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# Calorimetric Approach and Simulation for Scale-Up of a Friedel−Crafts Reaction

Lucia Gigante, Angelo Lunghi, Simone Martinelli, and Paolo Cardillo*
*Stazione sperimentale per i Combustibili, V.le A. De Gasperi, 3-20097 San Donato Milanese, Italy*

Luca Picello, Roberto Bortolaso, and Marco Galvagni
*Fabbrica Italiana Sintetici, Via Milano, 26-36041 Alte di Montecchio Maggiore, Vicenza, Italy*

Renato Rota
*Politecnico di Milano, Dip. di Chimica, Materiali e Ingegneria Chimica G. Natta, Via Mancinelli 7-20131 Milano, Italy*

## Abstract:

**The present study, on the optimisation of the scale-up of a Friedel−Crafts acylation, joins together experimental calorimetric techniques and simulation techniques. The adopted methodology involved the execution of isothermal tests at different temperatures, using the reaction calorimeter RC1, to obtain the heat flow versus time data. These data were used to perform a kinetic study of the reaction by using the simulation software BatchCAD. The reliability of the adopted kinetic model was confirmed by comparing the experimental data obtained by operating the desired reaction in adiabatic mode (in a Phi-Tec II calorimeter) with the predictions of the kinetic model in the same conditions. Using this kinetic equation it was possible to simulate the process under pilot-plant conditions. The good agreement between the model predictions and the experimental data confirmed the accuracy of the kinetic equations. Finally several large-scale production-plant simulations were carried out varying both dosing time and reaction temperature to maximise the space/time yield and minimise the thermal risks. This led to a high quality and safe process, saving a large part of the time (and money) usually spent in traditional scale-up procedures.**

## Introduction

The Fine Chemical Industries are increasingly under huge pressure because of increasing R&D costs and growing competition and pricing pressures; therefore, they need to speed-up the time-to-market to achieve market leadership.

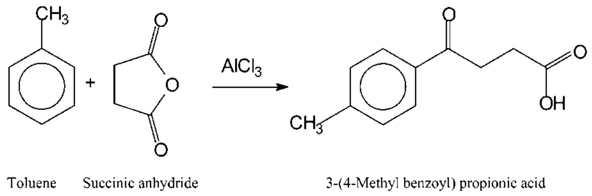
In Italy, most of the Chemical Industry is constituted by small- and medium-sized enterprises (SMEs) with a limited number of workers in each firm, and with the strong tendency to resort to outsourcing. This situation often prevents the complete identification of all the kinetic parameters related to the chemical production of new compounds that are essential to ensure the company's productivity and to comply with stricter and stricter laws on health and safety for people and environment. Both safety and economical aspects are critical points, particularly for SMEs.

The main aim of the present study was to develop a kinetic model for a Friedel−Crafts reaction using calorimetric data, obtained from the Mettler RC1[1] and other calorimetric techniques. This kinetic model was used with a commercial computer program (BatchCAD[2,3]) to simulate and optimise the actual process in terms of productivity and safety.

## Methodology

**Study of the Desired Reaction.** In this work we have studied the Friedel−Crafts acylation[4] of toluene with succinic anhydride and $AlCl_3$ as catalyst at low temperature.

The reaction scheme is shown as the following:



Preliminary DSC runs on the final reaction mass, reagents, and products showed that all samples do not decompose or oxidise exothermically within the temperature range 30−280 °C during a standard dynamic test (scanning rate 5 °C/min, static air atmosphere, sealed steel crucible, medium pressure). Therefore, we can assume that the final reaction mass is stable up to 280 °C.

The kinetic behaviour of the reaction system was studied by carrying out a series of isothermal reaction calorimeter (RC) experiments. The tests were run in batch mode, adding all succinic anhydride to the organic substrate (toluene) at the beginning of the experiment, using toluene as solvent

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* Author for correspondence. Telephone +39 02 51604209. Fax +39 02 514286. E-mail: cardillo@ssc.it.

