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In this Section of the journal, the literature on continuous flow synthesis (primarily organic synthesis and functional materials) from the period of January – March 2016 is presented. All the publications are listed ordered by journal name, with a Review article appearing at the end. In this quarter the number of papers on continuous flow organic synthesis is significantly higher than in the previous quarters. Also, the overall number of papers has increased by almost 30% as compared to any quarter in 2015. Let's hope that the trend continues throughout 2016!

1. Highlighted Articles

On-Demand Continuous-Flow Production of Pharmaceuticals in a Compact, Reconfigurable System

A. Adamo, R. L. Beingessner, M. Behnam, J. Chen, T. F. Jamison, K. F. Jensen, J.-C. M. Monbaliu, A. S. Myerson, E. M. Revalor, D. R. Snead

Science 2016, 352, 61-67

These authors have demonstrated a path breaking approach that leads to end-to-end synthesis of known active pharmaceutical ingredients (mainly hydrochlorides) and their formulation in a compact, reconfigurable manufacturing platform. This demonstration shows the path forward for decentralized pharmaceutical manufacturing through very neat integration of chemistry and robust engineering in a miniaturized form to achieve such a milestone in the science of chemical synthesis. The flexible plugand-play approach including membrane separation for work-up would enable the advancement in several domains associated with flow synthesis with real-time formulation. This approach would also pose a real technology challenge for the generic versions of drugs and so would give a significant advantage to innovators of new molecules.

Life Cycle Assessment of Multi-Step Rufinamide Synthesis - from Isolated Reactions in Batch to Continuous Microreactor Networks

D. Ott, S. Borukhova, V. Hessel

Green Chemistry 2016, 18, 1096–1116

Interconnections between different synthesis steps with a feed-back in terms of different indices (viz. atom economy, efficiency, solvent quantity, etc.) that govern the efficacy of chemistry are used for implementation for life cycle analysis for the multi-step flow synthesis of rufinamide. Use of harsh conditions for achieving a difficult activation and the use of chlorides for azide formation is novel. This will have interesting implications when it comes to scale-up. The proposed end goal of the extensive analysis to identify the best fully continuous multi-reaction network, having uninterrupted flow from the first step until the end product is obtained is laudable.

The non-Aqueous Synthesis of Shape Controllable Cu 2- x S Plasmonic Nanostructures in a Continuous-Flow Millifluidic Chip for the Generation of Photo-Induced Heating

T.-L. Cheung, L. Hong, N. Rao et al.

Nanoscale 2016, 8, 6609-6622

Synthesis of copper sulfide nanocrystals with different shapes and sizes in a non-aqueous surfactant-free environment is reported. The shape and size selectivity are demonstrated by simply controlling the flow rates and precursor concentrations. It is an important contribution to the flow synthesis as from the same precursors the synthesis approach leads to formation of copper-deficient covellite (CuS), spionkopite (Cu_{1.39}S), roxbyite (Cu_{1.75}S) and copper-rich djurleite (Cu_{1.94}S).

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Synthesis of Nitro-Containing Compounds through Multistep Continuous Flow with Heterogeneous Catalysts

H. Ishitani, Y. Saito, T. Tsubogo, S. Kobayashi

Organic Letters 2016, 18, 1346-1349

Synthesis of β -nitrostyrene derivatives from aromatic aldehydes and nitromethane and their following reactions with heterogeneous catalysts is an interesting synthesis approach for the nitration chemistry. Use of amino-functionalized silica gel as a catalyst for synthesis of several derivatives for over 100 hr with high selectivity has been reported. In the second step, reactions of β -nitrostyrenes with solid bases, immobilized bases, solid acids, and chiral supported metals and nonmetals used as catalysts has resulted in a library of nitro-containing organic compounds. This achieves an almost no work-up approach which is always desired by the synthesis community at large.

