



**HAL**  
open science

## **Stoichio-kinetic modeling and optimization of chemical synthesis: Application to the aldolic condensation of furfural on acetone**

Nadim Fakhfakh, Patrick Cognet, Michel Cabassud, Yolande Peres-Lucchese,  
Manuel Dias de Los Rios

► **To cite this version:**

Nadim Fakhfakh, Patrick Cognet, Michel Cabassud, Yolande Peres-Lucchese, Manuel Dias de Los Rios. Stoichio-kinetic modeling and optimization of chemical synthesis: Application to the aldolic condensation of furfural on acetone. *Chemical Engineering and Processing: Process Intensification*, 2008, 4 (3), pp.349-362. 10.1016/j.cep.2007.01.015 . hal-03580574

**HAL Id: hal-03580574**

**<https://hal.science/hal-03580574v1>**

Submitted on 18 Feb 2022

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

# Stoichio-kinetic modeling and optimization of chemical synthesis: Application to the aldolic condensation of furfural on acetone

Nadim Fakhfakh<sup>a</sup>, Patrick Cagnet<sup>a,\*</sup>, Michel Cabassud<sup>a</sup>,  
Yolande Lucchese<sup>a</sup>, Manuel Días de Los Ríos<sup>b</sup>

<sup>a</sup> *Laboratoire de Génie Chimique, UMR 5503 CNRS, INPT (ENSIIACET), UPS, 5 rue Paulin Talabot, BP 1301, 31106 Toulouse Cedex 1, France*

<sup>b</sup> *Cuban Research Institute for Sugar Cane Byproducts (ICIDCA), P.O. Box 4026, Havana City, Cuba*

---

## Abstract

The condensation reaction of furfural (F) on acetone (Ac) gives a high added value product, the 4-(2-furyl)-3-buten-2-one (FAc), used as aroma in alcohol free drinks, ice, candies, gelatines and other products of current life. This synthesis valorises the residues of sugar cane treatment since furfural is obtained by hydrolysis of sugar cane bagasse followed by vapor training extraction. In the face of numerous and complex reactions involved in this synthesis, it is very complicated to define the kinetic laws from exact stoichiometry. A solution allowing to cope the problem consists in identifying an appropriate stoichiometric model. It does not attempt to represent exactly all the reaction mechanisms, but proposes a mathematical support to integrate available knowledge on the transformation. The aim of this work is the determination of stoichiometric and kinetic models of the condensation reaction of furfural on acetone. Concentrations of reagents and products are determined by gas and liquid chromatography. Concentration profiles obtained at different temperatures are used to identify kinetic parameters. The model is then used for the optimization of the production of FAc. The interest of such tool is also shown for the scale up of laboratory reactor to a large scale. The anticipation of the reaction behaviour in large scale is crucial especially when the reactor presents important limitations of thermal exchange capacity.

*Keywords:* Furfural; Acetone; Chromatography; Aldolic condensation; Batch reactor; Stoichio-kinetic modeling

---

## 1. Introduction

Chemical industries of industrialized countries turn increasingly to products with high added value, especially in the sector of fine chemistry (pharmaceutical products, cosmetics, etc.). This type of industry [1–3] is different from traditional chemical industry. The fine chemical industry like in France is well known to be a strategic area which needs a lot of investments not only financial but in high level scientific knowledge for the R&D. The syntheses of such products are generally complex and involve secondary reactions which are to be minimized.

In this field, the faster development of processes is essential in order to answer the rapid evolutions of the market. The detailed studies of the mechanisms and kinetics of reactions are generally not carried out for reasons of duration and cost. Nevertheless, for optimization and advanced control of processes

of fine chemistry, it is necessary to obtain a reliable model of the system. This problem is often circumvented by the use of linear or quadratic polynomial models which parameters can quickly be identified by the installation of experimental planning [4]. Nevertheless, these models rapidly find their limits in a restricted field of validity and a difficulty of accounting for the dynamics of the syntheses.

Since fine chemical reactions are usually complex, their kinetics are poorly known. The real problem is the fast development of realistic and safety stoichio-kinetic models of the synthesis [5–8]. However, due to high purity requirements, environmental regulation and competitive pressure on the new products, the development of dynamic models has become an important objective.

The approach proposed does not depend on a detailed and predictive model of the process and at the same time it does not ignore what we already know about the process, such as material balances, heat and mass transfer characteristics, etc. Nevertheless, a stoichiometric model should describe the different stages of the synthesis, or the most important tendencies. It

---

\* Corresponding author. Tel.: +33 5 34 61 52 60; fax: +33 5 34 61 52 53.  
E-mail address: Patrick.Cagnet@ensiacet.fr (P. Cagnet).

can be obtained by creating pseudo-reaction (roundup of several reactions) or pseudo-compound (roundup of several compounds or addition of losses) [5]. The identified model can be used to calculate the kinetic of the different reactions determining thus the rate of the chemical transformation. This technique has been used with success by several researchers [9–15] for the modeling of chemical syntheses like the epoxidation of oleic acid [14], or the polymerization of acrylonitrile-styrene [10] carried out in batch reactors.

In several cases, the optimization problems of discontinuous reactor are formulated with two kinds of objectives: maximum conversion problem, the operative time is fixed a priori, or minimum time problem, the conversion rate of wished product is fixed a priori.

Garcia et al. [16] considered the first case. They converted the problem of optimal control into a non-linear problem solved by a reduced gradient algorithm (GRG) coupled with the golden search method. This tool allows to optimize simultaneously different variables (temperature, feed flow rate and amount of reactant, operation time, etc.) and to take into account bounds and linear and/or non-linear constraints on the variables. The use of constraints allows to reach a solution which is not only a numerical solution but which is closer to the experimental reality.

Aziz and Mujtaba [17] are interested to the consecutive reaction optimization in batch reactors. The optimization problems are formulated with environmental and operational constraints and solved by the control vector parameterisation (CVP) technique. Two different models are presented: a shortcut model, consisting of only mass balance and reaction kinetics, allows determination of the optimal reactor temperature profiles to achieve a desired performance. The optimal temperature profiles can then be used as a basis for the detailed design of the reactor (i.e. reactor volume, heating/cooling configuration, etc.). The detailed model, consisting of mass and energy balances, reaction kinetics and cooling/heating configuration, allows determination of the best operating conditions of already designed reactors.

In this work, the methodology is illustrated through its application to a complex chemical transformation: aldolic condensation of furfural (F) on acetone (Ac), which allows mainly two products noted (FAc) and (F<sub>2</sub>Ac) to be obtained. This synthesis valorises the residues of sugar cane treatment since furfural is obtained by hydrolysis of the sugar cane bagasse then extracted by vapor training. The (FAc) is used as aroma in several types of food industries. The study of this synthesis has been made with the collaboration of Cuban Research Institute for Sugar Byproducts (ICIDCA).

## 2. Theoretical part

### 2.1. Identification of a stoichiometric model

The stoichiometry of chemical transformation determines the proportions according to which the different constituents react or are formed. In general, these proportions are integer or semi-integer.

The stoichiometry of a reaction system involving NC species  $A_j$  ( $j = 1, \text{NC}$ ) and NR reactions  $R_i$  ( $i = 1, \text{NR}$ ), can be written:

$$\sum_{j=1}^{\text{NC}} v_{ij} A_j = 0 \quad (1)$$

where  $v_{ij}$  is the stoichiometric coefficient of  $A_j$  in the reaction  $R_i$ .

- If  $v_{ij} > 0$  then  $A_j$  is a product in the reaction  $i$ ;
- If  $v_{ij} < 0$  then  $A_j$  is a reactant in the reaction  $i$ ;
- If  $v_{ij} = 0$  then  $A_j$  is not involved in the reaction  $i$ .

For a batch reactor and a data base of NE experiments ( $k = 1, \text{NE}$ ), the mole number of the compound  $A_j$  in the chemical transformation, represented by several reactions  $R_i$ , is given by

$$n_{jk} = n_{jk}^0 + n^0 \sum_{i=1}^{\text{NR}} v_{ij} X_{ik} \quad (2)$$

where  $n_{jk}$  is the mole number of  $A_j$  in the experiment  $k$  at the instant  $t$ ,  $n_{jk}^0$  the initial mole number of  $A_j$  in the experiment  $k$ ,  $X_{ik}$  the extent of the reaction  $R_i$  in the experiment  $k$ , and  $n^0$  is the normalizing factor equal to the sum of the initial reactants mole numbers.

$$n^0 = \sum_{j=1}^{\text{NC}} n_{jk}^0, \quad k = 1, \text{NE} \quad (3)$$

For simplification reasons we note:

$$Y_{jk} = y_{jk} - y_{jk}^0 = \frac{n_{jk} - n_{jk}^0}{n^0} \quad (4)$$

Eq. (2) becomes:

$$Y_{jk} = \sum_{i=1}^{\text{NR}} v_{ij} X_{ik} \quad (5)$$

The equation system representing the whole set of equations can be put under the following matrix form:

$$[Y_{jk}] = [v_{ij}]^T [X_{ik}] \quad (6)$$

Or more simply:

$$Y = v^T X \quad (7)$$

Several techniques have been developed [5] allowing the identification of the stoichiometry of chemical syntheses. The first method proceeds with iterative way by constructing reaction by reaction a more and more complex system to improve the representativeness of the studied synthesis. The second method treats the problem in a more global manner and determines a stoichiometric matrix in only one stage: it is the singular values decomposition (SVD) method [18,19]. An approach called “target factor analysis” (TFA) [20] enables to know whether a postulated stoichiometry from a priori information is compatible with the abstract factors.

