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THE FUTURE OF BIOMEDICAL RESEARCH

CIPF Lecture Series

Continuous Flow in Medicinal Chemistry: opening new chemical space for Drug Discovery

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Date: **10/12/19- 12:30 h**
Place: Salón de Actos CIPF

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Continuous flow chemistry has recently emerged as a novel chemical tool that can help synthetic chemists to combine efficiency and sustainability. Implementation of this technology in the Pharma industry started more than 10 years ago in Development, where its main advantages (High control of the reaction variables, heat and mass transfer; access to novel process windows, easier reproducibility and scalability) have helped process chemist to improve procedure for active principal ingredient (API) synthesis.

However, this technology did not attract much attention in Discovery, where speedy preparation of a pool of target compounds is usually required. Batch protocols at this stage are robust to perform the synthesis of compound libraries in parallel using well established procedures. So, many Medicinal Chemists are still wondering what value Flow Chemistry can add at this stage.

In order to introduce this technology in a Drug Discovery setting, different methodologies have been developed to overcome current limitations of the batch platform, such as, escaping the flatland. Easy access to organometallic reagents by just flowing halogenated derivatives through a column filled with the corresponding metal (zinc[1] or magnesium[2]) allows to get compounds with increase C(sp^3) ratios and better pharmacokinetic properties.[3] More recently, the addition of photochemistry in flow has allowed medicinal chemists to access new chemical space in multigram amounts, overcoming the limitations of batch. These flow approaches are currently having an impact at all levels of the Drug Discovery process in our company, from Hit to Lead to Late Lead Optimization.

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[1] M. Berton, L. Huck, J. Alcázar, *Nat. Protoc.*, **2018**, *13*, 324.
[2] L. Huck, A. de la Hoz, A. Díaz-Ortiz, J. Alcázar, *Org. Lett.* **2017**, *19*, *3747*
[3] T. Tsukamoto, *ACS Med. Chem. Lett*. **2013**, *4*, 369.

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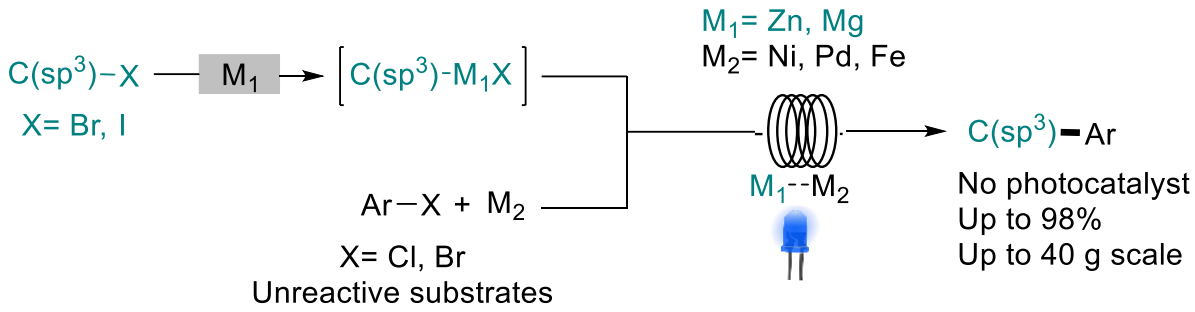

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