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A New Reaction Calorimeter for Screening Purposes during Process Development

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Abstract:

Calorimetry, in combination with thermal analysis, is an essential tool for a data-based assessment of thermal risks linked with the performance of chemical reactions at industrial scale. The energies of synthesis reactions or of decomposition reaction as well as the heat capacities of reaction masses can be measured by these techniques. The performance of the differential reaction calorimeter (DRC) from SETARAM in the determination of essential safety data was demonstrated using two example reactions. The differential reaction calorimeter was found to be a powerful screening tool in an organic synthesis laboratory or in a development laboratory, and it is especially well suited for a fast and low-cost determination of the thermal parameters of chemical reactions, even when only a few raw materials are available.

Introduction

One of the tasks of the chemist in charge of the development of an industrial process is to ensure the process safety. This means that he has to develop a process, which is robust against deviations from normal operating conditions.[1] Thus, at early stages of the process development, questions will be asked that require safety data to be able to evaluate thermal hazards, (i.e., the capability of a system to enter into a runaway reaction).

Thermal runaways are the cause of many incidents in process chemical industry, and some of them resulted in major accidents.[2] Thermal runaways are due to disturbances of the heat balance of a reactor, resulting in a fast increase of temperature in the reactor, which may result in a sharp increase of the pressure. Therefore, the chemist has to know the capability of a system to enter into a runaway reaction.

Considering a chemical reactor equipped with a jacket in which a cooling fluid circulates, if either the cooling system or the stirrer fails, heat removal is stopped and the reaction cannot be controlled anymore. If an important quantity of reagent, which has not been converted yet, remains in the reactor, its reaction will lead to a noncontrolled increase of the temperature. The maximum temperature reached during the reaction loss of control is called maximum temperature of the synthesis reaction (MTSR). At this point, a secondary decomposition reaction may be triggered and leads to a further temperature increase.

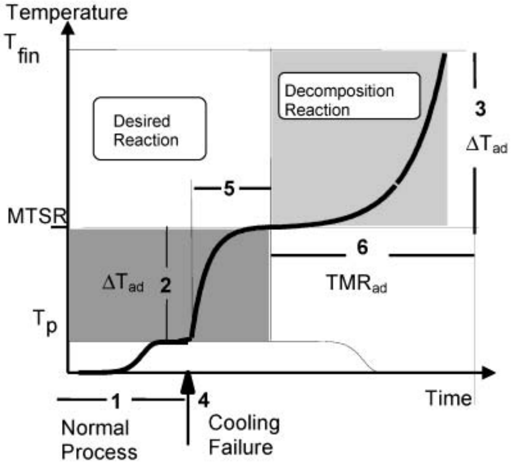

Figure 1. **Cooling failure scenario.**

A systematic examination of the phenomena occurring after a cooling failure allows drawing a so-called runaway scenario (Figure 1) from which the required thermal data can be drawn:[3] (1) the heat of the desired reaction, corresponding to the first step of the cooling failure scenario, (2) the heat of decomposition corresponding to the second step of the diagram, and (3) the heat capacity of the mixtures.

These data enable the evaluation of the time available before the beginning of the decomposition reaction starts at the MTSR. The MTSR depends on the accumulation of nonconverted reagents, the heat of reaction, and the heat capacity of the reaction mass.

The time to maximum rate under adiabatic conditions (TMR_{ad}), or time left before the explosion occurs, can also be calculated from the heat-release rate, the heat capacity, and the energy of activation of the reaction. This implies a kinetic study of the reaction, which can be restricted to a zero-order approximation when used for safety purposes only.

One way of obtaining this essential data about temperature, pressure, and energy is the experimental determination by thermal analysis and calorimetry.