## 2.2. Identification of kinetic model

The molar balance for a reactor operating in batch or semi-batch mode gives:

$$\frac{dn_j}{dt} = Fe_j + R_j V_r \quad (8)$$

with  $n_j$  is the mole number of  $A_j$  at instant  $t$ ,  $Fe_j$  the feed rate of the compound  $A_j$  ( $j = 1, NC$ ), and  $V_r$  is the reactor volume and

$$R_j = \sum_{i=1}^{NR} v_{ij} r_i \quad (9)$$

$R_j$  is the production rate if it is positive and consumption rate if it is negative and  $r_i$  is the rate of reaction  $i$ .

Eq. (8) may be written with extent of reaction, we obtain:

$$\frac{dX_i}{dt} = \frac{V_r}{n^0} r_i \quad (10)$$

In this work, the transformation is supposed to be a pseudo-homogeneous one and the kinetic law is written as a classical Arrhenius's law. It is important to emphasize that the form of the kinetic law and its degree of complexity depend on the user and the desired accuracy of the tendency model.

So, we have

$$r_i = k_i^0 e^{-E_{a_i}/RT} \prod_{j=1}^{NC} C_j^{a_{ij}} \quad (11)$$

where  $k_i^0$  is the pre-exponential factor for reaction  $i$ ,  $E_{a_i}$  the activation energy for reaction  $i$ ,  $C_j$  the concentration of constituent  $j$ , and  $a_{ij}$  is the order of constituent  $j$  in the reaction  $i$ .

According to (11), Eq. (10) may be written:

$$\frac{dX_i}{dt} = \frac{V_r}{n^0} k_i^0 e^{-E_{a_i}/RT} \prod_{j=1}^{NC} C_j^{a_{ij}} \quad (12)$$

The orders are assumed to be part of the data of the problem and are chosen a priori to be equal to the absolute value of the stoichiometric coefficients of every reactant. The identification of kinetic parameters (pre-exponential factor, activation energy) is determined by minimizing the difference between the experimental concentrations and those computed with the identified parameters for the different constituents according to the following criterion:

$$J = \sum_{k=1}^{NE} \sum_{j=1}^{NC} \frac{C_{0j}^0}{C_{1k}^0} (C_{jk}^f \text{id} - C_{jk}^f \text{exp})^2 \quad (13)$$

with

$$C_0^0 = \sum_{k=1}^{NE} C_{1k}^0 \quad (14)$$

and  $C_{1k}^0$  is the concentration of a key reactant in experiment  $k$ .

The whole procedure has been implemented on software, Batchmod [21].

The correlation coefficient ( $r$ ) is used to measure the ‘‘goodness of fit’’. It is defined as

$$r = \frac{\sum_{i=1}^N (x_i - \bar{x})(y_i - \bar{y})}{\sqrt{\sum_{i=1}^N (x_i - \bar{x})^2} \sqrt{\sum_{i=1}^N (y_i - \bar{y})^2}} \quad (15)$$

where  $x_i$  means data points and  $y_i$  means model points.

The average of the data points ( $\bar{x}$ ) and the model points ( $\bar{y}$ ) are simply given by

$$\bar{x} = \frac{1}{N} \sum_{i=1}^N x_i \quad \text{and} \quad \bar{y} = \frac{1}{N} \sum_{i=1}^N y_i \quad (16)$$

As the model better describes the data, the correlation coefficient will approach unity. For a perfect fit, the correlation coefficient will approach  $r = 1$ .

## 2.3. Optimization of chemical synthesis

The general procedure of optimization is formulated as the following [22]:

$$\begin{aligned} \min f(x), \quad x \in \mathfrak{R}^n; \quad g_i(x) = 0, \quad i = 1, m_e; \\ g_j(x) \leq 0, \quad j = m_e + 1, m; \quad x_l \leq x \leq x_u \end{aligned} \quad (17)$$

where  $f$  is the objective function to minimize,  $g_i$  the equality constraints,  $g_j$  the inequality constraints,  $m_e$  the number of equality constraints,  $m$  the total number of constraints,  $x_l$  the low limit of  $x$  variable, and  $x_u$  is the up limit of  $x$  variable.

The goal of the problem is to minimize a function  $f$  that depends on several variables. These variables are limited and submitted to equality and inequality constraints. In general, the function  $f$  is not linear and is not given under explicit shape of variables.

The optimization of a chemical synthesis is the determination of the working conditions (temperature, feed-rate, operative time), that maximize a synthesis criterion (output, concentration, etc.) under some constraints.

The resolution of the problem requires the discretisation of temperature profiles and feed-rates into finite intervals inside the interval of operation  $[t_0, t_f]$ , where  $t_0$  represents the initial time of operation and  $t_f$  the final time of operation. The interval  $[t_0, t_f]$  is discretised into a finite number ( $n_{\text{int}}$ ) of intervals. A function is defined to represent the evolution of the control variable  $v(t)$  in every time interval:

$$v(t) = \Phi(t, z_j), \quad t \in [t_{j-1}, t_j], \quad j = 0, n_{\text{int}} \quad (18)$$

where  $t$  is the commutation time and  $z_j$  is the temperature and feed-rate values in bounds of each interval.

In order to avoid complex temperature and feed profiles,  $\Phi$  function is assimilated to a simple function:

- A linear function for the temperature:

$$v(t) = z_{j-1} + (t - t_{j-1}) \left( \frac{z_j - z_{j-1}}{t_j - t_{j-1}} \right), \quad j \in [1, n_{\text{int}}] \quad (19)$$

The last temperature of interval  $j$  is supposed to be equal to the initial temperature of interval  $j + 1$ .

- A constant function for the feed-rate:

$$v(t) = a_j, \quad j \in [1, n_{\text{int}}] \quad (20)$$

The program determines the mass flow in every interval and supposes that it remains constant in this interval. The feed-rate is thus a succession of landings. The resolution of the optimization problem returns to the determination of  $(n_{\text{int}} + 1)$  temperatures and  $n_{\text{int}}$  values of feed-rate.

This optimization method allows to scale up a chemical reaction in batch reactor with safety constraints [23,24].

#### 2.4. Energy balance—thermal flux modeling

A classical Semenov-type analysis [25] is used to describe the exothermic reaction. The rate of heat production is proportional to the reaction speed, which means it is an exponential function of temperature. It is given by Eq. (21):

$$Q_{\text{released}} = V_r \Delta H k^0 \exp\left(-\frac{E_a}{RT}\right) C_{\text{initial}} \quad (21)$$

where  $Q_{\text{released}}$  is the heat flux released by the reaction,  $V_r$  the reacting volume,  $\Delta H$  the heat of reaction,  $k^0$  the pre-exponential factor of reaction,  $E_a$  the activation energy, and  $C_{\text{initial}}$  is the initial concentration.

The thermal flux evacuated out of the reactor is expressed by Eq. (22). It is proportional to a temperature difference between reacting solution and coolant fluid, exchange area and global heat transfer coefficient. A little variation of coolant fluid temperature induces a linear variation of thermal flux evacuated from the reactor:

$$Q_{\text{evacuated}} = UA(T_{\text{cf}} - T_{\text{reactor}}) \quad (22)$$

where  $Q_{\text{evacuated}}$  is the thermal flux evacuated with jacket reactor,  $U$  the global heat transfer coefficient,  $A$  the exchange surface reactor,  $T_{\text{cf}}$  the cooling fluid temperature, and  $T_{\text{reactor}}$  is the reactor temperature.

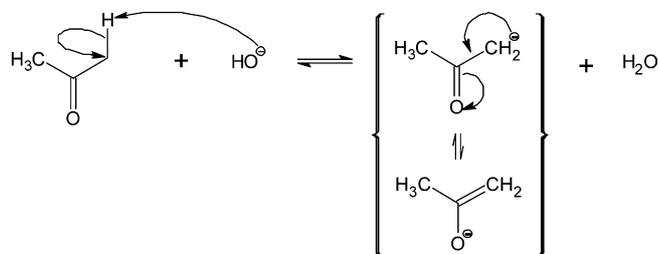
### 3. Experimental part

#### 3.1. Aldolic condensation of furfural on acetone

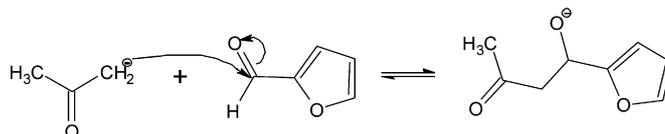
The aldolic condensation [26–29] of furfural (F) on acetone (Ac) takes place in alkaline medium. It implies the generation of a carbanion obtained from abstraction of a proton in alpha of acetone carbonyl function and leads to the 4-(2-furyl)-3-buten-2-one (FAC). Because of the symmetry of the acetone molecule, a second attack of the furfural can happen which then leads to the di-adding product, the 1,4-pentadien-3-one,1,5-di-2-furanyl (F<sub>2</sub>Ac).

