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ON C-H ACTIVATION

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IL09 – Merging C-H Activation and Flow Technology –  
Enabling the Scalable Synthesis of Pharmaceuticals

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Continuous flow processes form the basis of the petrochemical and bulk chemicals industry where strong competition drives the need for highly performing, cost-effective, safe and atom-efficient chemical operations. 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. 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. Owing to the small reactor volumes, the overall safety of the process is significantly improved, even when harsh reaction conditions are applied. Thus, microreactor technology offers a unique way to perform ultrafast, exothermic reactions, and allows the execution of chemistries which proceed via highly unstable or even explosive intermediates.<sup>1</sup>

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 rely on C–H activation and related chemistries including photoredox catalysis,<sup>2</sup> catalytic cross-dehydrogenative-coupling (CDC),<sup>3</sup> the direct arylation of arenes,<sup>4</sup> Fenton chemistry, and the C–H activation of methyl groups using Pd/O<sub>2</sub>.

### References

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