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Dedicated to Professor Valer Fărcăşan
at his 85th anniversary

MODELING AND SIMULATION OF PANTOLACTONE SYNTHESIS

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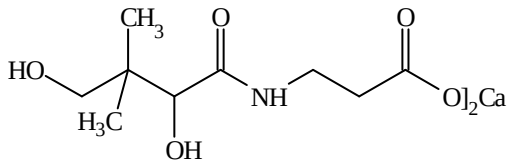
ABSTRACT. In this paper the mathematical model and the simulation for the discontinuous synthesis of racemic pantolactone (an intermediary product in the synthesis of calcium pantothenate) have been described. The chemical steps of the synthesis take place in two continuous stirred tank reactors, operated batchwise. The synthesis process consists of four reactions, which were studied. The first two reactions are highly exothermic. For a good quality of the product, the reactor temperature must be maintained between 12 – 14^{o}C. A control of reactor solution temperature was studied using PID controllers. The α,γ-dihydroxy-β,β-dimethyl-butyronitrile, obtained in the first two steps of the synthesis, is then hydrolyzed in acidic conditions in order to obtain racemic pantolactone. The mathematical model of the synthesis process was simulated using ChemCAD 5.0 software package. From the simulation results very valuable information can be obtained regarding real plant operation.

1. INTRODUCTION

Calcium pantothenate is one of the most used pro-vitamins in the therapy for the human beings and for the veterinary use. Pantothenic acid is a vitamin from the complex of vitamins B, it plays an important role in the metabolism [1, 8] (its biological active form is Coenzyme A). The chemical formula of calcium pantothenate is presented below:



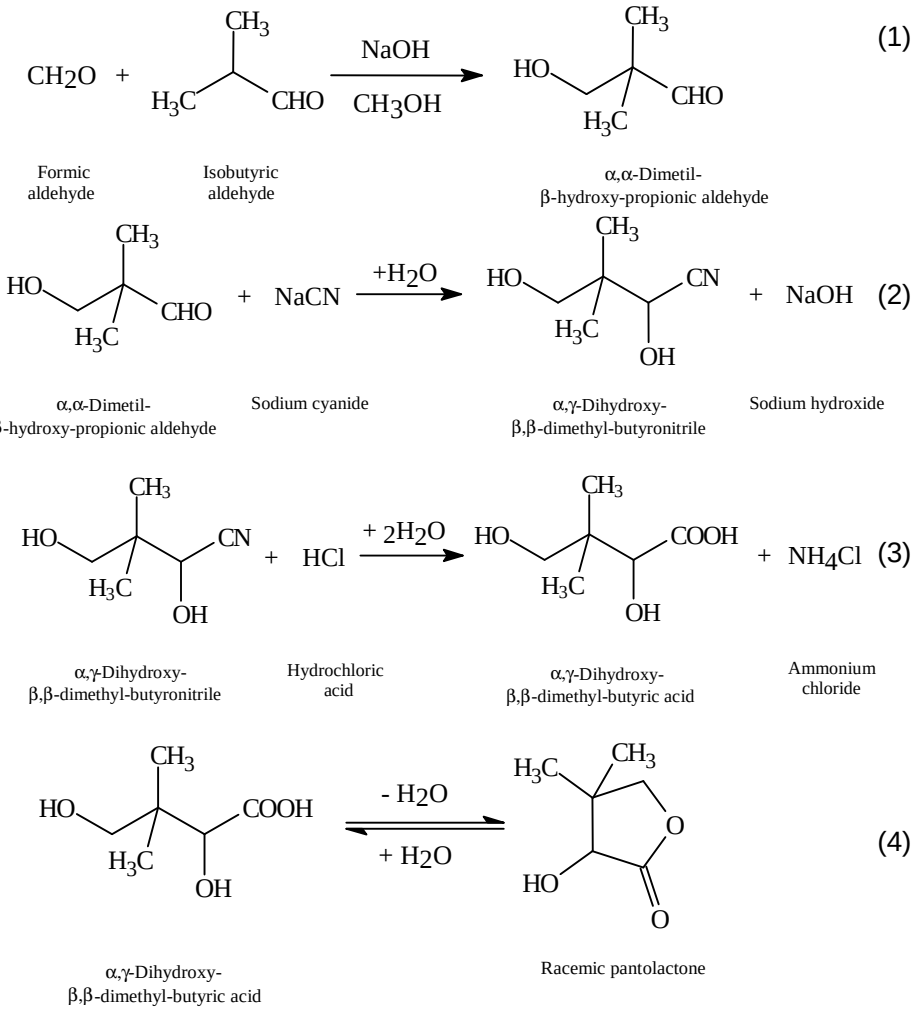
The synthesis of racemic calcium pantothenate is a complex process including chemical steps and physical separations of the intermediaries and the final product. The synthesis involves three major steps, the first step is the manufacture of pantolactone (α-hydroxy-β,β-dimethyl-γ-butyrolactone), the second step consists of the manufacture of sodium β-alaninate and in the final step of the synthesis these intermediaries are coupled resulting the final product [2].