The different steps for the formation of (FAC) molecule can be written:

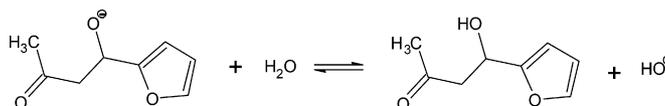
- Extraction of a proton on acetone and formation of the carbanion:



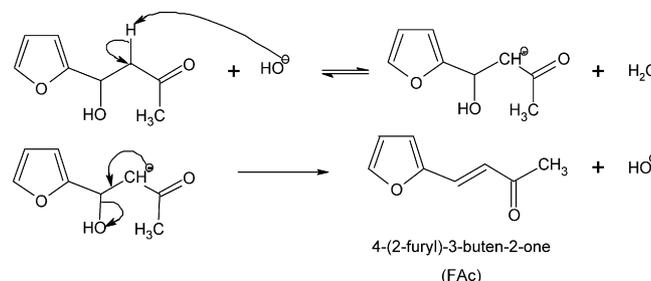
- Condensation of the carbanion on the carbon of furfural carbonyl function:



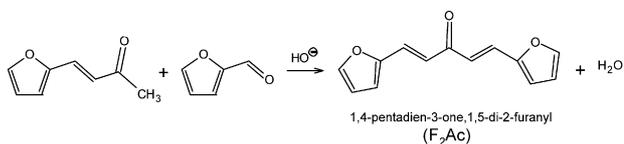
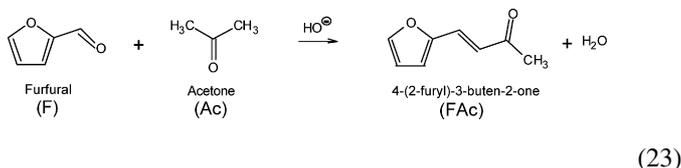
- Fixation of H<sup>+</sup> on the oxy-anion:



- Regeneration of hydroxide ion base and dehydration in basic medium:

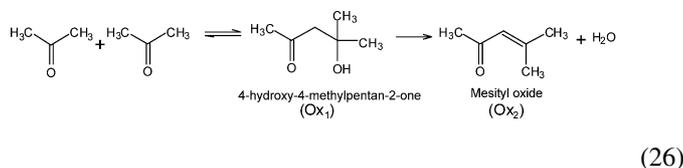
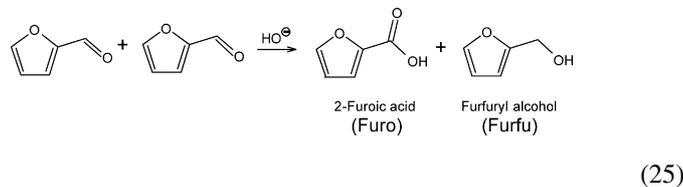


Finally, the reactions of formation of (FAC) and (F<sub>2</sub>Ac) are:



The reversibility of reactions (23) and (24) are negligible. Besides these two reactions, others may happen. Amongst the known reactions, furfural can react with itself in an oxydo-reduction reaction (Cannizzaro reaction) to give a higher

oxidation product, the 2-furoic acid (Furo), and a lower oxidation product, the furfuryl alcohol (Furfu) [30]. This reaction can take place in highly alkaline medium. On the other hand, acetone can react on itself to give the 4-hydroxy-4-methylpentan-2-one (Ox<sub>1</sub>), which after dehydration leads to the mesityl oxide (Ox<sub>2</sub>) [30].



All used chemicals have analytical grade. The 1,4-pentadien-3-one,1,5-di-2-furanyl is not commercialized, therefore, it has been prepared and purified in the laboratory.

### 3.2. Conditions of the reaction

The reactions are achieved in discontinuous mode in a jacketed glass reactor of 250 mL capacity (Fig. 1). The acetone and the furfural are charged in the reactor with equi-molar quantities. The solvent used is an equi-molar mixture of water and ethanol. The presence of ethanol in the medium favours the dissolution of FAc and F<sub>2</sub>Ac which are not soluble enough in water. An aqueous solution of sodium hydroxide (0.03 mol L<sup>-1</sup>) is injected to trigger the reaction. The temperature of the medium can be maintained constant thanks to a heating-cooling system. The reaction volume is constant and equal to 98 mL.

The initial compositions are chosen according to the suggestions of the Cuban Research Institute for Sugar Byproducts (ICIDCA). It was not varied because of industrial restrictions.

### 3.3. Analytical procedure

The concentrations of reagents and products are determined by gas and liquid chromatography. Only the acetone is measured by gas chromatography, the formed products (FAc and F<sub>2</sub>Ac) being heat-sensitives. For the two techniques, ethanol is used as an internal standard in addition to its solvent role.

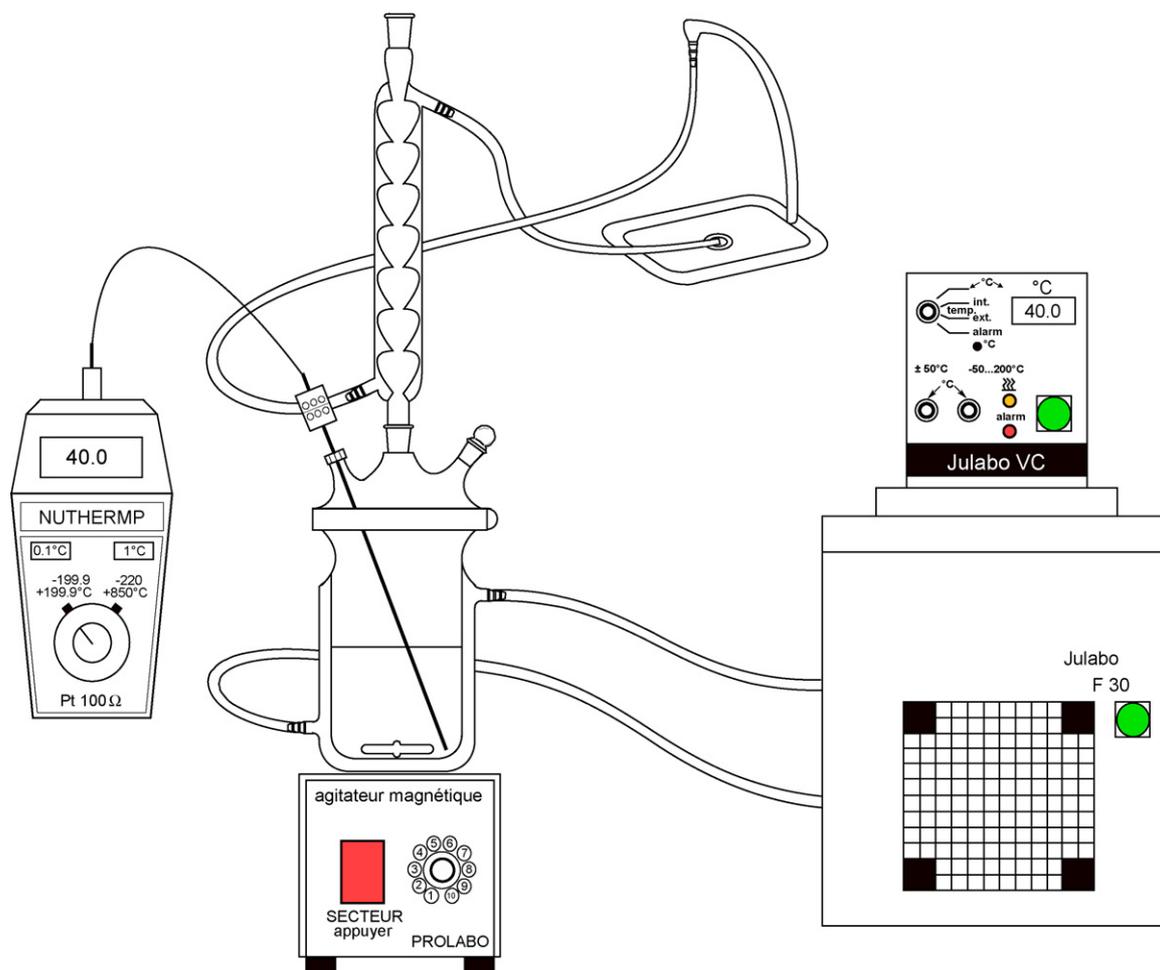


Fig. 1. Experimental equipment used for the chemical synthesis.

Table 1  
Wavelengths corresponding to a maximal UV absorption

Products	$\lambda_{\max}$ (nm)
Acetone	265
Furfural	274
FAc	322
F <sub>2</sub> Ac	382
2-Furoic acid	228
Furfuryl alcohol	220
Mesityl oxide	232
4-Hydroxy-4-methylpentan-2-one	232

For gas chromatography, the injections are realized in split mode. A flame ionization detector (FID) is used. A polar column (FFAP, 25 m × 0.32 mm i.d.) with a film thickness of 0.25  $\mu\text{m}$  separates the solvent and the matrix of components. The injector is maintained at a temperature of 250 °C. The flame ionization detector is heated until 300 °C. The initial temperature of the oven is 50 °C. After 1.5 min, the temperature increases quickly at the rate of 50 °C/min until 240 °C then it remains constant during 5 min. The total time of analysis is 10.3 min. Helium is used as the carrier-gas.

The products (F), (FAc) and (F<sub>2</sub>Ac) are measured by high performance liquid chromatography (HPLC) [31–36]. The system is equipped with UV-vis detector and an automatic injector of 25  $\mu\text{L}$  in full loop. An ODS Hypersyl C<sub>18</sub> 5  $\mu\text{m}$  column (125 mm × 4 mm i.d.) is used for the separation of the products.

Chemical compounds have different maximum UV absorption at different wavelengths. Table 1 shows the wavelength at which the maximum UV absorption is observed for the compounds of the synthesis. The use of three different wavelengths (265, 322 and 382 nm) allows to measure with precision the quantity of different compounds.

The eluent is a mixture of water and methanol. Fig. 2 summarizes the procedure of HPLC analysis adopted to follow the concentrations of the different compounds in the aldolic condensation of furfural on acetone.

