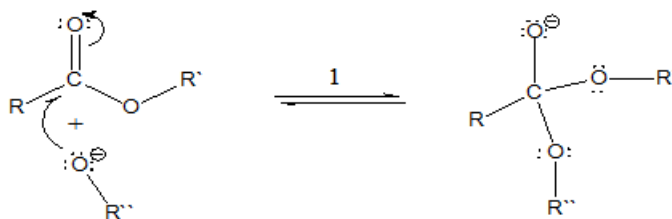


*The mechanism of the transesterification in basic background*

The reaction of transesterification in basic background in the presence of alcohol excess, takes place in two steps,

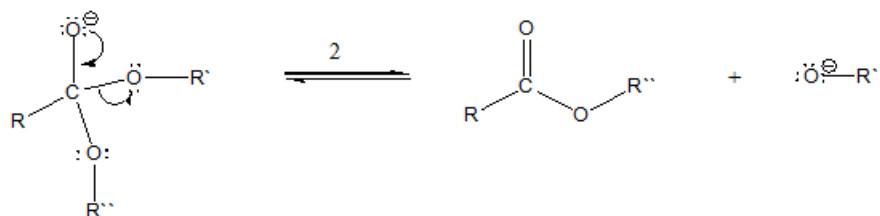
first an addition reaction, then the removal of an alkoxy group [7].

In the addition step, the nucleophilic alkoxy group attacks the ester in the tertiary carbon position.

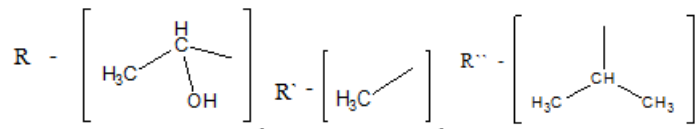


In the removal step, the alkoxy group of the initial ester is removed.

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Legend:

