

Catalytic cascade reactions for syntheses of sartanes in continuous flow

Katharina Hiebler, Heidrun Gruber-Woelfler

Institute of Process and Particle Engineering, Graz University of Technology, 8010
Graz, Austria

For the synthesis of active pharmaceutical ingredients (APIs), continuous-flow processes have gained increasing attention in the course of last years.^[1-3] As flow reactors have a lot of benefits including improved energy efficiency, reduced waste generation and safety, the Federal Drug Administration (FDA) aims for application of continuous synthesis in pharmaceutical manufacturing in order to establish more sustainable reaction protocols.^[1,4] Our work targets the development of catalytic cascade reactions for the syntheses of valsartan and sacubitril in continuous flow. The compounds are well known as APIs in a combination drug for the treatment of hypertension and chronic heart failure (Entresto[®], Novartis).^[5,6] The key step of our process, the formation of the biaryl unit, is a Suzuki-Miyaura cross-coupling reaction employing a novel heterogeneous palladium catalyst.^[7] In the first approach, the catalytic reaction will be carried out in a modular fixed bed reactor, developed in our lab.^[8] Furthermore, the utilization of benign solvents (EtOH, H₂O) and enzyme-catalyzed transformation is intended in order to implement a green reaction procedure in continuous flow.

The authors kindly acknowledge the funding by the H2020-FETOPEN-2016-2017 programme of the European commission (Grant agreement number: 737266-ONE FLOW)

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