(1) http://www.rxeforum.com/start_8_16−0.htm. Accessed 2003.
(2) *BatchCAD*, version 7.2; http://www.hyprotech.com/batchcad/default.asp. Accessed 2003.
(3) Lunghi, A.; Alós, M. A.; Gigante , L.; Feixas, J.; Sironi, E.; Feliu, J. A.; Cardillo, P. *Org. Process Res. Dev.* **2002**, *6*, 926.
(4) Groggings, P. H. *Unit Process in Organic Synthesis*, 3rd ed.; McGraw-Hill: New York, 1947.

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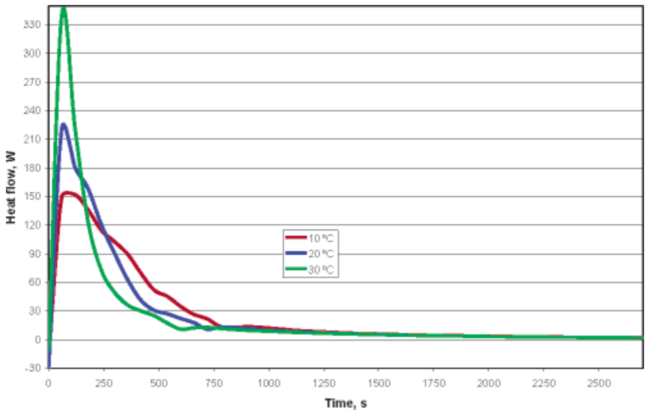

***Figure 1.*** **Experimental heat flow from RC1 tests.**

***Table 1.*** **RC1 experiments at 10, 20, 30 °C**

| process temperature [ °C] | $\Delta H_{\text{reac}}$ obtained [kJ] | $\Delta H_{\text{reac}}$ referred to succinic anhydride [kJ/mol] | specific heat of reaction mass [J/(kg$_{\text{mix}}$ × K)] | $\Delta T_{\text{ad}}$ [°C] |
|---|---|---|---|---|
| 10 | −60.52 | −86.46 | 1623 | 50.1 |
| 20 | −64.09 | −91.55 | 1739 | 49.5 |
| 30 | −61.11 | −87.29 | 1716 | 47.9 |

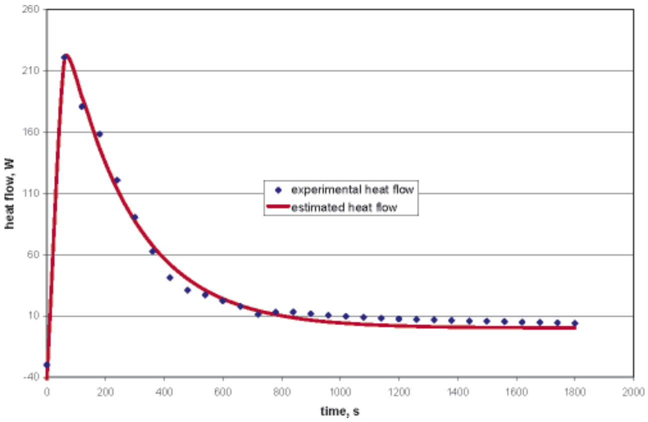

***Figure 2.*** **BatchCAD-fitted plot for the RC1 isothermal experiment at 20 °C.**

***Table 2.*** **Estimate of reaction order**

| reaction temperature [°C] | $k_1$ [1/s] | $k_2$ [1/s] | $m$ | $n$ | $\Delta H_{r1}$ [kJ/mol] | $\Delta H_{r2}$ [kJ/mol] |
|---|---|---|---|---|---|---|
| 10 | $2.8 \times 10^{-3}$ | $8.3 \times 10^{-3}$ | 1.5 | 0.6 | 10.0 | −96.5 |
| 20 | $4.3 \times 10^{-3}$ | $2.6 \times 10^{-2}$ | 1.0 | 0.8 | 10.0 | −101.6 |
| 30 | $6.5 \times 10^{-3}$ | $7.5 \times 10^{-2}$ | 1.7 | 0.9 | 10.0 | −97.3 |