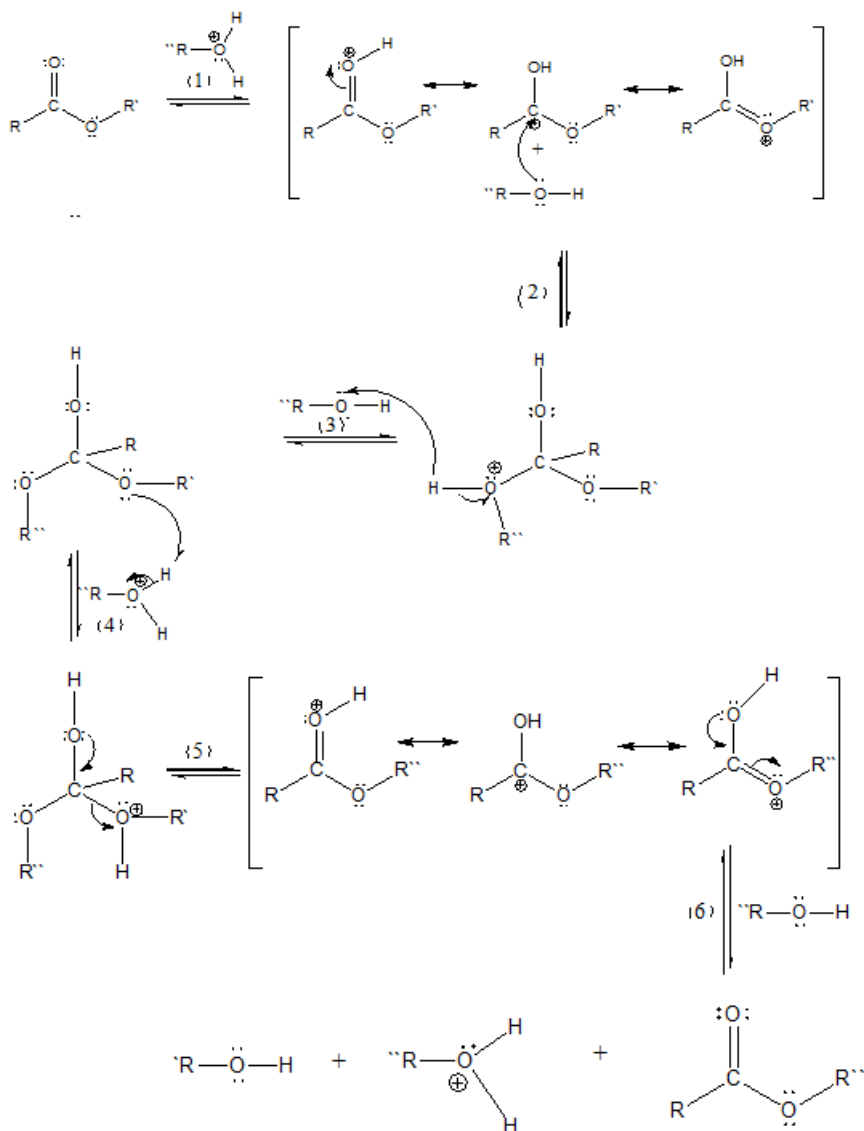


The result consists in the replacement of an alkoxy group with another alkoxy group in the ester molecule.

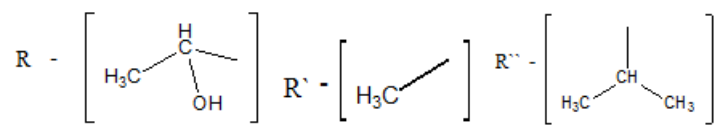
*The mechanism of the transesterification in acid background*

The mechanism of the transesterification in acid background is more complex and accomplished in more steps. In the first step, the protonation of the carbonyl group

by the acid takes place. In this way, the carbonyl group is activated for the next nucleophilic attack. Then the nucleophilic attack to the tertiary carbon atom takes place. The steps #3, #4, and #5 perform the proton transfer. Further step is the removal of the alcohol molecule which was initially located in the ester molecule. The last step is the deprotonation for obtaining the desired ester [5].



Legend:



The reactive distillation in acid background can take place in homogenous catalysis or in heterogeneous catalysis. In the homogenous catalysis procedures, the concentrated sulphuric acid is used as a catalyst while in the heterogeneous catalysis, acid polymers like cation exchange resins are used, playing a double role, as a catalyst and as packing for the distillation column.

Literature data on reactive distillation are more and more numerous lately, and research covers several aspects. Luyben and Yu [8] have proposed over the past decades new RD reaction systems including hundreds of publications and patents.

Reactive distillation (RD) is a technology with a considerable potential for industrial setting of liquid chemical reactions limited by chemical equilibrium and exothermic reactions, with a low consumption of raw materials. It is a process that combines chemical reaction with multi-component distillation in a single unit, reducing investment and operating costs. Due to the potential benefits of this technology, the study and information on the theoretical and experimental performance of the reactive distillation process is steadily increasing [9,10].

Because the reactive distillation implies combined effects of the reaction and separation by distillation, one must take into account the relevant variables for replication, in both units, for the design and operation. Therefore it is important to know the operating zones of a reactive distillation column (the zone controlled by reaction and the distillation zone) and understand the way in which the column is going to behave under the influence of the modified variables. In literature, it is presented a big variety of analysis, design and optimization models for the reactive distillation systems [11].

## Experimental part

### Method and materials

The experimental study of the methyl lactate transesterification with isopropanol in acid background consisted in:

- establishing the experimental array for transesterification reaction;
- observing the influence of independent variables on the reactive distillation results;
- proposing a mathematical model for the prediction of methyl lactate conversion into isopropyl lactate, in correlation with the process factors;
- collecting experimental data for setting-up the process flowsheet in view of process simulation

The materials for organic synthesis were methyl lactate 98.0% from Sygma Aldrich, isopropyl alcohol 99% from Chimopar Trading SRL, and concentrated sulphuric acid 98% from Chemical Company SRL.

The experimental study was performed in a laboratory installation [1] consisting of a batch distillation column with glass ring packing. At the top, the column is provided with a water cooler (20-25°C) for vapour condensation and in bottom, the mixture is progressively heated to the desired temperature with the aid of a rheostat.