Because the technology is very complex including a large category of operations, the mathematical models have been developed for the different steps of the synthesis. These mathematical models have been used to simulate

the process, in which purpose ChemCAD software package has been employed. The goals of modeling and simulation of these processes were to find the best operating points for the equipment, to try different control algorithms, to improve the energy consumption of the plant [5, 6, 7, 8].

In this paper the mathematical model for the discontinuous synthesis of racemic pantolactone has been described.

The chemical reactions for pantolactone synthesis are presented below [2]:



The process takes place in two CSTR (continuous stirred tank reactors), operated batchwise. First step of the synthesis consists in the preparation of a mixture containing formaldehyde and isobutyraldehyde using methanol as a

solvent. For a good control of the temperature, the reactor is equipped with an external jacket and an internal coil. As cooling agent a mixture of methanol and ethylene glycol, with a low temperature (-12^{o}C), is used. After the reactor mass temperature decreases below 12^{o}C a sodium hydroxide solution is added in the reactor. The sodium hydroxide catalyzes the first reaction between formaldehyde and isobutyraldehyde. The reaction 1 is highly exothermic (ΔH_1= - 36.45 kJ/mole). The reactor temperature must be maintained at less than 14^{o}C, for which purpose, PID controllers are used. The control of reactor temperature is achieved using the sodium hydroxide flow added into the reactor and the cooling agent flows (from the jacket and the coil of the reactor). The first reaction product is α,α-dimethyl-β-hydroxy-propionic aldehyde (oxymethyle).

After the reactor solution temperature goes below 12^{o}C, a sodium cyanide solution is added in the reactor. The reaction between α,α-dimethyl-β-hydroxy-propionic aldehyde and sodium cyanide is highly exothermic (ΔH_2= - 84.4 kJ/mole). The control of the reactor solution temperature (12 – 14^{o}C) is achieved using PID controllers, controlling sodium cyanide solution flow and cooling agent flows (from the jacket and the coil) as manipulated variables. The second reaction product is α,γ-dihydroxy-β,β-dimethyl-butyronitrile (nitrile).

The α,γ-dihydroxy-β,β-dimethyl-butyronitrile solution is then transferred in a different continuous stirred tank reactor (operated batchwise) and hydrolyzed in acidic condition in order to obtain an aqueous racemic pantolactone solution.

2. MODELING AND SIMULATION OF THE SYNTHESIS

The discontinuous synthesis of racemic pantolactone was modeled and simulated using ChemCAD 5.0 software package.

The parameters of the mathematical model for pantolactone synthesis are presented in tables 1, 2, 3 and 4 [8].

Table 1.

Synthesis reactors parameters

Characteristics	Reactor 1	Reactor 2
Reactor volume	4 m^3	6 m^3
Jacket volume	0.6 m^3	0.6 m^3
Coil volume	0.1 m^3	-
Heat transfer area (jacket)	12 m^2	15 m^2
Heat transfer area (coil)	1.5 m^2	-
Reactor diameter	1.4 m	1.8 m
Impeller diameter	0.6 m	0.8 m
Impeller speed	120 rpm	120 rpm
Motor power	6 kW	11 kW

Table 2.

