Going with the Flow – The Use of Continuous Processing for API Manufacturing

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Continuous flow processes form the basis of the petrochemical and bulk chemicals industry where strong competition, stringent environmental and safety regulations, and low profit margins drive the need for highly performing, cost effective, safe and atom efficient chemical operations. In contrast to the commodity chemical industry, however, the fine chemical industry primarily relies on its existing infrastructure of multipurpose batch or semi-batch reactors. Fine chemicals, such as drug substances and active pharmaceutical ingredients (APIs), are generally considerably more complex than commodity chemicals and usually require numerous, widely diverse reaction steps for their synthesis. These requirements generally make versatile and reconfigurable multipurpose batch reactors the technology of choice for their preparation. However, the advantages of continuous flow processing are increasingly being appreciated also by the pharmaceutical industry and, thus, a growing number of scientists, from research chemists in academia to process chemists and chemical engineers in pharmaceutical companies, are now starting to employ continuous flow technologies on a more routine basis [1].

Flow technology has considerable advantages in mass- and heat transfer, safety and ease of scale-up, when compared to traditional batch reactions. Furthermore, hazardous chemistries such as highly exothermic reactions, or those involving unstable or toxic intermediates can be operated safely in flow, whereby this technology acts as a powerful route-enabler.

In this lecture, contributions from our research group in the field of continuous flow processing will be highlighted. Emphasis will be given to highly atom efficient and process intensified chemical transformations useful for the synthesis of APIs or key intermediates that are often too hazardous to be executed in a batch reactor. These involve azide, diazomethane and nitration chemistry, oxidation reactions involving pure oxygen, and flow photochemistry/electrochemistry applications.

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[1] Gutmann, B.; Cantillo, D.; Kappe, C. O. *Angew. Chem. Int. Ed*. **2015**, 54, 6688.

Speaker Details

C. Oliver Kappe received his undergraduate and graduate education at the University of Graz. After periods of postdoctoral research work at the University of Queensland and at Emory University, he moved back to the University of Graz in 1996 to start his independent academic career. In 1999 he

became Associate Professor and in 2011 was appointed Full Professor for “Technology of Organic Synthesis” at the University of Graz. Professor Kappe has an extensive general experience and a 25 year track record in synthetic and physical organic chemistry, process intensification using batch microwave technology and flow chemistry/microreaction technology, communicated in >500 scientific publications. His current research interests involve continuous flow chemistry, API manufacturing, and process intensification technologies.