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Continuous API Synthesis using Heterogeneous Catalysis

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The pharmaceutical industry currently experiences a trend towards continuous manufacturing as there are many advantages, including better control of process conditions, effectively eliminating batch-to-batch variability, and the lack of scale-up problems, since even bench-top continuous systems can produce the desired quantities required in the pharmaceutical or fine-chemicals industry.
We present the development of continuous processes for the synthesis of active pharmaceutical ingredients (APIs). The set-ups include heterogeneous organometallic catalysts (titanocenes and Pd-complexes) that are ideally suited for these continuous processes. The covalent bond between the catalysts and the solid support effectively prevents metal leaching into the product. For this purpose we developed novel methods for catalyst immobilization [1, 2] including photolithographic techniques that allow a precise molecular control of the location and dispersion of the catalytic sites on the surface of the materials.
The application of the heterogeneous catalysts for the synthesis of chiral amines and substituted biphenyls [3] and the successful implementation in different lab-scale continuous flow systems, such as packed bed reactors, monolithic structures and microfluidic devices, showed that the continuous flow setups lead to improved practicability and flexibility of the processes. Thus, these novel reaction systems constitute promising alternatives to existing batch applications.
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