

# Organic Process Research & Development

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## *Editorial*

### Continuous Processes in Small-Scale Manufacture

The pharmaceuticals and fine chemical industries have been using batch and semibatch processing for over a hundred years, with little change in the equipment used—the large-scale equivalent of a three-necked flask, condenser, and stirrer, used by all organic chemists in the laboratory. Batch reactors have a number of advantages, particularly flexibility and the ability to be used for a wide range of chemistry. In addition, the equipment is suitable for a wide range of unit operations, including reactions, separations, and crystallisations. Of course, the batch reactor is not an ideal reactor for most scenarios but is a compromise—it may be the least worst option for each unit operation.

For many processes, however, the batch and semibatch reactor is far from ideal, e.g. fast exothermic processes or processes where poor mixing and mass transfer leads to low selectivity, and a continuous process may be preferable. At a recent conference on “Scale-Up of Chemical Processes” in Boston, MA, USA, several speakers indicated a changing attitude to continuous processes for fine chemical, intermediate, and possibly pharmaceutical manufacture and described recent progress in the field. Phoenix Chemicals in the U.K. already have a continuous process operating on about 300 t/a for a pharmaceutical intermediate. This includes not only a continuous reaction but also continuous extraction (which minimises solvent usage) and continuous oxidation of the cyanide waste.

The French company AETDEV has developed a multipurpose reactor, suitable for flexible continuous processing, which uses high temperatures but, at high selectivity, coupled with a short reaction time. Often these reactions are highly intense: i.e., they use little or no solvent. The reactor, which goes by the name of RAPTOR, is easy to clean for product changeover.

This reactor was used for a hydrogenation of an aromatic ring, for which the batch process used 4% catalyst and 4

volumes of solvent, giving 95% yield in 5–6 h. Using the RAPTOR technology, a continuous process gave >99% yield using only 0.4% catalyst without solvent in under 3 min. The product required no purification except for removal of catalyst.

Lonza chemists and engineers have spoken at a number of conferences about the progress they are making in using microreactors for fine chemical manufacture. At the Boston conference, reactors made by Ehrfeld (Germany) and Corning (France) were described for use in organolithium and Grignard chemistry. Up to tonne quantities of intermediates have already been produced using microreactors, with few scale-up issues.

Organic Process Research & Development has been aware of new developments in this area over the past decade, and the Nov/Dec 2001 special issue was devoted to Continuous Processing/Process Intensification. It now seems appropriate to have an updated special issue covering topics and processes which have developed in the intervening years.

Thus, this journal will, in 2008, include a special issue on Continuous Processing (Issue No. 5). We hope to attract authors from both academia and industry and are aiming for 20–25 papers. The papers could be review articles, descriptions of new technology, or reports of a batch process being, for various reasons, converted to a continuous process. All readers are invited to submit papers on this important topic. The deadline for receipt of manuscripts is the end of March 2008. Please contact Sue or myself if you wish to publish in this special issue.

Trevor Laird  
*Editor*

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