Heat transfer coefficients [3]

Heat transfer coefficients	Reactor 1	Reactor 2
Cooling agent (jacket)	831 W/m^2K	800 W/m^2K
Cooling agent (coil)	1932 W/m^2K	-
Heating agent (jacket)	-	6148.8 W/m^2K

Table 3.

Kinetic and thermodynamic parameters [4, 5]

Parameters	Reaction 1	Reaction 2	Reaction 3	Reaction 4
Heat of reaction	-36.45 kJ/mole	-84.4 kJ/mole	-190.8 kJ/mole	+23 kJ/mole
Kinetic data	$k_1 C_{NaOH} C_{Isobutyraldehyde}$	$k_2 C_{NaCN} C_{Oxymethyle}$	$k_3 C_{Nitrile} C_{HCl}$	$k_4 C_{Pantoic\ acid}$
Frequency factor	10^{11} m^3/kmole · s	$2 \cdot 10^{11}$ m^3/kmole · s	10^9 m^3/kmole · s	10^{10} m^3/kmole · s
Activation energy	73.2 kJ/mole	75 kJ/mole	83.7 kJ/mole	75.3 kJ/mole

Table 4.

Control systems parameters

Parameters	Proportional band	Integral time	Derivative time
PID 1 (NaOH solution)	150	5 min.	10 min.
PID 2 (jacket cooling agent)	200	2 min.	10 min.
PID 3 (coil cooling agent)	200	2 min.	10 min.
PID 4 (NaCN solution)	150	2 min.	1 min.

The synthesis processes were modeled and simulated with ChemCAD 5.0 software package.

The main window of the application for α,α-dimethyl-β-hydroxy-propionic aldehyde (oxymethyle) synthesis is presented in the figure 1.

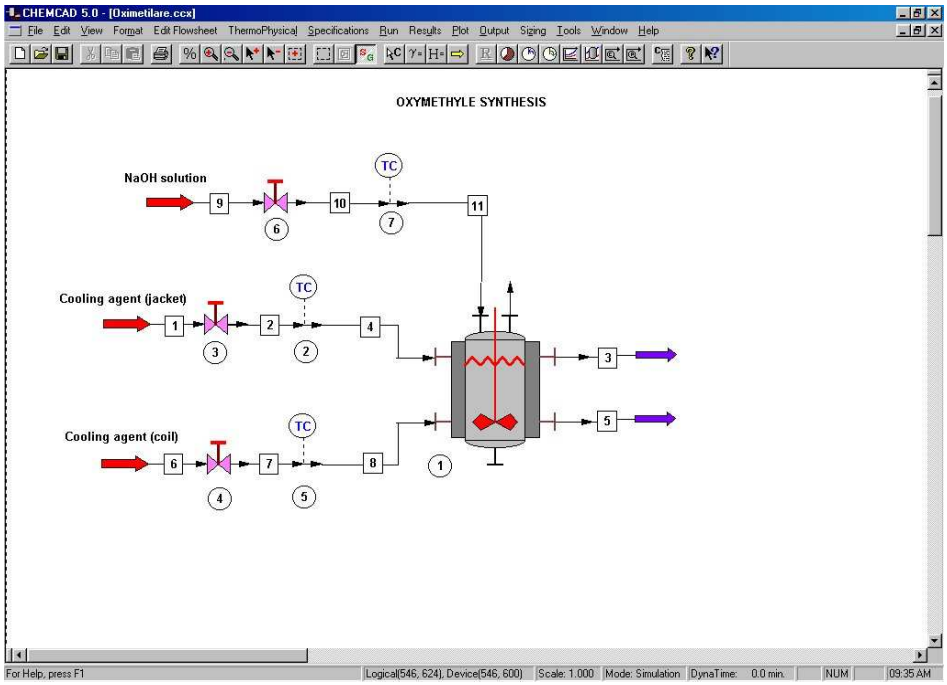


Figure 1. Simulation of α,α-dimethyl-β-hydroxy-propionic aldehyde synthesis

The main window of the application for α,γ-dihydroxy-β,β-dimethyl-butyronitrile (nitrile) synthesis is presented in the figure 2.