Organic synthesis

"Solvent-Free Continuous Operations Using Small Footprint Reactors: A Key Approach for Process Intensification" T. Ouchi, R. J. Mutton, V. Rojas, D. E. Fitzpatrick, D. G. Cork, C. Battilocchio, S. V. Ley ACS Sustainable Chemistry & Engineering **2016**, *4*, 1912–1916

"A Review on Continuous-Flow Microfluidic PCR in Droplets: Advances, Challenges and Future" Y. Zhang, H.-R. Jiang

Analytica Chimica Acta 2016, 914, 7-16

"Microfluidic Synthesis Enables Dense and Uniform Loading of Surfactant-Free PTSN Nanocrystals on Carbon Supports for Enhanced Ethanol Oxidation"

F. Wu, D. Zhang, M. Peng, Z. Yu, X. Wang, G. Guo, Y. Sun Angewandte Chemie International Edition **2016**, *55*, 4952–4956

"Influence of High Power Ultrasound on Brettanomyces and Lactic Acid Bacteria in Wine in Continuous Flow Treatment" L. Gracin, A. R. Jambrak, H. Juretić, S. Dobrović, I. Barukčić, M. Grozdanović, G. Smoljanić *Applied Acoustics* **2016**, *103*, 143–147

"Three New Trixane Glycosides Obtained from the Leaves of Jungia Sellowii Less. Using Centrifugal Partition Chromatography" Azevedo L, Faqueti L, Kritsanida M, et al. *Beilstein Journal of Organic Chemistry* **2016**, *12*, *674–683*

"Scope and Mechanism of the Highly Stereoselective Metal-Mediated Domino Aldol Reactions of Enolates with Aldehydes" M. E. Cinar, B. Engelen, M. Panthöfer, H.-J. Deiseroth, J. Schlirf, M. Schmittel *Beilstein Journal of Organic Chemistry* **2016**, *12*, 813–824

"Continuous Flow Negishi Cross-Couplings Employing Silica-Supported Pd-PEPPSI-Ipr Precatalyst" G. A. Price, A. R. Bogdan, A. L. Aguirre, T. Iwai, S. W. Djuric, M. G. Organ *Catalysis Science & Technology* **2016**, DOI: 10.1039/c6cy00331a

"Synthesis In Mesoreactors: Ru(Porphyrin)CO-Catalyzed Aziridination of Olefins under Continuous Flow Conditions" S. Rossi, A. Puglisi, M. Benaglia, D. M. Carminati, D. Intrieri, E. Gallo E *Catalysis Science & Technology* **2016**, DOI: 10.1039/C6CY00207B

"Continuous Flow Adsorption of Methylene Blue by Cellulose Nanocrystal-Alginate Hydrogel Beads in Fixed Bed Columns" N. Mohammed, N. Grishkewich, H. A. Waeijen, R. M. Berry, K. C. Tam *Carbohydrate Polymers* **2016**, *136*, 1194–1202

"Hydrodeoxygenation of Methyl Palmitate over MCM-41 Supported Nickel Phosphide Catalysts" Q. Guan, F. Wan, F. Han, Z. Liu, W. Li *Catalysis Today* **2016**, *259*, 467–473

"Scalable Synthesis of Palladium Icosahedra in Plug Reactors for the Production of Oxygen Reduction Reaction Catalysts" H. Wang, G. Niu, M. Zhou, X. Wang, J. Park, S. Bao, M. Chi, Z. Cai, Y. Xia *ChemCatChem* **2016**, *8*, 1658–1664

"Efficient Continuous Synthesis of High Purity Deep Eutectic Solvents by Twin Screw Extrusion" D. Crawford, L. Wright, S. James, A. Abbott *Chemical Communications* **2016**, *52*, 4215–4218

"Droplet Synthesis of Silver Nanoparticles by a Microfluidic Device" L. Xu, J. Peng, M. Yan, D. Zhang, A. Q. Shen *Chemical Engineering and Processing: Process Intensification* **2016**, *102*, 186–193

"Direct Photolysis of Benzoylecgonine under UV Irradiation at 254nm in a Continuous Flow Microcapillary Array Photoreactor" D. Russo, D. Spasiano, M. Vaccaro, R. Andreozzi, G. L. Puma, N. M. Reis, R. Marotta X *Chemical Engineering Journal* **2016**, *283*, 243–250

"Olive Mill Wastewater Valorisation through Phenolic Compounds Adsorption in a Continuous Flow Column" D. Frascari, A. E. M. Bacca, F. Zama, L. Bertin, F. Fava, D. Pinelli *Chemical Engineering Journal* **2016**, *283*, 293–303