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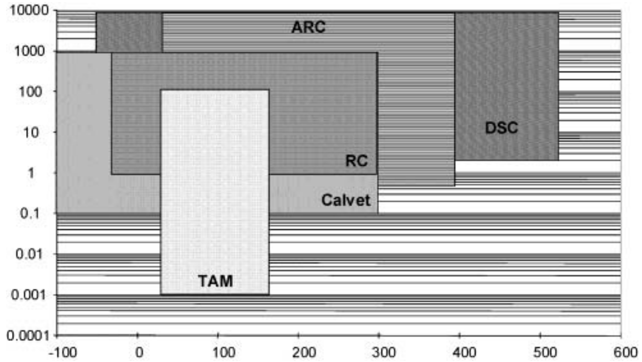

Figure 2. **Temperature in °C and sensitivity ranges in $W \cdot kg^{-1}$ of commonly used calorimetric methods in safety laboratories.**

2. Calorimeters for Safety Studies

There is a broad choice of various calorimeters based on different calorimetric principles available on the market, but safety studies impose specific requirements that only some calorimeters meet. The criteria for choosing the appropriate calorimetric method can be summarized as follows:

- The amount of sample available: on one hand, at early stages of the development of a process, only a few milligrams of samples may be available or may be “sacrificed” for safety studies. On the other hand, studying a runaway reaction will preferably not be performed at large scale.
- The sensitivity of the calorimeter is important, if only small heat-release rates have to be measured. This is especially important in the study of stability at storage or transportation, where even a heat release of a few milliwatts per kilogram may be critical. On the other hand, for tracking the steep part of a runaway reaction as required for vent-sizing purposes, there is no need for high sensitivity.
- The temperature and pressure range must be adapted to the process temperature range and also to the range in which secondary decomposition reactions may be triggered. Both parameters, temperature range and sensitivity, can be represented in a graphical form allowing the illustration of the ranges as an Arrhenius diagram (Figure 2).
- The operating conditions: the dynamic or scanning mode is well adapted for screening purposes in matters of thermal stability, whereas the capability of reproducing adequate process conditions is essential for the study of a synthesis reaction.

Therefore, four main kinds of calorimetric devices are commonly used in a safety testing laboratory: differential scanning calorimeters (DSC), Calvet calorimeters, adiabatic calorimeters, and calorimetric reactors.[4−6]

- DSC is a technique in which the change of the heat-flow rate difference between the sample and a reference sample is analyzed while they are subjected to a temperature scan.[7] DSC is a low-cost method using small amounts of sample: that is, a few milligrams of product. Setting up the experiment is easy and fast. Reagents are placed in the crucible and are submitted to a temperature ramp. Due to the small size of the sample to be introduced into the crucible, it is difficult to study heterogeneous mixtures quantitatively. Due to the small volume, special care is required to obtain representative samples of the reaction mass. Therefore, DSC is mainly used to study decomposition reactions in which the heat exchanged is very high and the high sensitivity of measurement is not needed. It is only rarely used to study the desired reaction.
- The Calvet calorimeter based on the Tian−Calvet principle has a furnace provided with two cylindrical cells in which the sample and reference are placed. Samples are surrounded by thermopiles enabling the integration of the energy released during the experiment. A few grams of product can be analyzed. Certain versions of the Calvet calorimeter enable the simulation of a chemical reaction in batch operation. Up to 12 mL of product can be analyzed. It is a very useful tool for measuring heat capacity and heat of reaction. For example, stirring is possible; therefore, it can be used to study the heat of reaction of heterogeneous mixtures with a good accuracy. The pressure can also be measured during a reaction.
- The purpose of adiabatic calorimeters is to simulate runaway conditions. In fact, true adiabatic conditions are difficult to carry out experimentally. Certain methods are based on Dewar calorimetry, avoiding heat losses by thermal insulation, whereas other methods avoid heat losses by adapting the temperature of the sample surroundings to the sample temperature. The problem is that, whichever technique is used, a part of the heat of reaction is used to heat up the crucible. Therefore, the so-called ϕ correction is of primary importance. With most of these calorimeters, a simultaneous measure of the pressure is also possible.
- Reaction calorimeters are instruments making possible the performance of chemical reactions under conditions close to those of industrial ones, while making possible quantitative measurements of the heat release rate. Traditional reaction calorimeters use only one reaction mass having a volume of about one liter.