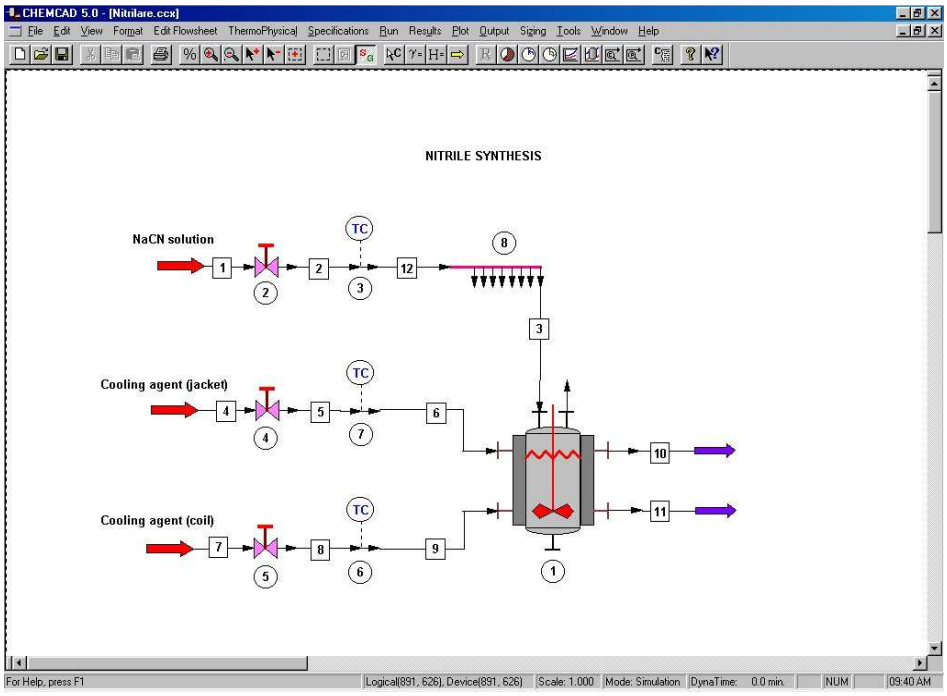


Figure 2. Simulation of α,γ-dihydroxy-β,β-dimethyl-butyronitrile synthesis

For both above applications, four PID control systems of reactor solution temperature were simulated. First temperature control system uses sodium hydroxide flow as manipulated variable. The second and third temperature control systems use jacket and coil cooling agent flows as manipulated variable. The fourth temperature control system uses sodium cyanide flow as manipulated variable.

The main window of the application for pantolactone synthesis (α,γ-dihydroxy-β,β-dimethyl-butyronitrile hydrolysis) is presented in the figure 3.

3. RESULTS AND DISCUSSIONS

The mathematical model of racemic pantolactone synthesis process was simulated using ChemCAD 5.0 software package.

The variation of the chemical species concentrations during the α,α-dimethyl-β-hydroxy-propionic aldehyde synthesis are presented in figure 4.

The variation of the temperatures (reactor mass, jacket cooling agent and coil cooling agent) during the α,α-dimethyl-β-hydroxy-propionic aldehyde (oxymethyle) synthesis are presented in figure 5.

