133f Modeling and Reactor Design for a Highly Exothermic Reactive System

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The importance of modeling for safe scale-up of processes is discussed by taking a recent example used in the synthesis of a key intermediate for an oncology product. The chemistry involves the conversion of a tertiary alcohol to the desired product, a primary alcohol. If the product in the solution is not quenched immediately, it is consumed to produce the undesired by-products. Accelerating Rate Calorimetry (ARC) experiments show that the mixture is thermally unstable with an onset temperature of approximately 20°C and decomposes rapidly with extremely high pressure and temperature rates. Semi-batch experiments were also performed at two isothermal temperatures on an autoMate calorimeter to capture the heat profile for the desired reaction. The goal is to identify the operating conditions so that the heat dissipated from the desired reaction is effectively removed without causing any localized temperature spikes possibly leading to a thermal run-away. A three step kinetic rate expression is postulated to fit both the heat and concentration profiles. The fitted model is then used in the selection of the best hypothetical reactor configuration to deliver good quality material under safe operating conditions. Experimental validation of the current reactor configuration is confirmed by successfully running both glass-plant and pilot plant scale batches safely and flawlessly.