## 4. Results and discussion

### 4.1. Identification of a stoichiometric matrix

Several reactions have been carried out at temperature of 24, 29, 34 and 40 °C and atmospheric pressure. The study has not exceeded 40 °C because the acetone ebullition temperature is 56 °C. The mole number variation of the compounds at 24 °C (Fig. 3) shows the disappearance of acetone and furfural and

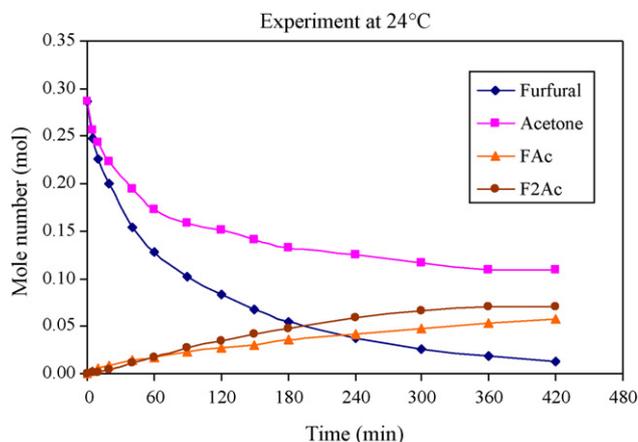


Fig. 3. Mole number evolution of the compounds at 24 °C.

the apparition of (FAc) and (F<sub>2</sub>Ac). The conversion of furfural approaches 95% while that of acetone is near 62%. The production of (F<sub>2</sub>Ac), more important than that of (FAc), explains the best conversion of the furfural. Furthermore, the analysis has not revealed the presence of either 2-furoic acid or furfuryl alcohol. Also neither (Ox<sub>1</sub>) nor (Ox<sub>2</sub>) was detected (Eq. (26)). Then suggested reactions for the synthesis are only reactions (23) and (24).

In order to verify the accuracy of the supposed stoichiometric matrix, it is necessary to verify that molar and mass balances are correct. Assuming that only reactions (23) and (24) occur, the molar balance can be written as

$$n_{\text{F}}^0 = n_{\text{F}} + n_{\text{FAc}} + 2n_{\text{F}_2\text{Ac}} \quad (27)$$

$$n_{\text{Ac}}^0 = n_{\text{Ac}} + n_{\text{FAc}} + n_{\text{F}_2\text{Ac}} \quad (28)$$

$$n_{\text{H}_2\text{O}} = n_{\text{FAc}} + 2n_{\text{F}_2\text{Ac}} \quad (29)$$

It is necessary to determine the number of moles of water formed during the synthesis to be able to establish the molar and mass balances. The formed water is not determined by chromatography but calculated according to Eq. (29). However, water present at the beginning in the medium does not appear in the balance and was taken into account in the concentration of the solvent.

The mass balance shows a deficit which increases with time and then decreases at the end of the synthesis (Fig. 4). The furfural and the acetone were more consumed than the prediction with the supposed reaction scheme. Supplementary reactions must therefore be added to the stoichiometric model. The Cannizaro reaction being rejected, the possibility of polymerization reactions was studied. The main reaction of polymerization men-

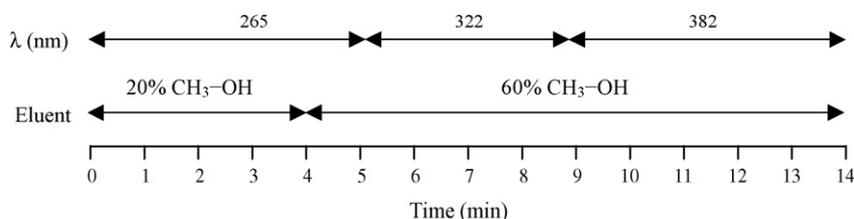


Fig. 2. Change of wavelength and eluent composition for the analysis by HPLC.

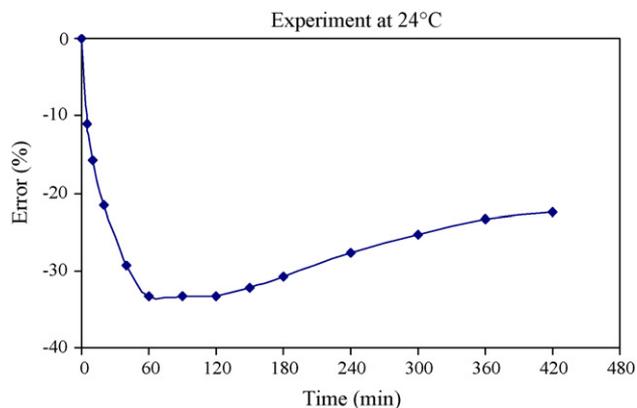


Fig. 4. Mass balance for the experiment at 24 °C ( $\text{H}_2\text{O}$  calculated from Eq. (21)).

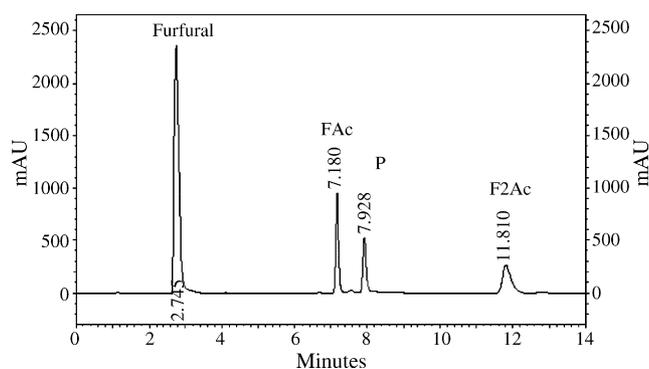


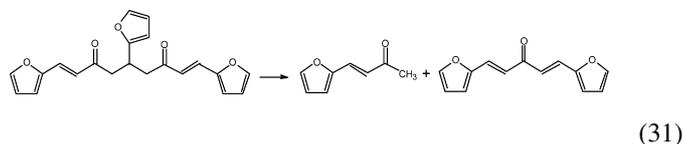
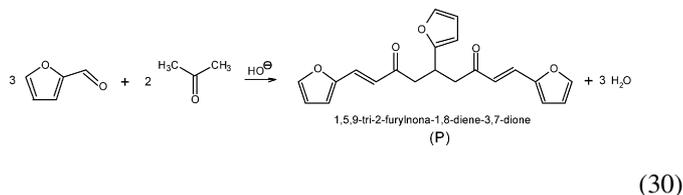
Fig. 5. Example of HPLC chromatogram (experiment at 40 °C, reaction time = 10 min).

tioned in the literature [37] is the formation of  $(\text{FAC})_n$  from the (FAC) in basic medium,  $n$  being superior or equal to 2.

In the HPLC chromatograms obtained, an unidentified peak can be noticed. It is present during the first minutes of the synthesis and then it disappears. It has a retention time near that of (FAC). The product (P) which corresponds to this peak is sensitive to the wavelength of 322 nm (Fig. 5).

To identify the product (P), we used the HPLC analysis coupled with mass spectroscopy (Fig. 6). This analysis revealed that this product has an important molar mass near  $350 \text{ g mol}^{-1}$ . The developed formula of (P) shown in Fig. 6 is one of possible formulas deduced from the fragments identified on the spectrum.

Since product (P) appears at the same time as (FAC), then it cannot be a polymer of the later. It is rather formed directly from the furfural and the acetone (Eq. (30)). This equation is only a representation and does not account for a chemical mechanism. It would then imply a five reactants encounter, which is not realistic. The product (P) disappears during the reaction, this disappearance could be represented by Eq. (31). HPLC and GC analyses has not reveal the presence of other products aside furfural, acetone FAc,  $\text{F}_2\text{Ac}$  and P, that is why the decomposition of P to FAc and  $\text{F}_2\text{Ac}$  is the most probable and not other products. Finally, it was suggested that this synthesis could be represented by the four reactions (23), (24), (30) and (31).



The molar balances associated to the reactions (23), (24), (30) and (31) become:

$$n_{\text{F}}^0 = n_{\text{F}} + n_{\text{FAC}} + 2n_{\text{F}_2\text{Ac}} + 3n_{\text{P}} \quad (32)$$

$$n_{\text{Ac}}^0 = n_{\text{Ac}} + n_{\text{FAC}} + n_{\text{F}_2\text{Ac}} + 2n_{\text{P}} \quad (33)$$

$$n_{\text{H}_2\text{O}} = n_{\text{FAC}} + 2n_{\text{F}_2\text{Ac}} + 3n_{\text{P}} \quad (34)$$

With the new reactions system proposed for the synthesis, the concentrations of (P) and water can be calculated by two ways, from the balance on acetone (Eqs. (33) and (34)), or from the balance on furfural (Eqs. (32) and (34)). The two methods have been tested and the values obtained were very close. Contrarily to the previous case (system of two reactions) the representation of the synthesis by four reactions allows to get a correct mass balance. The maximal error observed is 6.1% (Fig. 7).

The experiment carried out at temperatures of 24, 29, 34 and 40 °C allow to generate a range of input/output concentrations

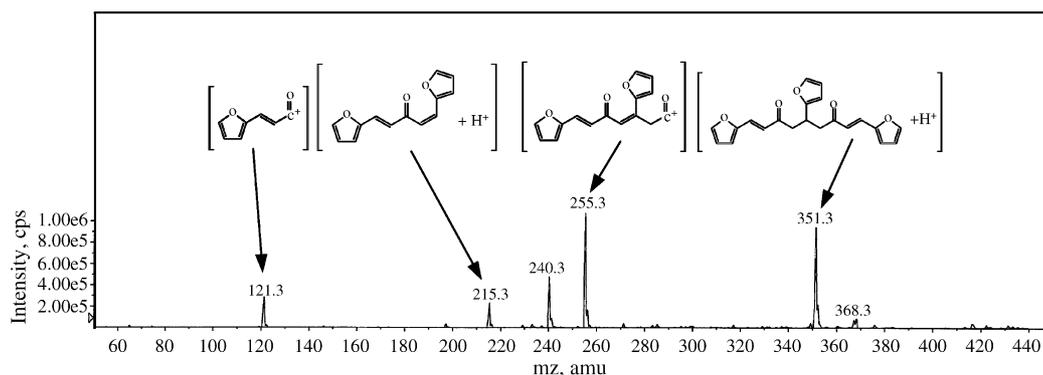


Fig. 6. Spectrum of mass spectroscopy (the peak at 240.3 amu is visible on the spectra of all analyzed samples).

