

Novel process windows as gate opener towards green chemistry

Citation for published version (APA):

Shahbazali, E., & Hessel, V. (2014). Novel process windows as gate opener towards green chemistry. In *Advances in innovative experimental methodology or simulation tools used to create, test, control and analyse systems, materials and molecules (NEXTLAB 2014)*, Rueilmalmaison, France, 2-4 April 2014)

Document status and date:

Published: 01/01/2014

Document Version:

Publisher's PDF, also known as Version of Record (includes final page, issue and volume numbers)

Please check the document version of this publication:

- A submitted manuscript is the version of the article upon submission and before peer-review. There can be important differences between the submitted version and the official published version of record. People interested in the research are advised to contact the author for the final version of the publication, or visit the DOI to the publisher's website.
- The final author version and the galley proof are versions of the publication after peer review.
- The final published version features the final layout of the paper including the volume, issue and page numbers.

[Link to publication](#)

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal.

If the publication is distributed under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license above, please follow below link for the End User Agreement:

www.tue.nl/taverne

Take down policy

If you believe that this document breaches copyright please contact us at:

openaccess@tue.nl

providing details and we will investigate your claim.

Novel Process Windows as Gate Opener Green Chemistry

Elnaz Shahbazali, Timothy Noël, Qi Wang, Volker Hessel

Eindhoven University of Technology, Department of Chemical Engineering and Chemistry,
Micro Flow Chemistry and Process Technology, Eindhoven, The Netherlands

Abstract

Micro Process Technology has given strong push to continuous chemical manufacture via facilitating heat and mass transfer (transport intensification). The next big step is to develop tailored process chemistry in flow under highly intensified conditions: Flow Chemistry. This has been coined Novel Process Windows [1-3] and has two research pillars, – the exploration of unusual and typically harsh process conditions (chemical intensification) and, in a more holistic picture, a completely new and often simpler process design (process-design intensification).

The 1,3-Huisgen cycloaddition (Click Chemistry), the Claisen and Johnson-Claisen rearrangements, the Heck C-C coupling, the Hantzsch dihydropyridine synthesis, the H₂O₂-based direct adipic acid synthesis, and more were processed harshly and chemically intensified [3-7]. Emphasis will be given on homogeneous catalysis applications in flow [4]. Click Chemistries can be integrated in multi-step (tandem, cascade, ...) synthesis which is done at the example of Rufinamide synthesis (Top200 5-ring drug) [3,4]. All reactions stand for generic approaches to boost reactivity via high-T, high-p, high-c (solvent-free; alternative solvent) concepts and more. The use of alternative energy for reaction activation will be exemplified at the Claisen rearrangement. A photo-route opens new synthetic possibilities which are further diversified by direct flow-to-flow coupling to the reaction forming the Claisen precursor [5]. Yet, regioisomers are formed via biradicalic intermediates. Then, the question to answer is – experimentally and theoretically (QM calculations) – if novel process windows can control the reaction course and in this way steer the product formation, i.e. the isomeric ratio. Recently, biotechnology and flow chemistry merged into enzymatic microreactors (alpha amino alcohols from Threonine Aldolase, transesterifications from Lipase) [6]. Main issue here is to achieve productivity, sufficient at least for pharma level. Starting from such new reaction designs, new process designs in flow are developed, such as the large-scale industrial direct adipic acid [7] and hydroformylation processes [4]; with major consequences on CAPEX/OPEX costs [6,8,9] sustainability [10], and energy consumption (heat integration, pinch analysis) [11].

- [1] V. Hessel, *Chem. Eng. Technol.* **32**, 11 (2009) 1655-1681.
- [2] V. Hessel, B. Cortese, M.H.J.M. de Croon, *Chem. Eng. Sci.* **66**, 7 (2011) 1426-1448.
- [3] V. Hessel, D. Kralisch, N. Kockmann, T. Noel, Q. Wang, Q., *ChemSusChem* **6**, 5 (2013) 746-789.
- [4] E. Shahbazali, V. Hessel, T. Noël, Q. Wang, *Nanotechnology Reviews* (2013) DOI: 10.1515/ntrev-2013-0017/
- [5] H. Kobayashi, B. Driessen, T. Noël, V. Hessel et al., *Tetrahedron* **69**, 14 (2013) 2885-2890.
- [6] I. Dencic, J. Meuldijk, M.H.J.M. de Croon, V. Hessel, *J. Flow Chem.* **1**, 1 (2011) 13-23.
- [7] M. Shang, T. Noël, Q. Wang, V. Hessel, *Chem. Eng. Technol.* **38**, 6 (2013) 1001-1009.
- [8] F. Benaskar, V. Hessel, L.A. Hulshof, J.C. Schouten et al., *J. Flow Chem.* **1**, 2 (2011) 74-89.
- [9] I. Vural-Gürsel, V. Hessel, Q. Wang, T. Noël, J. Lang, *Green Process. Synth.* **1**, 4 (2012) 309-404.
- [10] Q. Wang, I. Vural-Gürsel, M. Shang, V. Hessel, *Chem. Eng. J.* **234** (2013) 300-311.
- [11] I. Vural-Gürsel, Q. Wang, T. Noël, V. Hessel, J. T. Tinge, *Ind. Eng. Chem. Res.* **52**, 23 (2013) 7827-7835.

Elnaz Shahbazali, PhD student, Den Dolech 2- 5612 AZ, P.O. Box 513, Helix STW 1.38, 5600 MB
Eindhoven, The Netherlands, +31402478086, e.shahbazali@tue.nl