"Utilization of Milli-Scale Coiled Flow Inverter in Combination with Phase Separator for Continuous Flow Liquid-Liquid Extraction Processes"

I. V. Gürsel, S. K. Kurt, J. Aalders, Q. Wang, T. Noël, K. D. Nigam, N. Kockmann, V. Hessel *Chemical Engineering Journal* **2016**, *283*, 855–868

"Continuous Microreactor Synthesis of ZIF-8 with High Space–Time-Yield and Tunable Particle Size" Polyzoidis, T. Altenburg, M. Schwarzer, S. Loebbecke, S. Kaskel *Chemical Engineering Journal* **2016**, *283*, 971–977

"Microfluidic Synthesis of Monodispersed CDSE Quantum Dots Nanocrystals by Using Mixed Fatty Amines as Ligands" Z.-H. Tian, J.-H. Xu, Y.-J. Wang, G.-S. Luo *Chemical Engineering Journal* **2016**, *285*, 20–26

"Continuous Microfluidic Synthesis and Functionalization of Gold Nanorods" L. Uson, V. Sebastian, M. Arruebo, J. Santamaria *Chemical Engineering Journal* **2016**, *285*, 286–292

"Reaction Engineering Studies of the Continuous Synthesis of Cuins₂ and Cuins₂/Zns Nanocrystals" S. Tian, M. Fu, W. Hoheisel, L. Mleczko *Chemical Engineering Journal* **2016**, *289*, 365–373

"Design of Highly Selective Platinum Nanoparticle Catalysts for the Aerobic Oxidation of Ka-Oil Using Continuous-Flow Chemistry" A. M. Gill, C. S. Hinde, R. K. Leary, M. E. Potter, A. Jouve, P. P. Wells, P. A. Midgley, J. M. Thomas, R. Raja *ChemSusChem* **2016**, *9*, 417–417

"Scalability of Continuous Flow Production of Metal–Organic Frameworks" M. Rubio-Martinez, T. D. Hadley, M. P. Batten, K. Constanti-Carey, T. Barton, D. Marley, A. Mönch, K. S. Lim, M. R. Hill *ChemSusChem* **2016**, *9*, 938–941

"The Generation of a Library of Bromodomain-Containing Protein Modulators Expedited by Continuous Flow Synthesis" P. Filipponi, I. R. Baxendale

European Journal of Organic Chemistry 2016, 2000-2012

"An Efficient Continuous Flow Process for the Synthesis of a non-Conventional Mixture of Fructooligosaccharides" P. Zambelli, L. Tamborini, S. Cazzamalli, A. Pinto, S. Arioli, S. Balzaretti, F. J. Plou, L. Fernandez-Arrojo, F. Molinari, P. Conti *Food Chemistry* **2016**, *1*, 607–613

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D. Ott, S. Borukhova S, V. Hessel Green Chemistry 2016, 18, 1096–1116

"The Synthesis of Di-Carboxylate Esters Using Continuous Flow Vortex Fluidics" J. Britton, S. B. Dalziel, C. L. Raston *Green Chemistry* **2016**, *18*, 2193–2200

"Synthesis and Textural Characterization of Mesoporous and Meso-/Macroporous Silica Monoliths Obtained by Spinodal Decomposition"

A. Galarneau, Z. Abid, B. Said, Y. Didi, K. Szymanska, A. Jarzębski, F. Tancret, H. Hamaizi, A. Bengueddach, F. Di Renzo *Inorganics* **2016**, *4*, 9

"Microfluidic Biocatalysis Enhances the Esterification of Caffeic Acid and Methanol Under Continuous-Flow Conditions" S. S. Wang, Z. J. Li, S. Sheng, F. A. Wu, J. Wang *Journal of Chemical Technology and Biotechnology* **2016**, *91*, 555–562

"Isolation, Characterization and Evaluation of Photochemical Potential of Rice Husk-Based Furfural via Continuous Flow Reactor" H. Nsubuga, C. Basheer, H. A. S. Al-Muallem, A. N. Kalanthoden *Journal of Environmental Chemical Engineering* **2016**, *4*, 857–863