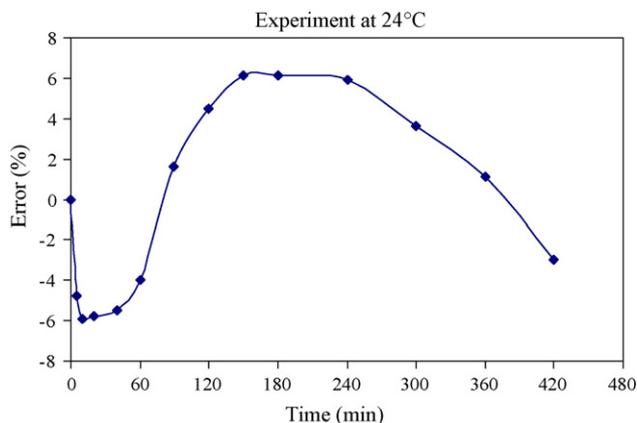


Fig. 7. Mass balance for the experiment at 24 °C (H<sub>2</sub>O calculated from Eq. (26)).

for the six components of the synthesis and therefore to feed the algorithm of calculation. The SVD method provides the following singular values:

$$(4.10217; 0.30914; 0.09268; 0.04932; 0.03277; 0.00037)$$

1            2            3            4            5

Knowing that the most important values indicate the number of necessary reactions for the description of the synthesis, it can be assumed that the chemical transformation can be described adequately by a system of four or five reactions.

According to the available knowledge about the transformation, it was postulated a stoichiometry with four reactions:

- The first reaction represents the formation of (FAC) from furfural and acetone.
- The second reaction represents the formation of (F<sub>2</sub>Ac) from (FAC) and furfural.
- The third reaction represents the formation of (P) from three moles of furfural and two moles of acetone.
- The fourth reaction represents the consumption of (P). One mole of (P) gives one mole of (FAC) and one mole of (F<sub>2</sub>Ac).

Table 2 contains the postulated stoichiometry and Table 3 contains the calculated stoichiometry. Eq. (35) allows the error between the target matrix and the calculated matrix for every reaction to be calculated:

$$\text{error}(i) = \sqrt{\frac{\sum_{j=1}^{\text{NC}} |v_{ij}^{\text{target}} - v_{ij}^{\text{calculated}}|^2}{\sum_{j=1}^{\text{NC}} |v_{ij}^{\text{target}}|^2}} \quad (35)$$

Table 2  
Target stoichiometric matrix

	F	Ac	FAC	F <sub>2</sub> Ac	P	H <sub>2</sub> O
Reaction 1	-1	-1	1	0	0	1
Reaction 2	-1	0	-1	1	0	1
Reaction 3	-3	-2	0	0	1	3
Reaction 4	0	0	1	1	-1	0

Table 3  
Calculated stoichiometric matrix

	F	Ac	FAC	F <sub>2</sub> Ac	P	H <sub>2</sub> O
Reaction 1	-0.983	-1.012	0.985	0.048	-0.017	0.980
Reaction 2	-1.037	0.043	-0.985	0.994	0.034	1.044
Reaction 3	-2.988	-2.022	-0.043	0.074	1.021	2.987
Reaction 4	-0.015	0.025	1.039	0.916	-1.034	0.016

Table 4  
Kinetic parameter values (reaction rate in mol L<sup>-1</sup> s<sup>-1</sup>)

	Activation energy, $E_a$ (J mol <sup>-1</sup> )	Pre-exponential factor, $k^0$
Reaction 1	74581.559	$3.7979 \times 10^8$
Reaction 2	35959.731	$2.2094 \times 10^2$
Reaction 3	58914.459	$4.4197 \times 10^4$
Reaction 4	117919.191	$9.5420 \times 10^{15}$

An error of 3.02% was obtained for the main reaction, 4.05% for the second reaction, 1.93% for the third reaction and 6.03% for the fourth reaction. Results show that the postulated stoichiometry is compatible with the abstract factors. The model can therefore be adopted for the identification of kinetic parameters.

#### 4.2. Determination of the kinetic parameters

The determination of the stoichiometry of the chemical transformation allows to find the proportions according to which the components react. The next step for modeling consists in identifying the kinetic parameters for each reaction. In this work, the transformation is supposed to be a pseudo-homogeneous one and the kinetic law is written as a classical Arrhenius's law. The orders of compounds are taken equal to absolute values of stoichiometric coefficients for the reactants and zero for the products. Table 4 gives the values of activation energy ( $E_a$ ) and pre-exponential factor ( $k^0$ ) identified according to Eq. (11).

The first reaction is sensitive to temperature; the production of (FAC) increases as temperature rises. The second reaction is less sensitive to temperature than the first. The third reaction which corresponds to the formation of (P) is far less activated by temperature than the fourth reaction which corresponds to the consumption of (P). The disappearance of (P) is so more rapid at 40 °C than at 24 °C.

From the kinetic parameters, the time-dependence of theoretical concentrations can be illustrated. The comparison between the time-dependence concentrations obtained from the experiment and from the model is given in Figs. 8–11. A statistical analysis is provided regarding the significance of the fitted kinetic parameters. Table 5 shows the correlation coefficients

Table 5  
Correlation coefficients

	F	Ac	FAC	F <sub>2</sub> Ac	P	H <sub>2</sub> O
Reaction at 24 °C	0.9995	0.9984	0.8915	0.9974	0.9267	0.9995
Reaction at 29 °C	0.9973	0.9986	0.9069	0.9986	0.9156	0.9973
Reaction at 34 °C	0.9953	0.9956	0.9041	0.9994	0.9051	0.9953
Reaction at 40 °C	0.9972	0.9991	0.9252	0.9970	0.9688	0.9972

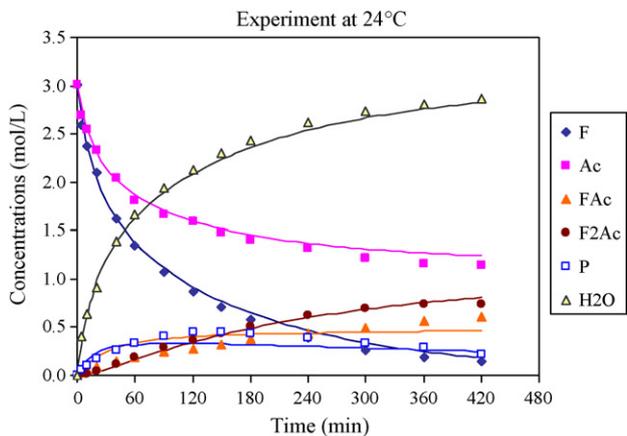


Fig. 8. Evolution of compound concentrations for the reaction at 24 °C (— model; (◆) experimental points).

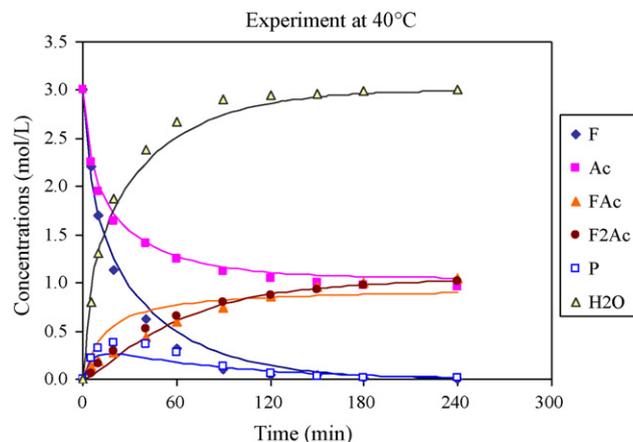


Fig. 11. Evolution of compound concentrations for the reaction at 40 °C (— model; (◆) experimental points).

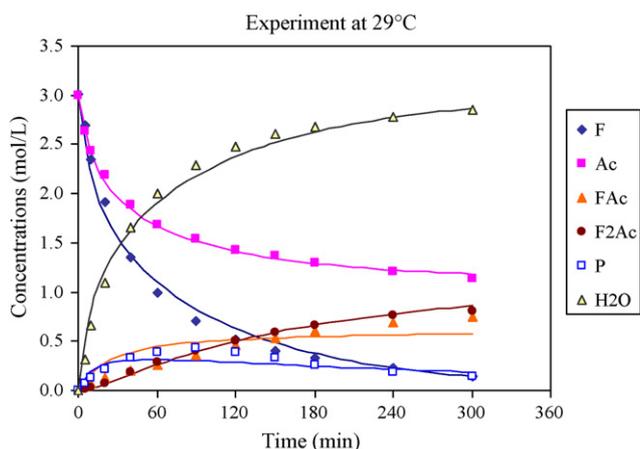


Fig. 9. Evolution of compound concentrations for the reaction at 29 °C (— model; (◆) experimental points).

obtained using Eq. (15). A good agreement was obtained between the experimental and model representation of furfural, acetone, (F<sub>2</sub>Ac) and water. However, the evolution of the compounds (FAc) and (P) is not as good. Behaviour of these intermediate components is the most difficult to predict

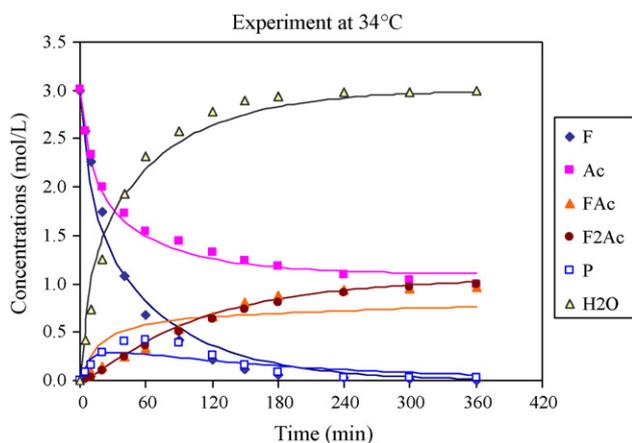


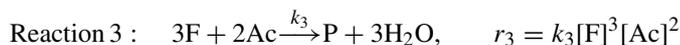
Fig. 10. Evolution of compound concentrations for the reaction at 34 °C (— model; (◆) experimental points).

because they play the role of reagents and products at the same time.