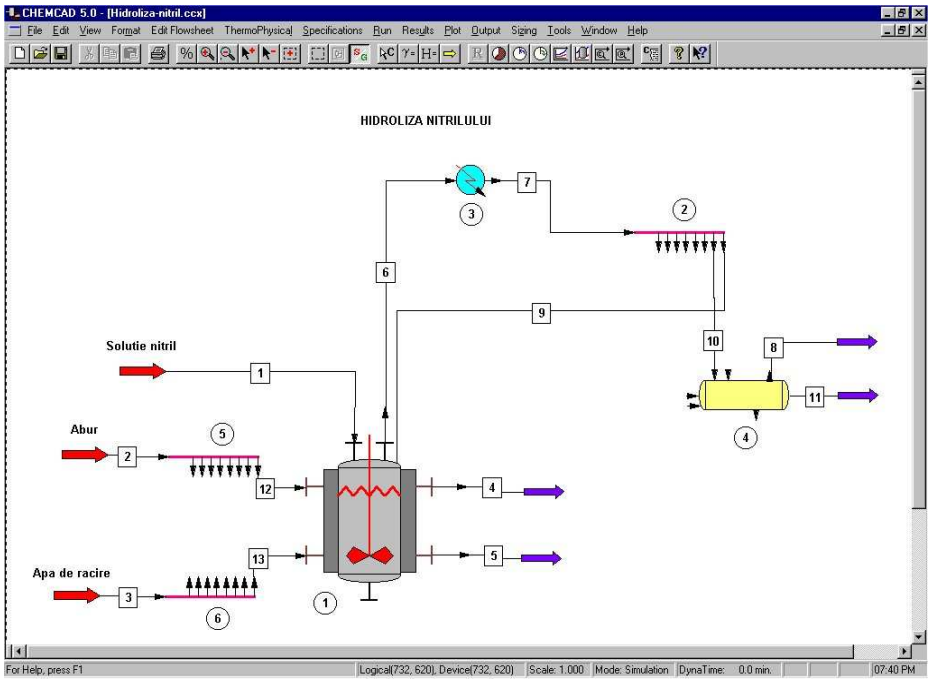


Figure 3. Simulation of racemic pantolactone synthesis

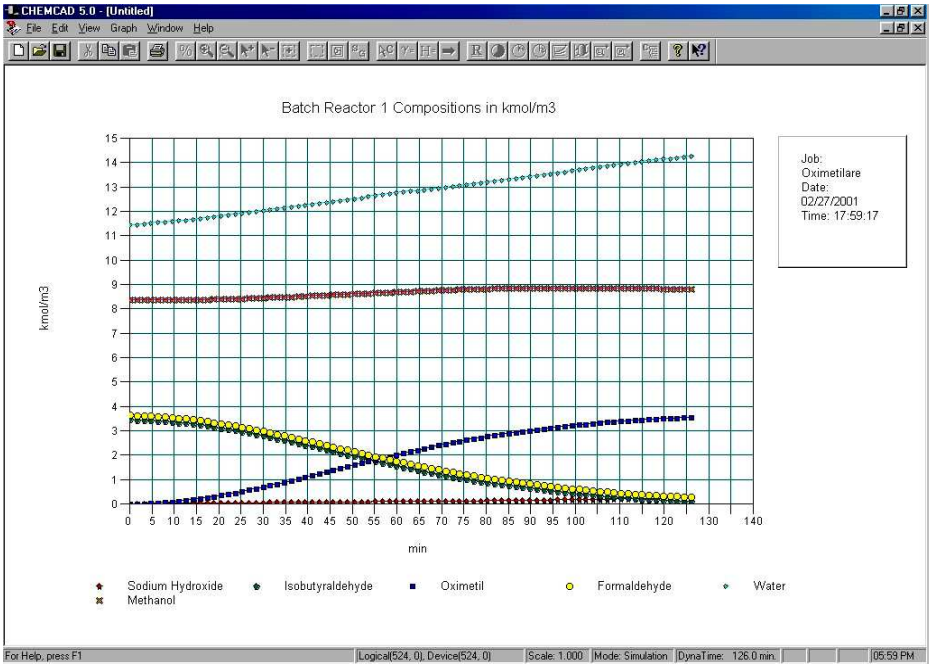


Figure 4. Variation of chemical species concentrations during the oxymethyle synthesis