The height of packing column, with the internal diameter of 20 mm, varied between 400 mm and 100 mm, corresponding to 2.4 theoretical plates and 1.7 respectively. The height equivalent to one theoretical plate (*HETP*) was 138 mm and 52 mm, respectively. The *HETP* was determined experimentally for the binary system methanol-isopropanol in range of  $x=0\div 0.5$  mole fraction.

The bottom flask was charged with the reactants and catalyst (the catalyst concentration was 3% wt in the reaction mass), and was progressively heated up to the

apparition of the reflux at the top of the column. The temperature in the bottom flask varied with the molar ratio isopropanol-methyl lactate between initial 82-91°C and increased during the experiment to a maximum of 130°C (to avoid thermal decomposition of the formed compound), as the methanol and the isopropanol were removed at the top. The separation was carried out in a batch giving a peak and a bottom fraction; the peak fraction is composed of the resulting methanol from reaction and the unreacted isopropyl alcohol; the isopropyl lactate ester together with the unreacted methyl lactate is obtained in the bottom fraction.

The temperature at the top of the column was initially 78-81°C, and the temperature rose to 84°C as the distillation continued. The reaction time (50-60 min) was long enough for reaching high conversions.

In the peak fraction, the concentration of methanol was determined by refraction index  $n_D^{20}$  with a refractometer ATAGO 3T using a calibration curve for the methanol-isopropanol binary mixture, as plotted in figure 1.

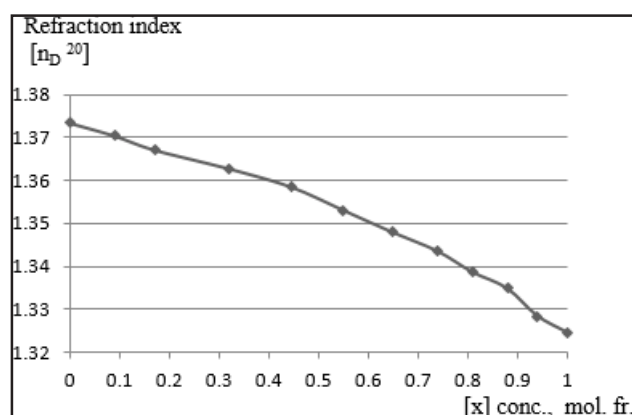


Fig. 1. Calibration curve of the methanol-isopropanol binary mixture

Depending on the methanol amount found in the peak fraction, the quantity of the reacted ester methyl lactate resulted from stoichiometric calculations and then the conversion was calculated with the relationship (1):

$$\text{conversion, \%} = \frac{\text{the amount of the reacted methyl lactate}}{\text{the amount of initial methyl lactate}} \times 100 \quad (1)$$

At first, the determinant factors were established:

- Molar ratio of reactants (alcohol: methyl lactate);
- The height of the packing in the column/ the number of theoretical plates;
- The column reflux ratio.

An important factor was considered to be the amount of catalyst, but preliminary research into esterification reactions has demonstrated that in case of homogeneous catalysis, the range of 3-5% wt of acid in the reaction mass is optimal.

In order to establish the effect of process factors, the three factors varied on two levels (minimum and maximum) so, a factorial experiment 2<sup>3</sup> was designed.

The variation levels of the reactants molar ratio were 2:1 and 4:1, for the number of theoretical plates were 1.7 and 2.4 (corresponding to 100 mm respectively 400 mm height of the packing) and for the reflux ratio 2 and 7 respectively.

The factors, the range and unit of variability for each factor are shown in table 1.

**Table 1**  
THE FACTORS VALUES AT TWO EXPERIMENTAL LEVELS

Factor	U.M.	Factor code	Central point $x_{j0}$	Variability unit $\Delta x_j$	Factor values at two levels	
					Inferior -	Superior +
Molar ratio Alcohol : Ester	-	$x_1$	3	1	2	4
The height of the packing (Number of theoretical plates)	mm (plates)	$x_2$	250 (2.1)	150	100 (1.7)	400 (2.4)
The reactive distillation column reflux ratio	-	$x_3$	4.5	2.5	2	7

The experimental array was subsequently established and it is shown in the table 2.