***Table 3.*** **Estimate of kinetic constants**

| reaction temperature [°C] | $k_1$ [1/s] | $k_2$ [1/s] |
|---|---|---|
| 10 | $2.4 \times 10^{-3}$ | $3.9 \times 10^{-2}$ |
| 20 | $4.3 \times 10^{-3}$ | $4.2 \times 10^{-2}$ |
| 30 | $7.2 \times 10^{-3}$ | $6.3 \times 10^{-2}$ |

***Table 4.*** **Estimate of Arrhenius parameters for the acylation**

| | $A_1$ [m$^3$ kmol$^{-1}$ s$^{-1}$] | $E_1$ [kJ/mol] | m |
|---|---|---|---|
| nucleophile attack | 37406 | 38.960 | 1 |
| | $A_2$ [m$^3$ kmol$^{-1}$ s$^{-1}$] | $E_2$ [kJ/mol] | n |
| product formation | 38.420 | 16.332 | 1 |

and aluminium chloride as catalyst to yield 3-(4-methyl benzoyl) propionic acid.

The RC1 tests showed that the reaction is exothermic: the shape of the RC1 curves obtained is typical of a reaction that accumulates a certain percentage of reactant (Figure 1). Accumulation increases when decreasing temperature. The reaction is usually performed close to 0 °C. Table 1 summarises the calorimetric data at three different temperatures deduced from the experiments summarised in Figure 1.

As the measured $\Delta T_{\text{ad}}$ is about 50 °C, the final temperature for the reaction mass cannot exceed 280 °C. Since DSC tests showed that the reaction mass is stable up to 280 °C, from these preliminary RC1 tests we can deduce that, in these conditions, the process does not show any runaway hazard.

The equations proposed to describe the system were:

$$C_4H_4O_3 + C_7H_8 + AlCl_3 \xrightarrow{1} \text{activated complex} + AlCl_3$$

$$\text{activated complex} \xrightarrow{2} C_{11}H_{12}O_3$$

The reaction rate equations proposed for these reactions are the following:

$$r_1 = k_1[C_4H_4O_3]^m$$

$$r_2 = k_2[\text{activated complex}]^n$$

This simplified reaction scheme, according to literature,[4] involves the formation of a not-isolating substance, the so-called "activated complex", and then the formation of the product. The influence of the toluene concentration on the reaction rates was not investigated since in all the experiments toluene was in large excess with respect to the stoichiometry. The partial reaction orders with respect to the succinic anhydride, $m$, and to the activated complex, $n$, which give the best fit of the heat flow versus time curves were determined using the "kinetic fitting environment" of the software BatchCAD from each isothermal experiment, as reported in Table 2.

After the reaction orders $m$ and $n$ were determined from all isothermal experiments, they were rounded and fixed as $n = 1$ and $m = 1$, and the fitting procedure was repeated to determinate the isothermal rate constants at three different temperatures, as summarised in Table 3. For the sake of example, Figure 2 shows a comparison between RC1 isothermal data and model simulation at 20 °C.

From the data summarised in Table 3, activation energy and preexponential factor values for the two reactions were determined according to the Arrhenius equation. The calculated values are summarised in Table 4 and Figure 3.

These kinetic data were assumed to model the thermal behaviour of the studied reaction. Kinetic equation was verified by comparison of simulated adiabatic Phi-Tec II runs

