Screening calorimetry on parallel small scale reactor systems

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The scale up of a reaction from bench top to production requires a good understanding of the process. To gain valuable information of the process in a short time pharmaceutical and chemical companies are starting to use parallel automated reactor systems.

Automated Laboratory Reactors (ALR) allow a precise control under repeatable conditions of critical reaction parameters (temperature, stirring). Performing reaction in parallel with further automation (pH control, dosing) allow to optimize reaction variables in short time and minimal effort. In addition, calorimetric information of each reaction can be obtained for scale up and risk analysis.
The risk assessment of any process should include the following questions:

- Under normal conditions, can the cooling system remove the heat produced by the reaction?
- What will happen if the cooling or power failure occurs? Can measures be takes to keep the process under control?

With the MultiMax ALR system METTLER TOLEDO offers a complete solution for calorimetric screening. Depending on the need two different sizes of reactors can be selected, either 4 reactors with a volume of 20 – 50ml or 2 reactors with a volume of 50 – 250ml each. All reactors have independent temperature and stirring control. For further automation multiple dosing and pH control can be added. Temperature can be controlled by varying the temperature of the reaction mass (T_r) or the temperature of the reactor jacket (T_j). The calorimetric principle based on the heat flow trough the reactor wall.

$$Q_{flow} = U \times A\left(T_j - T_r\right)$$

Q_{flow} : heat flow through reactor wall [W]
U : heat transfer coefficient [W/m^{2}K]
A : heat exchange area [m^2]

In the present work[1] a MultiMax RB04-50 (4 reactors with 50ml each) is used to achieve a better understanding of the first step of a Grignard reaction in an industrial process. The Grignard, as one of the key reaction to form covalent carbon bonds, is a strong exothermic reaction. Therefore a constant control of the reaction temperature is essential to prevent unexpected incidents such as evaporation of the solvent or decomposition.

The use of the MultiMax system helps to understand the process and gain valuable information for a safe transfer to production.

[1] Investigation of a Grignard Reaction at Small Scale; Dr. P. Reuse, Dr. O. Ubrich; METTLER TOLEDO GmbH