Recently, SETARAM has commercialized a new reaction calorimeter. This calorimeter developed in collaboration with Aventis and their Security laboratory in Neuville/ Saône will be presented in more detail following a study, which has been made at the Swiss Institute of Safety.

3. Description of the Differential Reaction Calorimeter

3.1. General Description of the Calorimeter. The new reaction calorimeter called differential reaction calorimeter (DRC) enables an easy and rapid determination of the most important thermodynamics data such as the heat of reaction and heat capacity of the reaction mass. It is very simple to use; its design is very similar to classical organic chemistry laboratory equipment. The instrument allows studying chemical reactions in the same conditions as those required by

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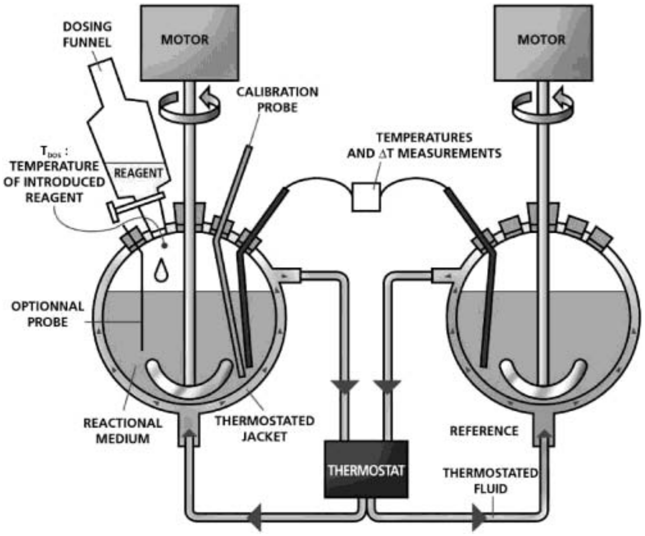

Figure 3. **Schematic view of the differential reaction calorimeter DRC from SETARAM.**

classical laboratory procedures because of the use of stirrers, a thermostatic jacket, and the possibility of adding liquids or gases in the reactor even during measurement.

3.2. Measurement Principles. The reaction calorimeter, DRC, continuously measures a temperature difference between the working reactor and the reference reactor (Figure 3). The reaction to be studied is performed in the working reactor, whereas the reference reactor only contains a solvent with physical properties close to those of the reacting mixture. The reference reactor enables the correction of the perturbations of the system to make possible an accurate determination of the heat of reaction and heat capacity. All phenomena that are not directly related to the reaction, such as temperature fluctuations of heat carrier, heat losses through the top of the reactor, and heat related to the stirring, can be corrected by using the reference reactor.

According to the temperature control of its surrounding, the DRC is classified as an isoperibolic calorimeter. Both reactors are double-enveloped spherical reactors connected in parallel. A heat-carrier fluid flows through the jackets, maintaining the reactor surroundings at a constant temperature with a ±0.01°C stability. The overall heat balance can be written:

$$q_{\text{R}} = UA(T_{\text{R1}} - T_{\text{R2}}) + (m_{\text{R}}c_{\text{pR}} + c_{\text{pi}})\frac{d(T_{\text{R1}} - T_{\text{R2}})}{\text{d}t} + \dot{m}c_{\text{pdos}}(T_{\text{R1}} - T_{\text{dos}}) \quad (1)$$

Measuring the temperature difference between both reactors ($T_{\text{R1}} - T_{\text{R2}}$) enables the determination of the heat-release rate of the reaction, if the heat transfer (UA) and the heat capacities of the reactor contents and the inserts ($m_{\text{R}}c_{\text{pR}} + c_{\text{pi}}$) are known. U is the overall heat-transfer coefficient through the reactor wall to the heat-carrier fluid flowing in the jacket. A is the exchange area that depends on the quantity of solvent in the reactor. The term mc_{pdos} ($T_{\text{R1}} - T_{\text{dos}}$) corresponds to the heat due to the feed, which may be at a different temperature (T_{dos}) than that of the reactor.