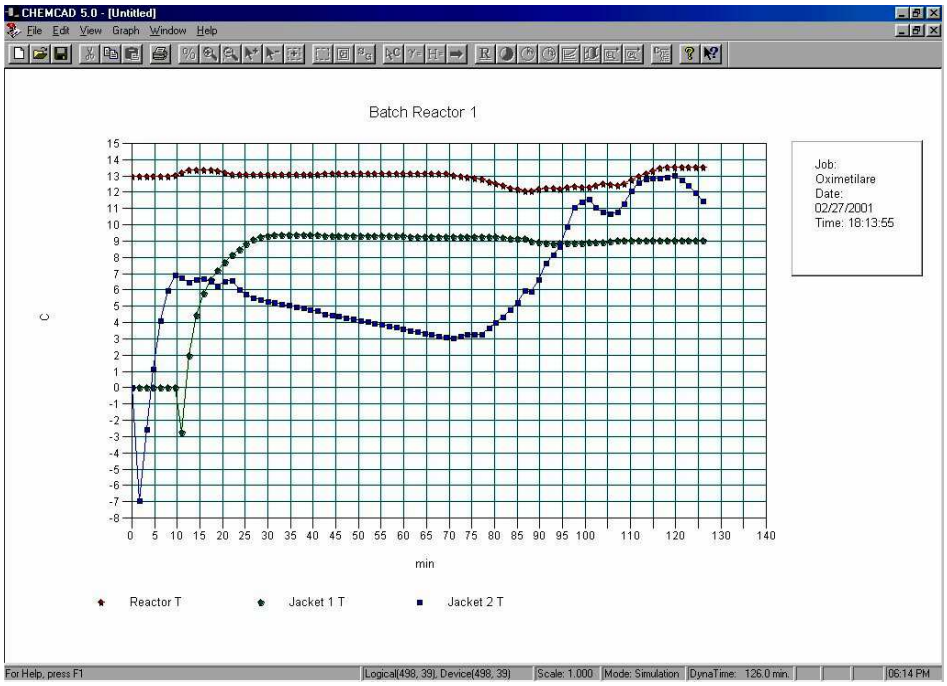


Figure 5. Variation of temperatures during the oxymethyle synthesis

The reactor mass temperature must be maintained between 12 and 14^{o}C (set point temperature 13^{o}C). If the reactor temperature exceeds 14^{o}C secondary reactions take place [2, 7]. During the α,α-dimethyl-β-hydroxy-propionic aldehyde synthesis the reactor temperature is good controlled between 12 and 14^{o}C.

The variation of the chemical species concentrations during the α,γ-dihydroxy-β,β-dimethyl-butyronitrile (nitrile) synthesis are presented in figure 6.

The variation of the temperatures (reactor mass, jacket cooling agent and coil cooling agent) during the α,γ-dihydroxy-β,β-dimethyl-butyronitrile synthesis are presented in figure 7.

From the figure 7 one can observe that the reactor solution temperature during α,γ-dihydroxy-β,β-dimethyl-butyronitrile synthesis is good controlled between 12 and 14^{o}C (set point temperature 13^{o}C).

The variation of the chemical species quantities from reactor the solution during racemic pantolactone synthesis (α,γ-dihydroxy-β,β-dimethyl-butyronitrile hydrolysis process) are presented in figures 8 and 9.

The real plant has only two PID control systems for the reactor temperature using sodium hydroxide and sodium cyanide flows as manipulated variables [2].

