Continuous-Flow Catalysis

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During the past twenty years, flow chemistry has emerged as an enabling tool to simplify, accelerate, integrate, scale-up and automatize chemical reactions [1]. Nowadays, it exhibits an inherently safer and greener nature over classical batch processes. Flow chemistry and catalysis have been demonstrated to represent an ideal match for the sustainable synthesis of an array of valuable products including biologically active substances, natural products and active pharmaceutical ingredients (APIs) [2–4]. Either heterogeneous or homogeneous catalytic reactions can be significantly advanced by the technical merits of continuous-flow processing and microreaction technology. Reactions involving gases, hazardous substances and reactive intermediates, as well as photo- and electrocatalytic transformations, can especially be facilitated by the benefits of flow chemistry. With increasing societal and economical pressure on sustainability, costs and quality, the pharmaceutical industry is gradually comprehending the concept of continuous-flow manufacturing, whilst the FDA (U.S. Food and Drug Administration) and the EMA (European Medicines Agency) are actively exploring this technology and its potentials [5]. This Special Issue therefore covered recent research on the subject of all aspects of catalytic reactions performed in various continuous-flow systems.

In a review paper by Fuse and co-workers, recent continuous-flow processes using metal-free homogeneous catalysts were surveyed [6]. The review compares continuous-flow results with conventional batch experiments and highlights the benefits and also the disadvantages of metal-free catalytic approaches utilizing either acidic, basic or miscellaneous catalysts.

In an excellent contribution by Tamborini and co-workers, flow-based chemoenzymatic synthesis of selected APIs is presented [7]. A bioreactor was exploited to yield valuable amide and ester intermediates, which were next processed into the final API by means of in-line purification and continuous-flow hydrogenation.

Sá and co-workers investigated the effect of palladium doping on a nano-nickel catalyst during the hydrogenation of sulcatone under continuous-flow conditions [8]. The authors observed that doping enhanced hydrogen activation on the catalyst, which was found to be a rate-limiting step using kinetic isotopic measurements and theoretical calculations.

Gruber-Woelfler and co-workers reported the optimization of a chemoenzymatic tandem reaction under flow conditions and demonstrated its application for the synthesis of pharmacologically active substances, resveratrol and pterostilbene [9]. The process involved the enzymatic decarboxylation of coumaric acid followed by a telescoped Heck coupling of the corresponding vinylphenol intermediate with an aryl iodide using a heterogeneous palladium catalyst in a packed bed reactor.

Selva and co-workers reported a two-step sequence by combining batch and flow protocols for upgrading aminodiols regioisomers derived from glycerol [10]. Initially, catalyst-free N-acetylation furnished the corresponding amide intermediates, which were next transformed into the desired amide-acetal products by means of selective continuous-flow acetalization in the presence of a solid acid catalyst.

Len and co-workers demonstrated an interesting continuous-flow protocol for the oligomerization of glycerol under microwave activation in the presence of potassium carbonate as a readily available homogeneous basic catalyst [11]. The effects of temperature

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and residence time were thoroughly investigated to strategically control the distribution of oligomers.

This collection gave excellent recent examples on how catalysis and flow chemistry can jointly advance the synthesis and manufacture of valuable products and their useful intermediates.

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