101f Continuous Reactive Precipitation in a Y-Mixer

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Continuous precipitation of pharmaceutical compounds frequently offers clear advantages over batch processing. For precipitations where a uniformly small (<10 μm) particle size distribution is required, equipment configurations generating uniformly high supersaturation are needed. Opposed jet reactors used at the industrial or lab scale can achieve rapid mixing, producing uniformly high supersaturation and offering high throughput. We have previously used the competitive-parallel fourth Bourne reaction to evaluate the mixing effectiveness in the continuous Y-mixer (opposed-jet). Mixing quality in the Y-mixer shows rapid mixing (<10 ms) at a mean jet velocity of 10 m/s.

An equal-volume mixing model based on the growth of eddies is developed based on Baldyga and Bourne (1999) for conditions of no reaction, infinitely fast, and competitive-parallel reactions. Comparison of these results then allows the assignment of a mixing time that corresponds to 95% completion of physical mixing. Experimental results for selectivity of the fourth Bourne reaction in the Y-mixer over a range of jet velocities, jet diameters and viscosities permits connection of this mixing time to those postulated by turbulent mixing theory. A Corrsin-like model combining meso- and micromixing mechanisms appears to be most appropriate. A second model based on the reaction and diffusion of species in stagnant fluid films shows good agreement with experiment near the poor mixing limit (low jet velocities).

Application of the Y-mixer to the reactive precipitation of model compounds was studied over a range of supersaturation. The progress of the precipitation is followed directly by magnification and dark-field illumination of the exit tube, both under flow and immediately after rapid stopped flow. The number of particles can be tracked after flow has stopped to describe induction times longer than 100 ms. The visual appearance of particles during flow is used to measure times less than 100 ms. Experimental induction times showed significant differences under different reactant concentration ratios. This result is not predicted by the eddy growth model, but is accounted for in a simplified diffusion-reaction model. This suggests that diffusion-induced interfacial gradients on a length scale smaller that of eddies are important in reactive precipitation.

General guidelines for manipulation of particle size distribution in continuous reactive precipitation are suggested including mixing and concentration effects.