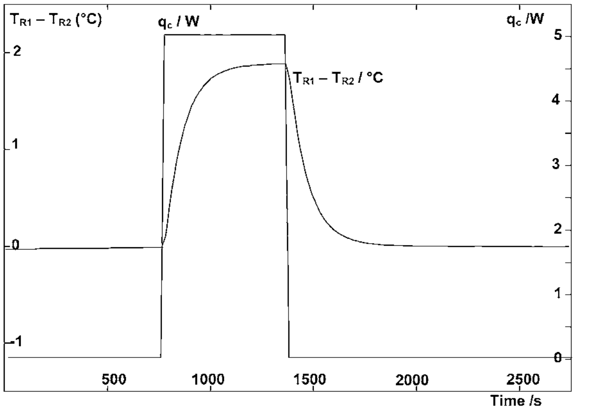

Figure 4. **Calibration of the differential reaction calorimeter by Joule effect.**

A Joule effect probe made up of a special alloy is used to calibrate the calorimeter (Figure 4). The power used for calibration (q_{c}) can be set up to 10 W. If, during the calibration, no reaction takes place and the reactor is not fed, the heat balance may be written:

$$q_{\text{c}} = UA(T_{\text{R1}} - T_{\text{R2}}) + (m_{\text{R}}c_{\text{pR}} + c_{\text{pi}})\frac{d(T_{\text{R1}} - T_{\text{R2}})}{\text{d}t} \quad (2)$$

The heat-transfer characteristics are obtained by integration of the signal over time:

$$UA = \frac{\int_0^\infty q_{\text{c}}\text{d}t}{\int_0^\infty (T_{\text{R1}} - T_{\text{R2}})\text{d}t} \quad (3)$$

The specific heat capacity of the reactor's contents can be obtained by evaluating the thermal relaxation after the calibration heater has been switched off. eq 2 can be integrated:

$$(T_{\text{R1}} - T_{\text{R2}})_{(t)} = (T_{\text{R1}} - T_{\text{R2}})_{(t_0)} + \frac{q_{\text{c}}}{UA}[1 - \text{e}^{-(t-t_0)/\tau}] \quad (4)$$

with the time constant,

$$\tau = \frac{m_{\text{r}}c_{\text{pR}} + c_{\text{pi}}}{UA} \quad (5)$$

The heat capacity of the inserts (c_{pi}) is determined by a calibration using a solvent with a known specific heat capacity.

3.3. Calorimeter Features. Reactors are made up of glass and use a glass stirrer with PTFE blades and metal inserts (temperature probe and Joule effect probe). The temperature in the working reactor and the one in the reference reactor are measured using a platinum−tantalum-cased probe. Three kinds of reactors can be adapted on the reaction calorimeter. Two double-enveloped spherical reactors having respectively a volume of 250 and 500 mL, are available. The double-enveloped Keller-type reactor has a volume of 100 mL. Such small-volume reactors allow working with small quantities of reagent and solvent, rending the calorimeter useful for studies carried out on expensive products such as those in the pharmaceutical industry.

Reactors have a central port, which receives the agitation bearing through which the stirrer passes. Agitation speed inside the reactors is fixed by stirring motors. Reactors also have four connection pipes, which enable the introduction of the temperature and calibration probes as well as any other accessory (a pH probe, for example). Reagents are added in the calorimeter using a dosing funnel or a driven syringe pump. All the accessories are held in place using glass pipes. Therefore, installing and starting up the DRC are very easy operations.

Since this calorimeter is operated as a differential calorimeter, the question of symmetry and especially of loss of symmetry during a reaction arises.

3.4. Effect of Loss of Symmetry on the Performance of the Differential Calorimeter. Equation 1 assumes the same calorific sensitivity (UA) in both measure and reference reactors, but during performance of a reaction this term may vary either due to the change of the heat-exchange area of the measure reactor resulting from addition of a reactant in semi-batch operation or due to a viscosity change in the measure reactor resulting from the chemical reaction.