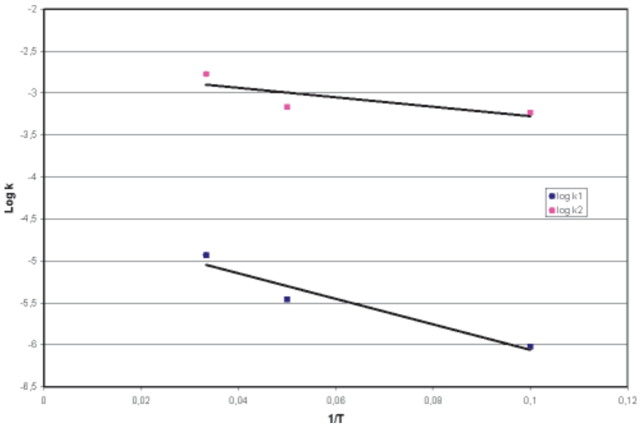

*Figure 3.* **Arrhenius plot of the experimental data.**

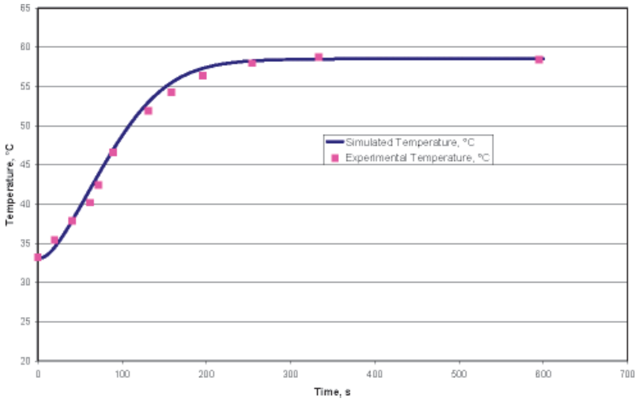

*Figure 4.* **Comparison between predicted and experimental data under adiabatic conditions.**

*Table 5.* **Phi-Tec II experimental conditions**

| | |
|---|---|
| toluene | 35 g |
| aluminum chloride | 10.5 g |
| succinic anhydride | 4 g |
| conditions | adiabatic |
| stirrer | 200 rpm |
| Φ factor | 1.35 |

(using BatchCAD) and actual Phi-TecII[5,6] test cell data. The Phi-Tec II experimental conditions are summarised in Table 5, while the observed and calculated adiabatic temperature plots are shown in Figure 4.

The good agreement between experimental and predicted data confirms the reliability of the developed kinetic model.

## Pilot-Plant Process and Simulation

Pilot-plant process was carried out using a 1.5 m$^3$ steel jacketed reactor. The heat-transfer system is composed by two service fluids, which are fed into a 0.21 m$^3$ jacket on a drain/fill mode. A manual controller allows heating and cooling the reactor to the required operation temperature. Figure 5 illustrates the reactor configuration.

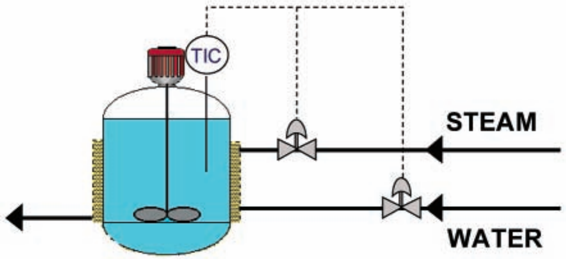

*Figure 5.* **Pilot plant sketch. Fluid conditions are steam at 127 °C, and cooling water−glycol ether at −20 °C.**

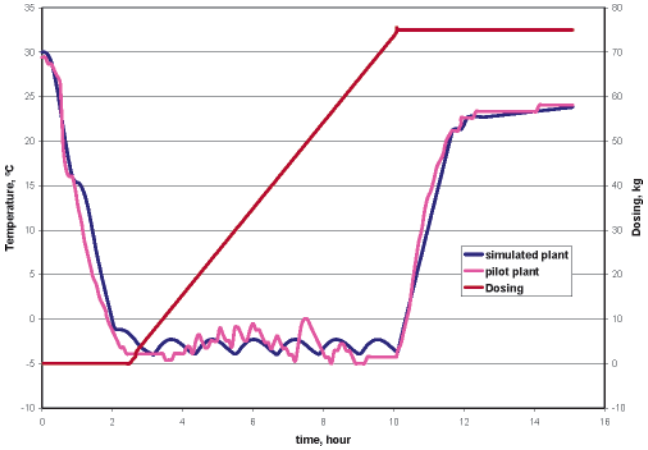

*Figure 6.* **Comparison between pilot-plant experiments and model predictions.**

