Continuous manufacturing as an enabling tool with green credentials in pharmaceutical chemistry

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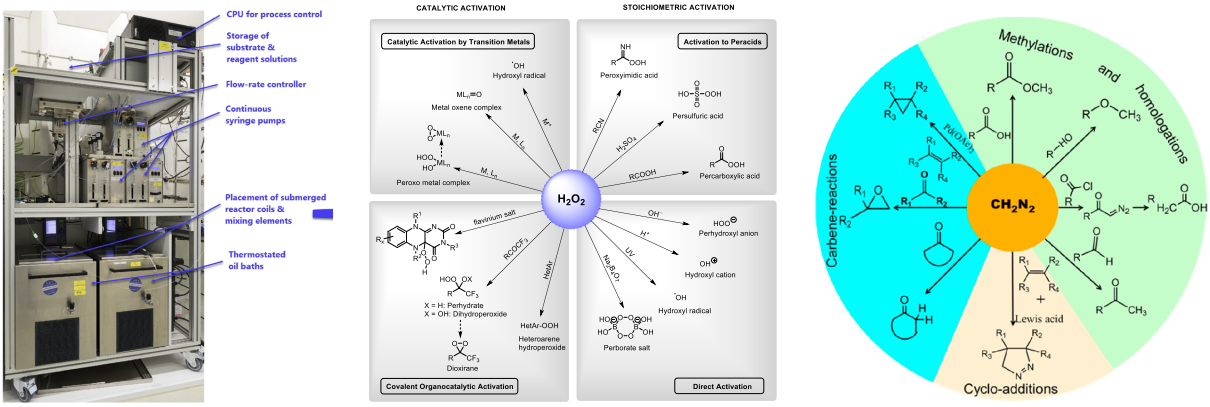
Continuous manufacturing is at the interface of chemistry and engineering and represents an area of high potential in the green chemistry landscape.[1] It is an enabling technology which offers process intensification, synthesis shortcuts and sophisticated separations, amongst other attributes.[2] The combination with process analytical technology (PAT) permits prediction of the reaction outcome through reaction simulation, and supports reactor selection and identification of optimal reaction conditions.[3]



This presentation will describe two case studies from Novartis Chemical R&D to outline how practical, but unstable, reagents can be used in a safe manner for key chemical transformations.[4] Use of hydrogen peroxide[5] and diazomethane[6] will be showcased, beginning by building a mechanistic understanding of the use of these classical reagents with toolbox studies on model compounds. In each case the knowledge is then translated into flow chemistry campaigns to supply pharmaceutical intermediates for clinics. A use of feedstock reagents with wide-utility, coupled with an increase in process throughput and safety underscore the impact of continuous manufacturing as a tool for green processing.

[1] P. Poechlauer, J. Colberg, S. Koenig, B. Martin et al., *Org. Process Res. Dev.,* **2013**, 17, 1472
[2] S. G. Newman, K. F. Jensen, *Green Chem.*, **2013**, 15, 1456
[3] F. Susanne, B. Martin, F. Venturoni et al., *Org. Process Res. Dev.,* **2017**, 21, 1779
[4] B. Martin, H. Lehmann, H. Yang, B. Schenkel et al., *Current Opinion in Green and Sustainable Chemistry*, **2018**, 11, 27
[5] B. Martin, J. Sedelmeier, J. Haber, B. Schenkel et al., *Green Chem.*, **2017**, 19, 1439
[6] H. Yang, B. Martin, B. Schenkel, *Org. Process Res. Dev.,* **2018**, 22, 446