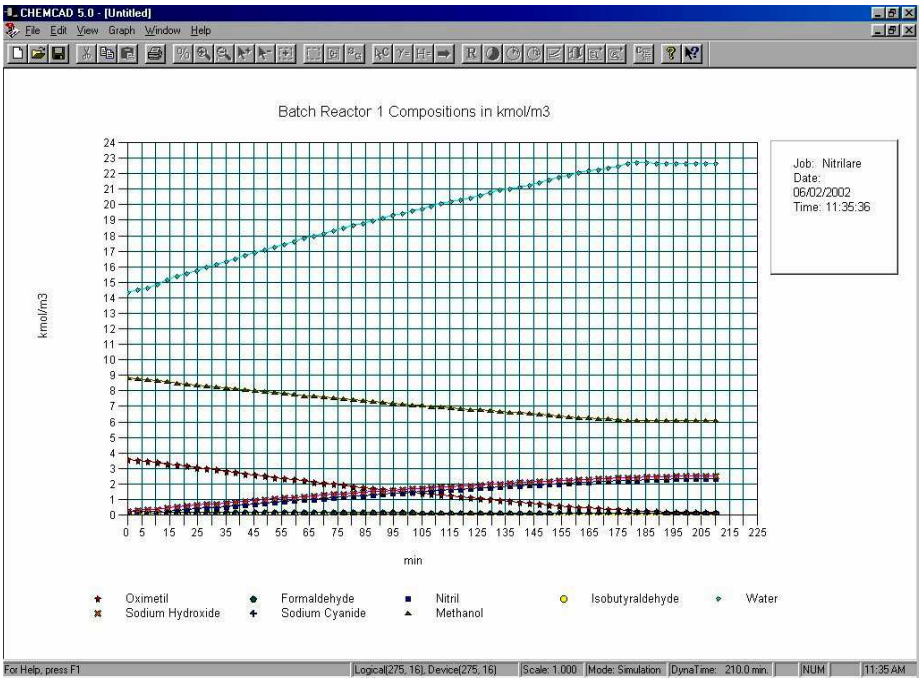


Figure 6. Variation of chemical species concentrations during the nitrile synthesis