During normal operation conditions, the reactor is charged with 649.5 kg of toluene, 199.9 kg of aluminium chloride, and after 2.5 h, during which reactor temperature is brought to −4 °C, 75 kg of succinic anhydride is charged in semi-batch mode, during 7.5 h. At the end of the dosing, the temperature is raised to 25 °C. Under these conditions, no accumulation of succinic anhydride occurs in the reactor, and temperature profile could be classified as QFS (quick onset, fair conversion and smooth profile).[7]

The process has been then simulated under normal conditions, comparing the real and the simulated data. Figure 6 shows reactor temperature and addition as a function of time in the two cases.

We can see that experimental and predicted profiles are quite similar, thus confirming the reliability of the developed kinetic model.

## Optimisation of the Pilot-Plant Process by Simulation

According to the DSC tests and to RC1 experimentation, the process does not involve any thermal hazard. The final reaction mass is thermally stable in the 30−280 °C range of temperature, and the measured $\Delta T_{ad}$ of the desired reaction is 50 °C which leads to a maximum final temperature of about 50 °C in the pilot-plant conditions. However, such operating conditions require large times for cooling, dosing, and heating. Consequently, several large-scale production-plant simulations using the BatchCAD simulation environment were run to optimise the process in terms of productivity without introducing any thermal hazard.

At first, dosing time was strongly reduced, and the final heating was eliminated. In this case the optimal configuration found, in terms of both safety and productivity, was a dosing

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(5) Singh, J. Enhanced vent sizing calorimeter: application and comparison with existing devices. International Symposium on Runaway Reactions, CCPS, Boston, MA, 1989; p 313.

(6) http://www.helgroup.co.uk. Accessed 2003.

(7) Steensma, M., Westerterp, K. R. *Ind. Eng. Chem. Res.* **1990**, *29*, 1259.