"Artificial Fluorogenic Substrates in Microfluidic Devices for Bacterial Diagnostics in Biotechnology" C. E. M. Krämer, W. Wiechert, D. Kohlheyer *Journal of Flow Chemistry* **2016**, *6*, 3–7

"Continuous-Flow Biochemical Reactors: Biocatalysis, Bioconversion, and Bioanalytical Applications Utilizing Immobilized Microfluidic Enzyme Reactors" L. Hajba, A. Guttman

Journal of Flow Chemistry 2016, 6, 8–12

"Application of Enzyme-Immobilization Technique for Microflow Reactor" H. Yamaguchi, T. Honda, M. Miyazaki *Journal of Flow Chemistry* **2016**, *6*, 13–17 "A Microfluidic Toolbox for the Development if In-Situ Product Removal Strategies in Biocatalysis" S. Heintz, A. Mitic, R. H. Ringborg, U. Krühne, J. M. Woodley, K. V. Gernaey *Journal of Flow Chemistry* **2016**, *6*, 18–26

"NADH Oxidation in a Microreactor with an Oscillating Magnetic Field" A. S. Katarina, P. G. Hojnik, P. Nikolina, N. Maja, L. B. Zelić *Journal of Flow Chemistry* **2016**, *6*, 27–32

"Continuous Lipase B-Catalyzed Isoamyl Acetate Synthesis in a Two-Liquid Phase System Using Corning[®] AFR[™] Module Coupled with a Membrane Separator Enabling Biocatalyst Recycle" U. Novak, D. Lavric, P. Žnidaršič-Plazl *Journal of Flow Chemistry* **2016**, *6*, 33–38

"Catalytic Pseudomonas Taiwanensis VLB120∆C Biofilms Thrive in a Continuous Pure Styrene Generated by Multiphasic Segmented Flow in a Capillary Microreactor" B. Halan, R. Karande, K. Buehler, A. Schmid

Journal of Flow Chemistry 2016, 6, 39–42

"Microfluidic Multiple Cell Chip Reactor Filled with Enzyme-Coated Magnetic Nanoparticles — An Efficient and Flexible Novel Tool for Enzyme Catalyzed Biotransformations" F. Ender, D. Weiser, B. Nagy, C. László, B. Csaba, P. Pálovics, L. Poppe *Journal of Flow Chemistry* **2016**, *6*, 43–52

"Characterization of Microchannel Hemodialyzers Using Residence Time Distribution Analysis" M. Coblyn, A. Truszkowska, G. Jovanovic *Journal of Flow Chemistry* **2016**, *6*, 53–61

"Magnetic Catalysts as Nanoactuators to Achieve Simultaneous Momentum-Transfer and Continuous-Flow Hydrogen Production" Y. Liu, J. Zhang, X. Zhang, B. Li, X. Wang, H. Cao, D. Wei, Z. Zhou, A. K. Cheetham *Journal of Materials Chemistry* **2016**, *4*, 4280–4287

"Development of a Novel Process to Mitigate Membrane Fouling in a Continuous Sludge System by Seeding Aerobic Granules at Pilot Plant"

M. Sajjad, I. S. Kim, K. S. Kim Journal of Membrane Science **2016**, 497, 90–98

"Selective Catalytic Oxidation of Benzene over Cu/Ti/HZSM-5 under Low Oxygen Pressure for One Step Synthesis of Phenol" A. Okemoto, Y.-h. Tsukano, A. Utsunomiya, K. Taniya, Y. Ichihashi, S. Nishiyama Journal of Molecular Catalysis A: Chemical **2016**, 411, 372–376

"Ultrafine Palladium Nanoparticles Immobilized into Poly (4-Vinylpyridine)-Based Porous Monolith for Continuous-Flow Mizoroki-Heck Reaction"

R. P. Jumde, M. Marelli, N. Scotti, A. Mandoli, R. Psaro, C. Evangelisti *Journal of Molecular Catalysis A: Chemical* **2016**, *414*, 55–61

"Increased Cyclic Guanosine Monophosphate Levels and Continuous-Flow Left-Ventricular Assist Devices: Implications for Gastrointestinal Bleeding"

