Accelerating small organic molecules scale up with data-rich experimentation

Ekaterina Trushina[1,2] Joshua Derasp[1,2] Matthew Reish[1,2] Wenyu Zhang[1,2] Arcadia Lau[1,2] Jason Hein[1,2,3]
[1]Department of Chemistry, University of British Columbia, Vancouver, British Columbia, Canada [2]Acceleration Consortium, University of Toronto, Toronto, Ontario, Canada [3]Department of Chemistry, University of Bergen, Bergen, Norway

Correspondence to: Ekaterina Trushina etrushina@chem.ubc.ca

1. Introduction

Vast majority of automated platforms in chemistry are discovery focused with the main goal to accelerate identification and testing of promising drug candidates or high-performance materials [1]. However champion molecules scale up and industrial deployment often become very time and resource consuming due to chemical and process challenges as well as addressing safety, environmental and economical concerns. Our team's goal was to develop workflow to support and accelerate small organic molecules scale up leveraging benefits of automation and data rich experimentation.

2. Results and Discussion

The proposed workflow (Fig. 1) is based on existing capabilities of our team as well as ongoing developments to complete meaningful pipeline. All our work focuses on principle of flexible automation [2] leveraging benefits of commercially available and in-house developed modules allowing high flexibility of developed workflows.

It shall be noted that importance of purification optimization is often overlooked despite the process being extremely challenging yet crucial for quality of the final target. Therefore, in our approach we introduce opportunity for parallel optimization of the synthesis and purification. Our team has developed and currently validating two automated platforms for optimization of liquid-liquid extraction (LLE) and crystallization – two ubiquitous purification techniques.

In relation to synthesis, our capabilities are rooted in use of variety of online reaction monitoring tools in order to gather extensive datasets allowing deeper understanding of reaction mechanism and kinetics. Starting investigation from smaller scale (5-50 mL) on our custom automated kinetics platform, continuing on medium scale (50-500 mL) with the use of Easymax automated reactor (industry standard for automated synthesis) and DILC system [3], we aim to complete our optimization on custom scale up platform (up to 1 L) to access scalability of optimized protocols.

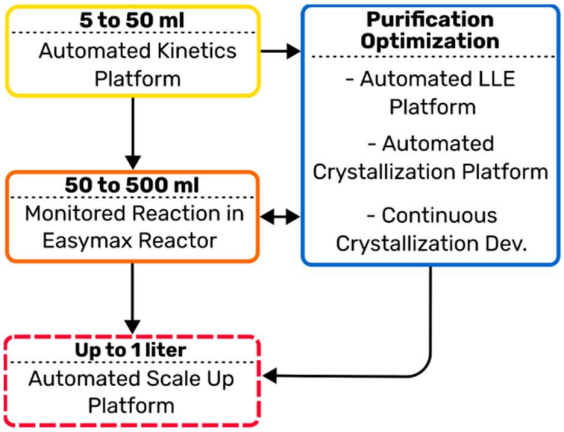

Fig. 1: Automation scale up pipeline (solid line – existing capabilities; dashed line – under development)

3. Conclusion

Developed automated workflow is devoted to scale up acceleration via use of data-rich experimentation, streamlining process optimization with self-driving labs as well as reducing long term cost through use of automation.

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