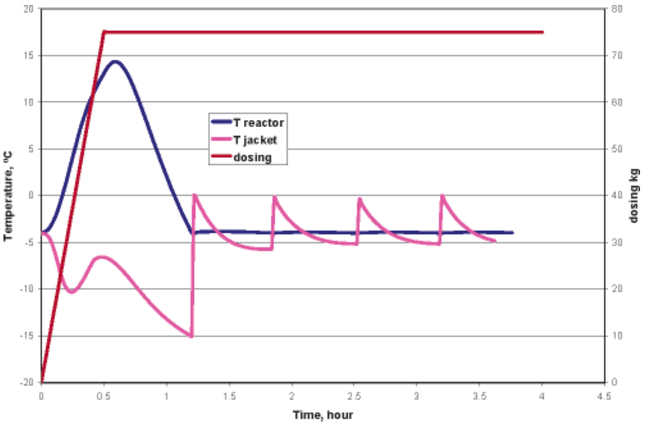

***Figure 7.*** **Simulated temperature profile for a semibatch process with dosing time equal to 0.5 h.**

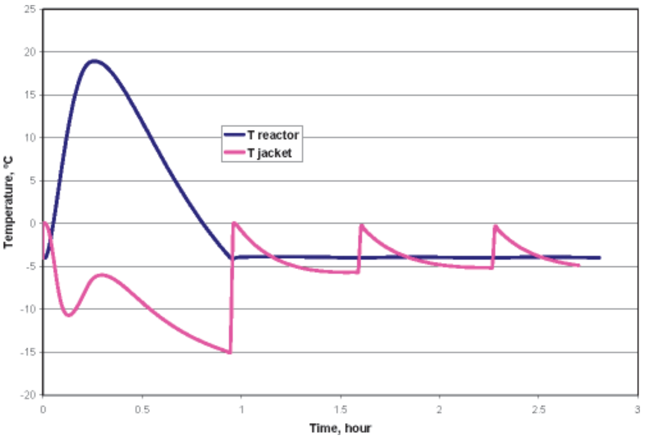

***Figure 8.*** **Temperature profile in batch reactor with initial temperature equal to 0°C.**

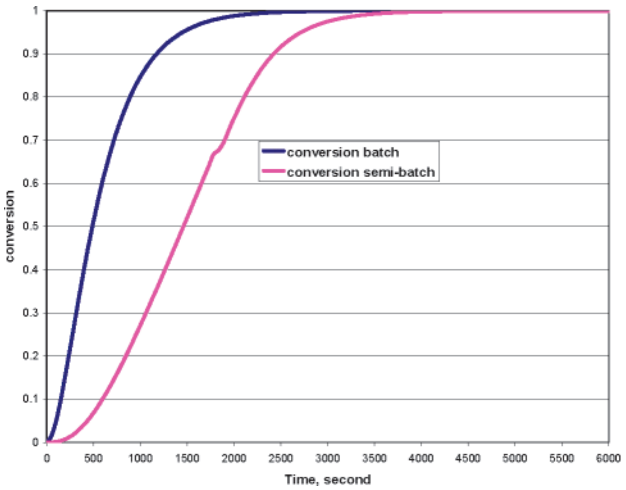

***Figure 9.*** **Comparison of conversion for batch and semi-batch reactors.**

time equal to 0.5 h as shown in Figure 7. We can see that also in this case no safety problems arise, while the reaction is completed in about 1 h after completing the dosing of succinin anhydride.

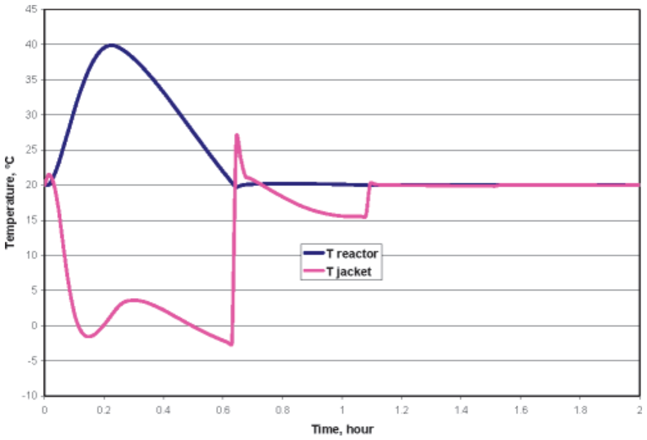

***Figure 10.*** **Temperature profile in batch reactor with initial temperature equal to 20°C.**

Therefore, the more severe batch conditions were investigated. Figure 8 shows the simulated reactor and jacket temperature profiles in a batch reactor operating at the same temperature and charge conditions as the semi-batch reactor. We can see that also in the batch mode the reactor temperature is lower than 20 °C during the whole process. This means that, as previously discussed, the process can be performed in safe conditions also in a batch reactor.

Furthermore comparing the conversion of the succinic anhydride in semi-batch and batch mode (Figure 9) we can see that, as expected, the batch mode leads to a complete conversion in a shorter time.

Even more severe conditions can be utilised without compromising the process safety, as shown in Figure 10, where the reactor temperature profile in batch mode and an initial temperature of 20 °C is reported.

Comparing the results of this last figure with those of the normally adopted operating conditions (reported in Figure 6), we can note the large reduction in the process time without compromising the process safety.

## Conclusions

This study presents an application of coupling calorimetric experiments with simulation models to obtain a short-cut methodology able to optimise the scale-up of chemical processes, both in safety and economic terms. Limited targeted experiments with Mettler RC1 along with the capabilities of the software BatchCAD easily produced a reliable kinetic model that has been verified by comparison with adiabatic calorimeter and pilot-plant data. The simulation in different industrial conditions has been used to optimise the whole process in terms both of productivity and safety.

Good characterisation of the reactant system allows a quicker scale-up, promptly recognising any mistakes and inadequacy. In this particular case the applied methodology permitted drastic reduction of the reaction time and avoidance of the initial cooling period.

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