#### 4.3. Optimization of the synthesis

In the previous paragraphs, a stoichio-kinetic model of aldolic condensation of furfural on acetone has been determined. This model gives a satisfactory representation of the synthesis behaviour and can be used therefore for its optimization.

The stoichiometric matrix adopted is



##### 4.3.1. Optimization at laboratory scale

In this section, the amounts of reactants are the same as there used for experiments, corresponding to an initial concentration of 3 mol L<sup>-1</sup> for furfural and acetone in batch mode. The operation time is equal to 4 h.

The criterion to maximize is the final FAc yield, defined as the ratio between the mole number of FAc present at the end of operation, and the mole number of initial acetone loaded in the reactor (Eq. (36)):

$$\text{criterion} = \frac{\text{mole number of (FAc) at the end of operation}}{\text{mole number of initial acetone}} \quad (36)$$

The temperature domain used is

$$20^\circ\text{C} \leq \text{temperature} \leq 40^\circ\text{C}$$

The minimal and maximal temperature choice has been guided by the experimental domain that has been covered with the experimental tests. In particular, the highest temperature has been limited to 40 °C. Taking a larger domain would lead to solutions for which the validity of the model would be very

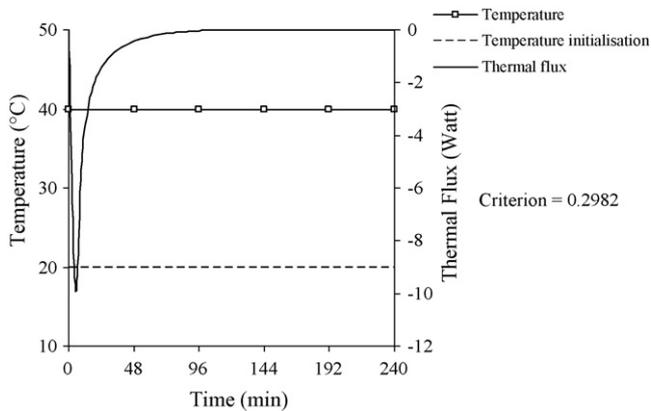


Fig. 12. Results of the simulation in discontinuous mode at laboratory scale.

uncertain. Moreover, at atmospheric pressure, the temperature is limited by 56 °C the acetone boiling point.

- Working in discontinuous mode (Batch), the best isotherm is 40 °C, the maximum thermal flux generated is equal to 10 W (Fig. 12) and FAc yield approaches 29.82%. Feeding acetone could lead to large amount of furfural together with low concentration of acetone. It would then favour F<sub>2</sub>Ac formation. It was then decided to feed furfural.

By comparing the aldolic condensation of furfural on acetone to a thermodynamic system, it is clear that this system loses energy since the synthesis is exothermic, which explains the negative values of the thermal fluxes in the different figures.

- While applying a feed-rate of  $2.2916 \times 10^{-4} \text{ kg min}^{-1}$  during 2 h and looking for the best isotherm, the optimal temperature is 40 °C, the thermal flux reaches a maximum of 1.5 W and the yield lies around 28.5% (Figs. 13 and 14). When reducing the feeding time to 1 h, the optimal temperature is always 40 °C, the thermal flux reaches 2.8 W and the chemical yield is slightly improved and becomes 28.87% (Figs. 15 and 16). By decreasing the feeding time to 30 mn, the optimal temperature does not change (40 °C), the thermal flux increases to 5.2 W. Furthermore, the obtained chemical yield is about 29.43%. This result is the nearest one compared to the discon-

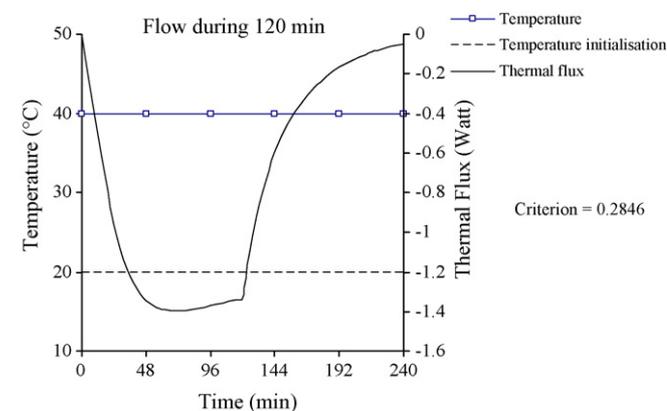


Fig. 13. Results of the simulation in semi-continuous mode at laboratory scale with a furfural feed-rate during 120 min.

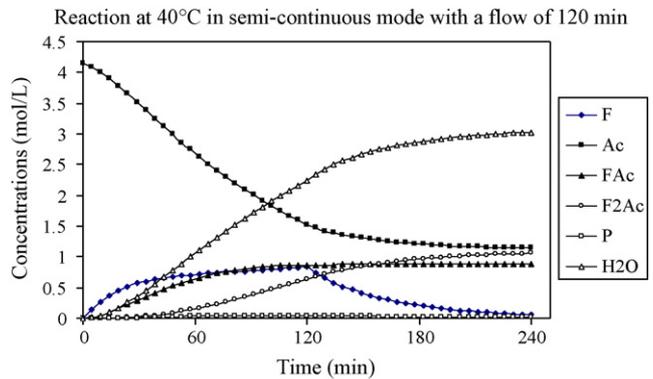


Fig. 14. Evolution of compound concentrations of the reaction at 40 °C in semi-continuous mode with a furfural feed-rate during 120 min (calculated points with smoothing).

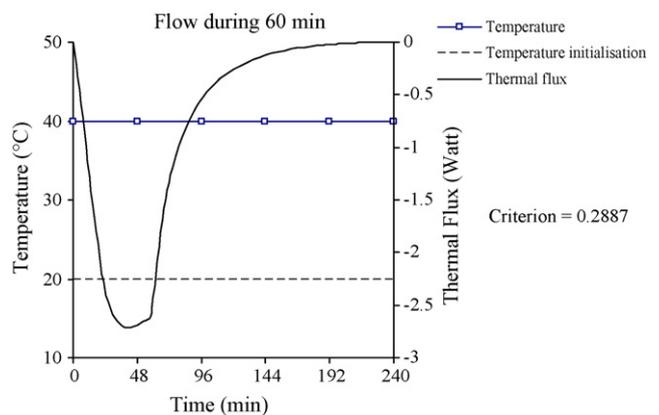


Fig. 15. Results of the simulation in semi-continuous mode at laboratory scale with a furfural feed-rate during 60 min.

tinuous mode (Figs. 17 and 18). Table 6 summarizes operative conditions obtained for the different problems treated in semi-continuous and discontinuous mode at laboratory scale.

Heat generated in batch mode can be easily removed at laboratory scale. In the opposite, it is difficult to evacuate this heat at industrial scale. The cooling capacity of discontinuous reactors (type agitated tank) is generally limited. Especially, the ratio sur-

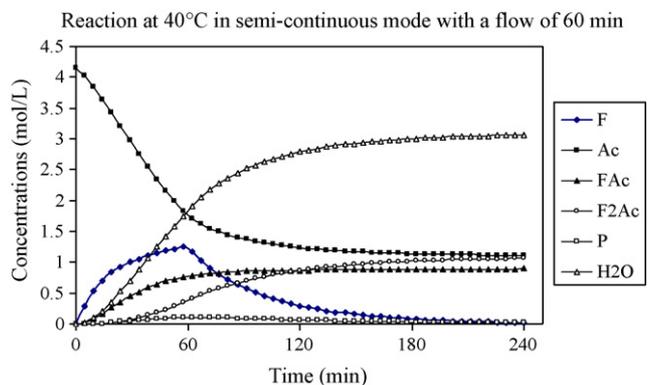


Fig. 16. Evolution of compound concentrations of the reaction at 40 °C in semi-continuous mode with a furfural feed-rate during 60 min (calculated points with smoothing).

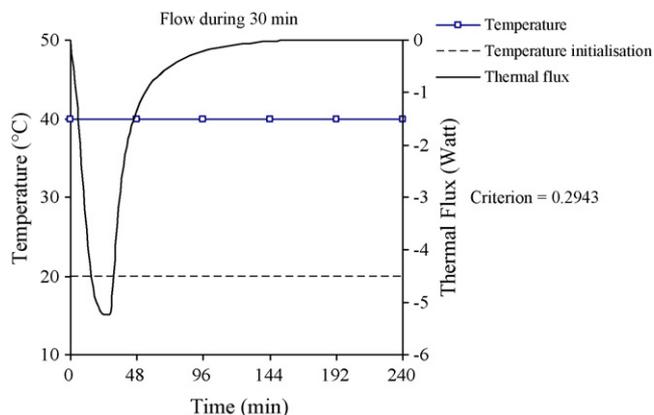


Fig. 17. Results of the simulation in semi-continuous mode at laboratory scale with a furfural feed-rate during 30 min.