To study the effect of a volume increase in the sole measure reactor, a semi-batch reaction was simulated by charging 100 mL of water into both measure and reference reactors. Then 100 mL (doubling of volume) of water was added to the measure reactor only with a simultaneous heat input from the calibration heater. The added water was maintained at the same temperature as that of the measure reactor, avoiding the perturbation by the sensible heat of addition. From the heat input of 15 kJ the integration of the signal using a linear interpolation of *UA* rends 13.1 kJ (−12.7%). As a comparison, a simultaneous addition of 50 mL of water to both reactors was also performed: the integration of the signal gives 13.4 kJ (−10.7%). The results can be improved by taking into account the nonlinear variation of the heat-exchange area (*A*) using a spreadsheet: the first experiment gives 14.5 kJ (−3.3%), and the second, 14.2 kJ (−5.3%).

The other common cause for loss of symmetry is viscosity change. A series of calibrations was performed with water in the measure reactor and poly(ethylene glycol) (PEG 3000) solutions 500 and 700 $g \cdot L^{-1}$ in water into the reference reactor. These concentrations represent a change of the viscosity by ca. 140 mPa•s. The calorific sensitivities (*UA*) increased by 0.37 and 0.47 $W \cdot K^{-1}$, but this had no significant effect on the determination of the specific heat capacities, which remained constant at 4.10 ± 0.03 $J \cdot g^{-1} \cdot K^{-1}$. The PEG solution was added into the reference reactor to maintain the specific heat capacity of the measure reactor contents constant.

To ensure conditions that are closer to practical ones, a semi-batch reaction was simulated by charging 100 mL of a 500 $g \cdot L^{-1}$ solution of poly(ethylene glycol) in water into both measure and reference reactors. Then 50 mL of water was added to the measure reactor and within the same time was added 50 mL of the same PEG solution into the reference reactor with a simultaneous heat input from the calibration heater. The added solution was maintained at the same temperature as that of the measure reactor, avoiding the perturbation by the sensible heat of addition. This procedure allows for checking the effect of the sole viscosity on calorimetric measurement. From the heat input of 15 kJ the integration of the signal using a linear interpolation of *UA* rends 13.5 kJ (−10.0%). As a comparison, a simultaneous addition of 50 mL of the PEG 3000 solution to both reactors was performed: the integration of the signal gives 13.2 kJ (−12.0%). The results can be improved by taking into account the nonlinear variation of calorific sensitivity (*UA*) using a spreadsheet: the first experiment gives 14.7 kJ (−2.0%), and the second, 14.2 kJ (−5.3%).

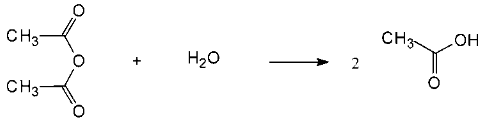

Figure 5. **Reaction scheme of the hydrolysis of acetic anhydride.**

These results are within the commonly accepted tolerance of ±15% for safety screening, showing that the approximation made in eq 1 is valid in this frame.

To test the calorimeter under more realistic conditions, two reactions have been studied in the DRC, using the isothermal batch and semi-batch operation.

4. Example 1: Hydrolysis of Acetic Anhydride

4.1. Reaction. The first reaction studied is a classical “calibration” reaction for calorimeters: the hydrolysis of acetic anhydride (Figure 5). It is a fast reaction well suited for checking the dynamic response of a calorimeter. It has been studied in batch mode using the DRC and the 250-mL reactors.

Acetic anhydride was obtained from Fluka (Fluka 45830, puris. p.a. ACS ≥ 99.5%). Deionized water was used.

4.2. Experimental Procedure. The reaction has been performed as an isothermal batch operation at three different temperatures 10, 25, and 40 °C. The reactor is thermally equilibrated at working temperature and only contains the solvent: 150 g (8.33 mol) of water. A heated dosing funnel, maintained at the temperature of the experiment, was used to introduce 12 g (0.12 mol) of acetic anhydride in one portion. The reference reactor contains 160 g of water, which is almost equal to the final reaction mass in the working reactor. In these conditions, symmetry is maintained between both reactors; hence, *U* and *A* are very similar in both reactors, and *UA* may be measured only once at the end of the experiment.