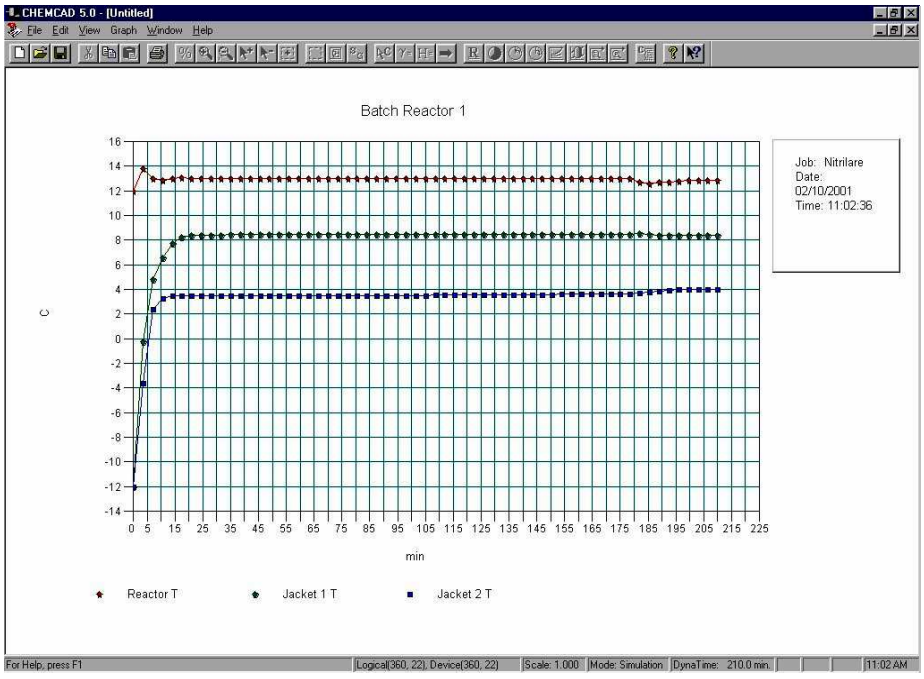


Figure 7. Variation of temperatures during the nitrile synthesis

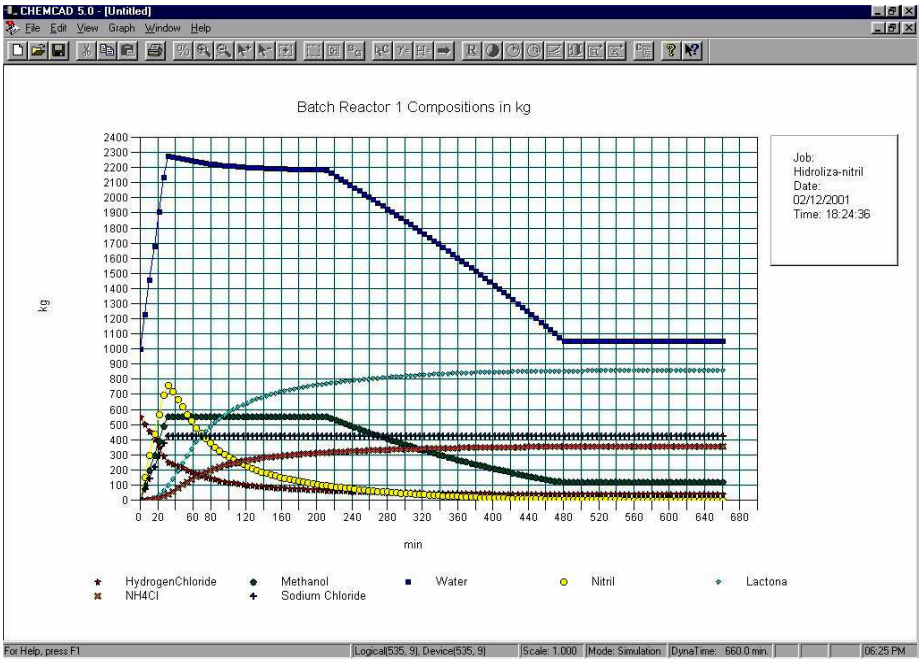


Figure 8. Variation of chemical species quantities from the synthesis reactor (1)

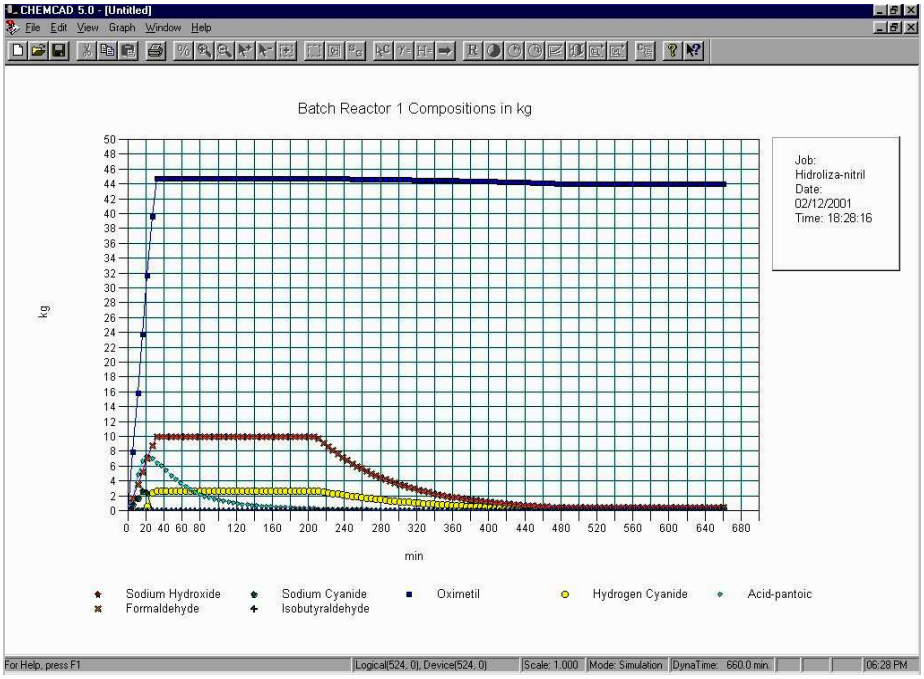


Figure 9. Variation of chemical species quantities from the synthesis reactor (2)

Comparing the simulation results obtained with two temperature control systems and the simulation results obtained using the others two control systems for reactor temperature (using the cooling agent flows), one can observe that the introduction of the supplementary temperature control systems leads to cooling agent economy (10 – 15 %). The annual cooling agent economy is $2,500.

In addition, the introduction of supplementary temperature control systems leads to a better reactor temperature control in comparison with the present situation used in practice, with benefic consequences on the quality of the product.

4. CONCLUSIONS

In this paper the discontinuous synthesis of racemic pantolactone was presented. The mathematical model of the synthesis process was simulated using ChemCAD 5.0 software package. The variations of different parameters (concentration of chemical species, reactor solution temperature, cooling and heating agent temperature) during the synthesis were presented.

The model proved to be a reliable tool for analyzing pantolactone synthesis process. Using the model of the synthesis process and the simulation results (for different operational conditions) very valuable information can be obtained for the real plant operation (temperature control improvement, reduction of cooling agent consumption, investigation of different control strategies etc.).

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