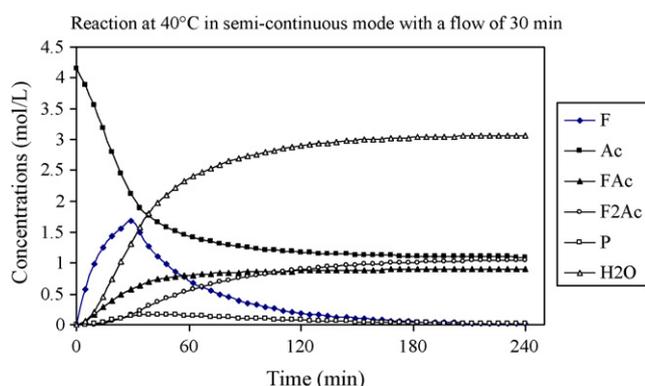


Fig. 18. Evolution of compound concentrations of the reaction at 40°C in semi-continuous mode with a furfural feed-rate during 30 min (calculated points with smoothing).

face/volume decreases when the reactor size increases and the exchange coefficients degrade especially for glass lined reactors.

#### 4.3.2. Extrapolation to industrial scale

A 3 m<sup>3</sup> industrial reactor is chosen (cylindrical shape, diameter of 1.4 m, height of 1.95 m and area of 10 m<sup>2</sup>). The amounts of reagents introduced are multiplied by 3 × 10<sup>4</sup> compared to those used at laboratory scale. The reacting volume is about 2850 l.

Reagents and solvents	
Furfural	828 kg (8.618 kmol)
Acetone	501 kg (8.626 kmol)
Ethanol	1050 L (17.990 kmol)
Water	450 L (24.934 kmol)
Sodium hydroxide	1.8 kg (0.045 kmol)

The optimal operating mode is batch, as suggested by the consecutive/competitive reaction scheme. At 40°C, the maximum thermal energy released is about 300 kW (10 W at laboratory scale). Eq. (22) is used to estimate the maximum thermal flux evacuated by the jacket of the reactor considering a global heat transfer coefficient equal to 150 W m<sup>-2</sup> K<sup>-1</sup> [38], a minimal exchange surface of 10 m<sup>2</sup> and a difference of 10°C between the cooling fluid temperature and the reaction temperature. The reactor can only evacuate 15 kW. A safety constraint becomes necessary.

Table 6

Operative conditions obtained for different problems in semi-continuous and discontinuous mode (reaction time 240 min)

Feed-rate time (min)	120	60	30	Batch
Feed-rate (kg min <sup>-1</sup> )	2.2916 × 10 <sup>-4</sup>	4.5833 × 10 <sup>-4</sup>	9.1667 × 10 <sup>-4</sup>	Batch
Temperature (°C)	40	40	40	40
Thermal flux (W)	1.4	2.7	5.2	10
Output (%)	28.46	28.87	29.43	29.82

By respecting this limit, the synthesis can be carried out in discontinuous mode at a temperature of -10.3°C. The resulting yield is 1.5% smaller than at a laboratory scale. Interest of discontinuous mode at the industrial scale is rather poor.

The problem to solve consists, firstly, to maximize the yield of FAc by working at high temperature, and secondary, to impose a safety constraint of 15 kW in order to respect the limits of the reactor cooling system, minimizing thus the thermal run-away risks. The semi-continuous mode becomes necessary.

The aim of this part is to determine a furfural feed-rate profile at 40°C, under a security constraint of 15 kW. The criterion to maximize is still the same (Eq. (36)). Research is under the following constraints:

- Limits of the feed-rate:

$$0 \text{ kg min}^{-1} \leq \text{flow} \leq 15 \text{ kg min}^{-1}$$

- Gradient of the feed-rate:

$$\left( \frac{\Delta D}{\Delta t} \right)_{\max} = \pm 2 \text{ kg min}^{-2}$$

- To introduce 828 kg of furfural in the reactor in 240 min, the necessary feed-rate is 3.45 kg min<sup>-1</sup>. With this feed-rate and the temperature of 40°C, the thermal flux reaches 21.7 kW (Figs. 19 and 20). This value is superior to the limit supported

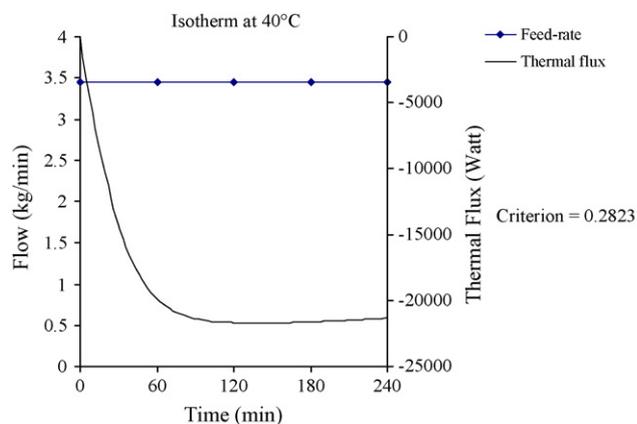


Fig. 19. Results of the simulation in semi-continuous mode at industrial scale with a furfural feed-rate during 240 min.

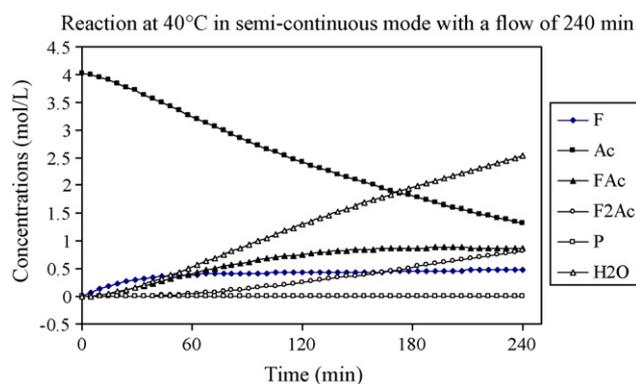


Fig. 20. Evolution of compound concentrations of the reaction at 40 °C in semi-continuous mode with a furfural feed-rate during 30 min (calculated points with smoothing).

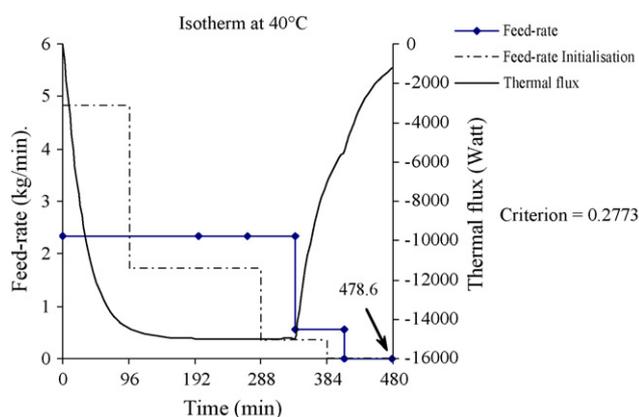


Fig. 21. Results of the simulation in semi-continuous mode at industrial scale.

by the reactor cooling system. It is necessary to increase the operative time to be able to limit the thermal flux to 15 kW.

- To respect the safety constraint, the maximal time of the reaction is multiplied by two (480 min). Optimal feed-rate profile at 40 °C generating a thermal flux lower than 15 kW can then be determined. The first interval of the operating time is also introduced as a variable to be optimized by the calculation algorithm.

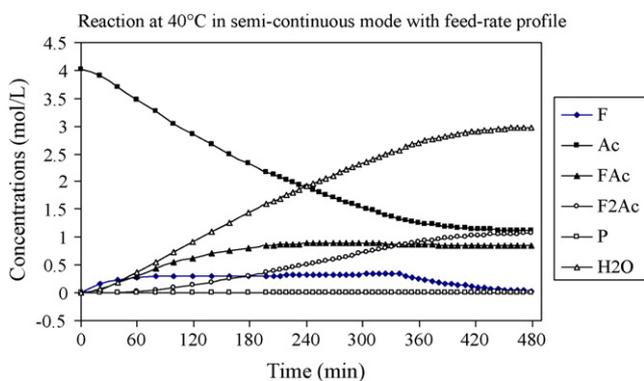


Fig. 22. Evolution of compound concentrations of the reaction at 40 °C in semi-continuous mode with a furfural feed-rate during 30 min (calculated points with smoothing).

The optimization result is presented Fig. 21. The furfural feed-rate is constant during 338 min and the generated thermal flux does not exceed 15 kW. The rest of the furfural amount is fed in the fourth interval. The total time of the synthesis is 478.6 min at the end of which the output is 27.73%. Fig. 22 represents the evolution of product and reagent concentrations as a function of time.

## 5. Conclusion

The results obtained for the stoichiometric identification show that the algorithm is able to find out a good representation of the transformation from solely the initial and final concentrations.

The identified kinetic constants allow to simulate the curves representing the evolution of reagents and products concentrations taking part in the synthesis. For compounds that are only products or reagents, the experimental points and the simulation are in good agreement. On the other hand, for compounds that are simultaneously reagent and product, the model does not perfectly fit the experiments, but the description of compounds evolution remains correct.

The optimization of aldolic condensation of furfural on acetone has been realized by maximizing the chemical yield of FAc. As expected from the reaction scheme and the values of kinetic constants, the best criterion is obtained for a synthesis in discontinuous mode (batch) realized at the temperature of 40 °C, which represents the maximal limit imposed for the research of optimal operating conditions.

Although this synthesis is not very exothermic, the extrapolation to industrial scale has been realized by integrating some thermal limitations (heating/cooling rate, thermal evacuation capacity) that remain a crucial problem for big capacity jacketed reactors.