4.3. Results. The evolution of the working reactor temperature as a function of time allows following the reaction progress qualitatively: that is, the temperature returns to its initial value (baseline) after about 45 min at 40 °C. In the example shown in Figure 6, the maximum heat release rate was found ca. 90 $W \cdot kg^{-1}$, which would require a rather high cooling capacity for an industrial reactor. The reaction enthalpy is obtained by integration of the temperature difference with time using the Joule effect calibration performed at the end of the experiment with a horizontal

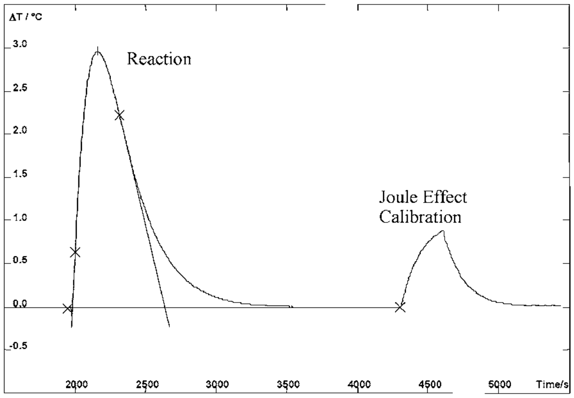

Figure 6. **Thermogram of the hydrolysis of acetic anhydride with water at 40 °C.**

Table 1: **Measured enthalpy of reaction for the hydrolysis of acetic anhydride**

temperature in °C	10	25	40
enthalpy of reaction in kJ·mol^{-1}	57.6	57.7	58.3

baseline also drawn from the end of the experiment. The results are summarized in Table 1.

The average value is $-\Delta H_R = 57.9$ kJ·mol^{-1} with a standard deviation of 0.67%. This value compares well with values from literature: $-\Delta H = 60.4$ kJ·mol^{-1} between 15 and 35°C[8] and $-\Delta H = 58.3$ kJ·mol^{-1} at 30°C.[9]

For this relatively fast reaction, the differential reaction calorimeter gives reproducible results with a good accuracy when compared to literature data.

5. Example 2: Esterification of Propanoic Anhydride by 2-Butanol

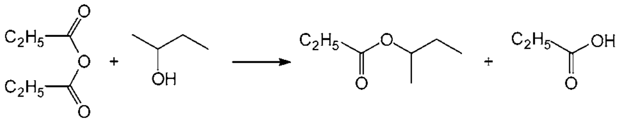

Figure 7. **Reaction scheme of the esterification of acetic anhydride by 2-butanol.**

5.1. Reaction. As a second example, a slow reaction was chosen: the esterification of propanoic anhydride by 2-butanol (Figure 7). This reaction is weakly exothermic, its kinetics may be influenced by catalysis, and there is no secondary decomposition reaction. Therefore, it is often used as a test reaction for calorimetry.[10,11] In the conditions we used, it is slow and well adapted to the study of reactant accumulation a in semi-batch reactor and to test the thermal sensitivity of the calorimeter.

Propanoic anhydride was obtained from Fluka (Fluka 81942, purum 98%) as well as butanol-2 (Fluka 19440, puris. p.a. ≥99.5%).

Table 2: **Results of esterification reaction in the batch mode**

temperature in °C	60	70	80
conversion at the end of the experiment	0.868	0.934	0.968
enthalpy of reaction in kJ·mol^{-1}	−62.5	−58.1	−63.3

5.2. Reaction Performed as Batch Reaction. The study was first performed in the batch mode at three different temperatures: 60, 70, and 80 °C. Seventy-five grams (ca. 0.56 mol) of propanoic anhydride were charged into the working reactor, and 43 g (ca. 0.58 mol) of 2-butanol were added; 130 g of water was placed in the reference reactor. To calculate the heat of reaction, it was necessary to know which quantity of reagent had reacted. Therefore, after reaction, the degree of conversion was obtained by chemical analysis of the final reaction mass by gas chromatography.

