

Real time calorimetry without calibration: a new tool for reaction optimization

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The optimization of chemical processes is the primary goal of chemists and engineers in pharmaceutical and chemical process development. A new concept of real time heat measurement allows chemists and engineers to develop robust and simple chemical processes. In the past companies developed open-loop systems to optimize chemical processes. As a prerequisite to optimization, the kinetics of the chemical system considered must be determined. This was done by coupling calorimetry and spectroscopic measurements. Although efficient, the method was also strongly dependent on the accuracy of the kinetic data.

Recently companies have been using real time techniques to establish a more simple process design. A real time optimization implementing a closed-loop algorithm presents strong advantages. The idea is to use real time information combined with a feed back model. *In situ* techniques, including IR spectroscopy, are primarily used.

However, the method described above has some disadvantages. For example, online heat data is unavailable. Heat flow information is crucial for optimization purposes as well as to verify if the process remains within certain boundaries. The optimization of the process has to consider safety and scale-up issues.

In this paper, a new methodology is presented, which allows users to obtain the heat evolution *in situ* in real time without perturbation of the system. The methodology is not affected by large exothermic reactions or by realistic changes in viscosity and heat transfer coefficient. Examples are included that show how the user benefits from this new concept.