## Appendix A. Nomenclature

$a$	order of the constituent in the reaction
$C$	concentration of the constituent
$E_a$	activation energy of Arrhenius law
$Fe$	feed rate
$\Delta H$	heat of reaction
$J$	optimization criterion
$k^0$	pre-exponential factor of Arrhenius law
$n$	mole number
$N$	number of points
$NC$	number of constituents
$NE$	number of experiments
$NR$	number of reactions
$r$	rate of reaction
$R$	gas constant ( $8.314 \text{ J K}^{-1} \text{ mol}^{-1}$ )
$R_j$	overall rate of production of species $j$
$t$	time
$T$	temperature
$U$	global heat transfer coefficient
$V$	$(NC \times NC)$ orthonormal matrix

$V_r$	reactor volume
$x$	data point
$X$	extent of reaction
$y$	model point
$Y$	(NE $\times$ NR) data matrix

#### Greek symbols

$\lambda$	wavelength
$\nu$	stoichiometric coefficient

#### Subscripts

Ac	acetone
exp	measured
F	furfural
FAc	4-(2-furyl)-3-buten-2-one
F <sub>2</sub> Ac	1,4-pentadien-3-one,1,5-di-2-furanyl
H <sub>2</sub> O	water
$i$	refers to reactions or to point number
id	calculated
$j$	refers to constituents
$k$	refers to experiments
P	1,5,9-tri-2-furylnona-1,8-diene-3,7-dione

#### Superscripts

0	initial
f	final
T	transpose

#### References

- [1] P.J. Le Meur, L'ingénierie en chimie fine: définitions et fonction, *Inf. Chim.* 343 (1992) 95–101.
- [2] P. Pollak, La chimie fine rêves et réalités, *Inf. Chim.* 288 (1987) 195–203.
- [3] E. Polastro, S. Tulcinsky, La R&D en chimie fine, pour quoi faire? *Inf. Chim.* 383 (1996) 82–84.
- [4] G.E.P. Box, W.G. Hunter, J.S. Hunter, *Statistics for Experimenters*, Wiley, 1978.
- [5] Garcia, V., Exploitation des modèles de tendance stœchiométriques et cinétiques pour l'optimisation des réacteurs discontinus de chimie fine, Ph.D. Thesis, INP Toulouse, France, 1993.
- [6] Sedrati, Y., Stratégie expérimentale pour la détermination des modèles stoéchio-cinétiques, Ph.D. Thesis, INP Toulouse, France, 1999.
- [7] Toulouse, C., Conduite optimale sous contraintes de sécurité des réacteurs batch ou alimentés de chimie fine, Ph.D. Thesis, INP Toulouse, France 1999.
- [8] J. Villermaux, C. Georgakis, Problèmes actuels dans la mise en œuvre des réactions discontinues, *Entropie* 23 (137/138) (1987) 45–51.
- [9] O. Abel, A. Helbig, W. Marquardt, H. Zwick, T. Daszkowski, Productivity optimization of an industrial semi-batch polymerization reactor under safety constraints, *J. Proc. Cont.* 10 (2000) 351–362.
- [10] G.D. Cawthon, K.S. Knaebel, Optimization of semibatch polymerization reactions, *Comp. Chem. Eng.* 13 (1/2) (1989) 63–72.
- [11] C. Filippi, J.L. Greffe, J. Bordet, J. Villermaux, Tendency modelling of semibatch reactors for optimization and control, *Chem. Eng. Sci.* 41 (4) (1986) 913–920.
- [12] C. Filippi-Bossy, J. Bordet, J. Villermaux, S. Marchal-Brassely, Batch reactor optimization by use of tendency models, *Comp. Chem. Eng.* 13 (1/2) (1989) 35–47.
- [13] S. Marchal-Brassely, J. Villermaux, J.-L. Houzelot, J.L. Barnay, Optimal operation of a semi-batch reactor by self-adaptive models for temperature and feed-rate profiles, *Chem. Eng. Sci.* 47 (9–11) (1992) 2445–2450.
- [14] A. Rastogi, A. Vega, C. Georgakis, H.G. Stenger Jr., Optimization of catalyzed epoxidation of unsaturated fatty acids by using tendency models, *Chem. Eng. Sci.* 45 (8) (1990) 2067–2074.
- [15] A. Rastogi, J. Fotopoulos, C. Georgakis, H.G. Stenger Jr., The identification of kinetic expressions and the evolutionary optimization of specialty chemical batch reactors using tendency models, *Chem. Eng. Sci.* 47 (9–11) (1992) 2487–2492.
- [16] V. Garcia, M. Cabassud, M.V. LeLann, L. Pibouleau, G. Casamatta, Constrained optimization for fine chemical productions in batch reactors, *Chem. Eng. J. Biochem. Eng. J.* 59 (3) (1995) 229–241.
- [17] N. Aziz, I.M. Mujtaba, Optimal operation policies in batch reactors, *Chem. Eng. J.* 85 (2002) 313–325.
- [18] D. Bonvin, D.W.T. Rippin, Target factor analysis for the identification of stoichiometric models, *Chem. Eng. Sci.* 45 (12) (1990) 3417–3426.
- [19] P. Tsobanakis, S.H. Lee, J.A. Phillips, C. Georgakis, Adaptive stoichiometric modeling and state estimation of batch and fed-batch fermentation processes, in: *Am. Inst. Chem. Engrs., Annual Meeting*, San Francisco, California, November 9, 1997.
- [20] J.W. Hamer, Stoichiometric interpretation of multireaction data: application to fed batch fermentation data, *Chem. Eng. Sci.* 44 (10) (1989) 2363–2374.
- [21] Batchmod: Stoichiometric identification software, License INPT, 1997.
- [22] M. Cabassud, P. Cognet, V. Garcia, M.V. Le Lann, L. Rigal, G. Casamatta, Modelling and optimisation of the lactic acid synthesis by the alkaline degradation of fructose in a batch reactor, *Chem. Eng. Commun.* 192 (2005) 758–786.
- [23] C. Toulouse, J. Cezerac, M. Cabassud, M.V. Le Lann, G. Casamatta, Optimisation and scale-up of batch chemical reactors: impact of safety constraints, *Chem. Eng. Sci.* 51 (10) (1996) 2243–2252.
- [24] C. Toulouse, M. Cabassud, M.V. Le Lann, G. Casamatta, Opérations optimales dans les réacteurs discontinus sous contraintes de fonctionnement, *Entropie* 210 (1998) 29–34.
- [25] N.N. Semenov, *Z. Phys.* 48 (1928) 571–581.
- [26] T. Bottin-Strzalko, Effet de structure sur la réversibilité de la condensation aldolique: Réaction des phosphonoesters et du benzaldéhyde, *Tetrahedron* 29 (24) (1973) 4199–4204.
- [27] J.E. Dubois, P. Fellmann, Influence de la géométrie de l'énolate sur la stéréochimie de la condensation aldolique, *Tetrahedron Lett.* 16 (14) (1975) 1225–1228.
- [28] P. Fellmann, J.E. Dubois, Condensation aldolique: effets de substituants alcoyles sur la stéréochimie de la réaction entre un énolate et un aldéhyde ou une cétone, *Tetrahedron* 34 (9) (1978) 1343–1347.
- [29] G. Kyriakakou, M.C. Roux-Schmitt, J. Seyden-Penne, Stéréosélectivité de la condensation aldolique. Réaction du benzaldéhyde et d'énolates carbénates magnésiens  $\alpha$ -chlorés, *J. Organomet. Chem.* 47 (2) (1973) 315–320.
- [30] N.L. Allinger, M.P. Cava, D.C. De Jongh, N.A. Lebel, C.L. Stevens, *Chimie organique – volume II: Réactions*, 3<sup>ème</sup> édition, McGraw Hill, 1981.
- [31] A.L. Bailey, G. Wortley, S. Southon, Measurement of aldehydes in low density lipoprotein by high performance liquid chromatography, *Free Rad. Biol. Med.* 23 (7) (1997) 1078–1085.
- [32] P. Chambel, M.B. Oliveira, P.B. Andrade, J.O. Fernandes, R.M. Seabra, M.A. Ferreira, Identification of 5,5'-oxy-dimethylene-bis(2-furaldehyde) by thermal decomposition of 5-hydroxymethyl-2-furfuraldehyde, *Food Chem.* 63 (4) (1998) 473–477.
- [33] E. Ferrer, A. Alegría, R. Farré, P. Abellán, F. Romero, High-performance liquid chromatographic determination of furfural compounds in infant formulas: changes during heat treatment and storage, *J. Chromatogr. A* 947 (2002) 85–95.
- [34] P. Ho, T.A. Hogg, M.C.M. Silva, Application of a liquid chromatography method for the determination of phenolic compounds and furans in fortified wines, *Food Chem.* 64 (1999) 115–122.
- [35] S. Kermasha, M. Goetghebeur, J. Dumont, R. Couture, Analyses of phenolic and furfural compounds in concentrated and non-concentrated apple juices, *Food Res. Int.* 28 (3) (1995) 245–252.

- [36] F. Lo Coco, C. Valentini, V. Novelli, L. Ceccon, High-performance liquid chromatographic determination of 2-furaldehyde and 5-hydroxymethyl-2-furaldehyde in honey, *J. Chromatogr. A* 749 (1996) 95–102.
- [37] A.A. Patel, S.R. Patel, Synthesis and characterization of furfural-acetone polymers, *Eur. Polym. J.* 19 (3) (1983) 231–234.
- [38] S. Cramer, R. Gesthuisen, Simultaneous estimation of the heat of reaction and the heat transfer coefficient by calorimetry: estimation problems due to model simplification and high jacket flow rates-theoretical development, *Chem. Eng. Sci.* 60 (2005) 4233–4248.