The results are summarized in Table 2. At 60 and 70 °C, the reaction does not reach completion after 20 h (time at which the study was stopped). At 80 °C, after 20 h, the conversion is practically complete.

These values were corrected by the heat of mixing ($\Delta H_{mix} = +\ 4.2$ kJ·mol^{-1}).[12]

The average value of the enthalpy of reaction obtained for the three temperatures is $-\Delta H_R = 61.63$ kJ·mol^{-1} with a standard deviation of 4.6%. The heat of reaction is independent of the temperature and compares well with literature values: $-\Delta H_R = 60$ kJ·mol^{-1} [13,14] $-\Delta H_R = 64$ kJ·mol^{-1},[15] $-\Delta H_R = 63.7-69.5$ kJ·mol^{-1}.[16]

This shows that the differential reaction calorimeter allows obtaining reliable results for enthalpies of reaction even for slow reactions, which requires a good thermal sensitivity especially at the end of the experiment, where the heat release rate is low and becomes difficult to distinguish from the measurement noise. In such cases, it is essential to complete the measurement by a chemical analysis.[17]

5.3. Reaction Performed as Semi-Batch Reaction. As described in the Introduction, the accumulation of reagents in a semi-batch reactor is essential information for the safety assessment. Therefore, this relatively slow reaction was also performed in the semi-batch mode, that is, with an addition of one of the reagents.

About 100 g (ca. 1 mol) of propanoic anhydride was initially charged into the working reactor, 57 g of 2-butanol (0.77 mol) was added at a constant rate during 100 min using a pump and a balance. The reagent was added in the working reactor only; 170 g of propanoic anhydride was placed in the reference reactor. The variation of reaction volume is about 70 mL in the working reactor.

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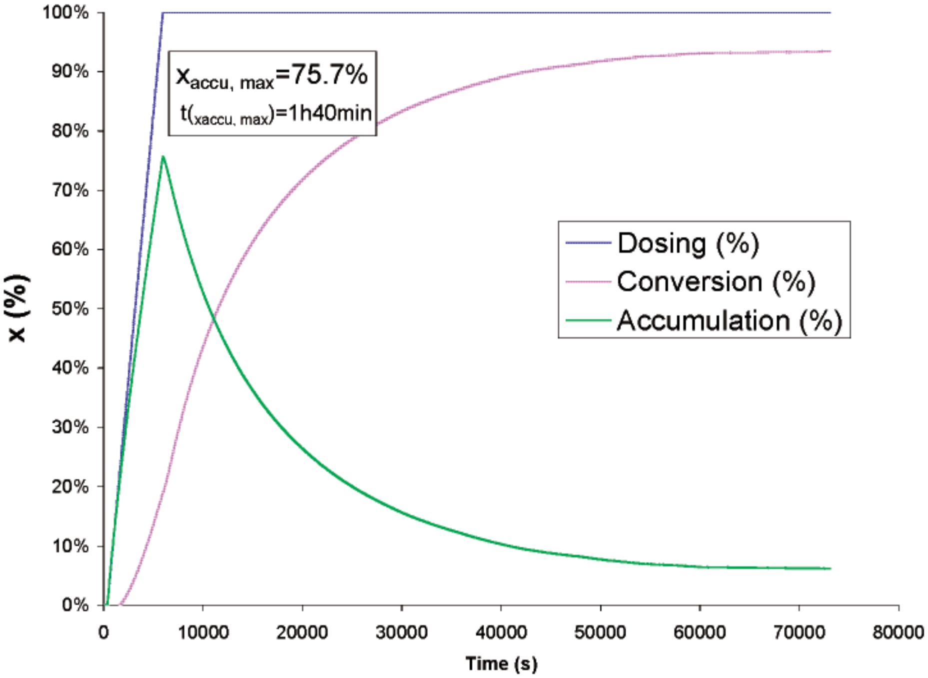

Figure 8. **Feed, conversion, and accumulation in function of time during the esterification of propanoic anhydride with isobutanol at 70 °C as semi-batch reaction.**