**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

In order to establish the optimal conditions of the reactive distillation system for the transesterification reaction in acid background with the obtaining of isopropyl lactate, the conversion of methyl lactate into isopropyl lactate was experimentally determined according to the experimental schedule in table 2. Results are shown in table 3.

Because the shape of the mathematical model is unknown from elsewhere, it can be chosen freely, and then the model must be tested. A linear model was proposed to predict the methyl lactate conversion in isopropyl lactate:

$$y = A_0 + A_1x_1 + A_2x_2 + A_3x_3 \quad (2)$$

where  $y$  - represents the methyl lactate conversion in isopropyl lactate (IPL);

$x_1$  - the molar ratio of the reactants;

$x_2$  - the number of theoretical stages in the column;

$x_3$  - the reflux ratio;

$A_0 \div A_3$  - regression coefficients.

The parameters of the mathematical model  $A_0$ ,  $A_1$ ,  $A_2$  and  $A_3$ , where determined by regression analysis with the facilities offered by Excel. The model (eq.3) resulted:

$$y = 8,727 + 7,330x_1 + 18,419x_2 + 1,084x_3 \quad (3)$$

A good linear correlation between the dependant variable  $Y$  and the independent variables  $X$  was demonstrated by the high determination coefficient  $R^2 = 0.9963$  and the small standard error of the estimation (0.8623). Also, analysis of variance (ANOVA), demonstrated that the coefficients of eq.3 are statistically significant at 95% confidence level, since  $P$ -value is smaller than 0.05 for all coefficients.

**Table 3**

EXPERIMENTAL RESULTS AT ISOPROPYL LACTATE OBTAINING BY TRANSESTERIFICATION

Experiment code	Conversion of methyl lactate, %
0.	84.2
1.	89.7
2.	75.1
1.2.	69.6
3.	71.9
1.3.	77.3
2.3.	57.2
1.2.3.	62.7

All coefficients are positive and this shows that the conversion increases with all three process factors ( $x_1$ ,  $x_2$ ,  $x_3$ ) increasing.

By applying the model, the predicted values of conversions resulted and, comparing with the experimental data, one can observe acceptable absolute errors, as seen in table 4.

**Table 4**

ERROR ANALYSIS AT DETERMINING MODEL PARAMETERS

Experiment code	$Y$ predicted	$Y$ experimental	Absolute errors
0.	84.2	85.0	0.8
1.	89.7	89.8	0.1
2.	75.1	74.3	-0.8
1.2.	69.6	69.3	-0.3
3.	71.9	71.6	-0.3
1.3.	77.3	76.7	-0.6
2.3.	57.2	57.0	-0.2
1.2.3.	62.7	63.8	1.1

The equation (3) applies in the experimental limits with a confidence of 95% but it can be extrapolated with caution beyond these limits for simulation purposes.

## Conclusions

This work was dedicated to the obtaining of isopropyl lactate in transesterification of the methyl lactate with isopropanol by reactive distillation.

The influence of the process factors was studied in the laboratory, by establishing an experimental array with three factors at two levels: molar ratio isopropanol: methyl lactate at 2:1 and 4:1, the height of the packing was

equivalent with 1.7 and 2.4 theoretical stages, respectively and the reactive distillation column reflux ratio was 2 and 7, respectively. The results showed that methyl lactate conversion increases with increasing each of three factors: the molar ratio of reactants, the number of theoretical plates and the reflux ratio. The highest conversion, 89.82%, was obtained at the molar ratio isopropanol: methyl lactate 4: 1, using a column with 2.4 theoretical stages and at a reflux ratio of 7.

A mathematical model for the prediction of the methyl lactate conversion as a function of the three factors was proposed. It is a linear correlation. The equation's coefficients were determined by regression. The quality of the correlation was proved by a good determination coefficient ( $R^2=0.9963$ ) and by the analysis of variance (ANOVA) which showed that coefficients are statistically significant at 95 % confidence level.

In correlation with these experimental data, a flow sheet of the industrial process for manufacturing of isopropyl lactate can be elaborated for transesterification in acid background under optimum conditions.

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