Table 3: **Results of esterification reaction in the semi-batch mode**

temperature in °C	70	80
conversion at the end of the experiment	0.934	0.968
enthalpy of reaction in kJ·mol^{-1}	−56.8	−57.6

Table 4: **Results of esterification reaction in the batch mode**

temperature in °C	60	70	80
measured rate constant in L·mol^{-1}·h^{-1}	0.031	0.088	0.226
rate constant from literature in L·mol^{-1}·h^{-1}	0.041	0.093	0.219

The determination of the reaction enthalpy was performed using eq 1, that is, the sensitive heat of the feed was taken into account. The results are summarized in Table 3.

The average of the measured values of the reaction enthalpy in the semi-batch mode is $-\Delta H_R = 57.2 \pm 0.4$ kJ·mol^{-1}. This value is slightly inferior to the value obtained in the batch mode but remains in good agreement with literature values.

The reagent addition as a function of time makes possible the quantitative determination of the instantaneous thermal conversion (X_{th}). In turn, the determination of the thermal conversion, linked with the measure of the percentage of addition enables obtaining the thermal accumulation of reagent:

$$X_{acc} = 1 - X_{th}(t) = 1 - \frac{\int_0^t q_R(t')\mathrm{d}t'}{\int_0^\infty q_R(t')\mathrm{d}t'} \qquad (6)$$

The comparison of the feed with thermal conversion for the 70 °C reaction is represented in Figure 8.

Since butanol is only present in stoichiometric default, the accumulation is maximum (ca. 80%) at the end of the addition and corresponds to an adiabatic temperature rise of 82 °C. This means that a temperature of MTSR = 152 °C could be reached in case of a cooling failure at this instant. In these conditions, the reaction is by far not feed-controlled.

5.4. Kinetic Analysis of the Esterification. For single reactions such as the present esterification, thermal conversion is identical to the chemical conversion. Thus, the kinetics can be evaluated from the experiments performed in the batch-mode by using:

$$X_{th}(t) = \frac{\int_0^t q_R(t')\mathrm{d}t'}{\int_0^\infty q_R(t')\mathrm{d}t'} \qquad (7)$$

Thus, the heat release rate curve (expressed in W/kg) as a function of time can be transformed into conversion curves as a function of time, which content can, in turn, be directly used for the kinetic evaluation. The esterification of propanoic anhydride with 2-butanol is known to be a second-order reaction.[11] The rate constant k was calculated from the experiments performed at 60, 70, and 80 °C respectively and compared to values from a previous work.[18] The results are summarized in Table 4.

An activation energy of 84.4 kJ·mol^{-1} was calculated from these rate constants and agrees well with the value found in the previous work.[18]

Conclusions

Calorimetry, in combination with thermal analysis, is an essential tool for a data-based assessment of thermal risks

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linked with the performance of chemical reactions at industrial scale. The energies of synthesis reactions or of decomposition reaction, as well as the heat capacities of reaction masses, can be measured by these techniques. The performance of the Differential Reaction Calorimeter DRC from SETARAM was demonstrated using two example reactions.

The first and fastest reaction (hydrolysis of acetic anhydride) allowed showing the calorimeter performance in terms of tracking a fast reaction performed in the batch mode. The values of reaction enthalpy are in good agreement with values from the literature.

The second and slowest reaction could be studied in the semi-batch mode as well as in the batch mode. With this example, the performance of the calorimeter for the determination of the reaction enthalpy requiring a good caloric sensitivity was shown. In the semi-batch mode, the accumulation of nonconverted butanol could be quantitatively measured, allowing the establishment of the failure scenario on which the safety study will be based.

Furthermore, since the heat-release rate of a reaction is proportional to its rate, calorimetric methods give access to kinetic data. The examples shown in this paper illustrate the performance of the differential reaction calorimeter in the determination of kinetic data.

The differential reaction calorimeter was found to be a powerful screening tool in an organic synthesis laboratory or in a development laboratory and is especially well suited for a fast and low-cost determination of the thermal parameters of chemical reactions, even when only a few raw materials are available.

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