L. Grosman-Rimon, L. C. Tumiati, A. Fuks, I. Jacobs, S. D. Lalonde, D. Z. Cherney, V. Rao *The Journal of Thoracic and Cardiovascular Surgery* **2016**, *151*, 219–227

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"Continuous Flow Photochemistry as an Enabling Synthetic Technology: Synthesis of Substituted-6(5H)-Phenanthridinones for Use as Poly(ADP-Ribose) Polymerase Inhibitors" Y. Fang, G.K. Tranmer

MedChemComm 2016, 7, 720-724

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MedChemComm 2016, 7, 732-732

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"Continuous Flow Magnesiation or Zincation of Acrylonitriles, Acrylates, and Nitroolefins. Application to the Synthesis of Butenolides" M. A. Ganiek, M. R. Becker, M. Ketels, P. Knochel *Organic Letters* **2016**, *18*, 828–831

"Short Flow-Photochemistry Enabled Synthesis of the Cytotoxic Lactone (+)-Goniofufurone" M. Ralph, S. Ng, K. I. Booker-Milburn *Organic Letters* **2016**, *18*, 968–971

"Generation and Synthetic Application of Trifluoromethyl Diazomethane Utilizing Continuous Flow Technologies" B. U. Pieber, C. O. Kappe *Organic Letters* **2016**, *18*, 1076–1079

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"High-Temperature Boc Deprotection in Flow and Its Application in Multistep Reaction Sequences" A. R. Bogdan, M. Charaschanya, A. W. Dombrowski, Y. Wang, S. W. Djuric *Organic Letters* **2016**, *18*, 1732–1735

"Asymmetric Synthesis of N-Boc-(R)-Silaproline via Rh-Catalyzed Intramolecular Hydrosilylation of Dehydroalanine and Continuous Flow N-Alkylation" J. Y. Chung, M. Shevlin, A. Klapars, M. Journet

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"Continuous-Flow Process for Selective Mononitration of 1-Methyl-4-(Methylsulfonyl) Benzene" Z. Yu, P. Zhou, J. Liu, W. Wang, C. Yu, W. Su

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"Development of an Intermittent-Flow Enantioselective Aza-Henry Reaction Using an Arylnitromethane and Homogeneous Brønsted Acid–Base Catalyst with Recycle" S. V. Tsukanov, M. D. Johnson, S. A. May et al.

Organic Process Research & Development 2016, 20, 215–226

"The Use of Gases in Flow Synthesis" C. J. Mallia, I. R. Baxendale Organic Process Research & Development **2016**, 20, 327–360

"Controlled Flow Precipitation as a Valuable Tool for Synthesis" P. Filipponi, A. Gioiello, I. R. Baxendale *Organic Process Research & Development* **2016**, *20*, 371–375

"Selective Olefin Reduction Using Hydrazine Hydrate and O₂ under Intensified Continuous Flow Conditions" B. Pieber, D. P. Cox, C. O. Kappe Organic Process Research & Development **2016**, *20*, 376–385

"Toward the Waste-Free Synthesis of Fine Chemicals with Visible Light" R. Ciriminna, R. Delisi, Y.-J. Xu, M. Pagliaro Organic Process Research & Development **2016**, *20*, 403–408

"Rapid and Scalable Access into Strained Scaffolds through Continuous Flow Photochemistry" D. Blanco-Ania, S. A. Gawade, L. J. L. Zwinkels et al. Organic Process Research & Development **2016**, *20*, 409–413

"Microwave Promoted Transcarbamylation Reaction of Sulfonylcarbamates under Continuous-Flow Conditions" I. Kumpiņa, R. Isaksson, J. Sävmarker, J. Wannberg, M. Larhed Organic Process Research & Development **2016**, 20, 440–445

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"Experience with Scale-up of Low-Temperature Organometallic Reactions in Continuous Flow" S. Laue, V. Haverkamp, L. Mleczko *Organic Process Research & Development* **2016**, *20*, 480–486

"Toward a Large-Scale Approach to Milnacipran Analogues Using Diazo Compounds in Flow Chemistry" S. T. R. Müller, A. Murat, P. Hellier, T. Wirth T. *Organic Process Research & Development* **2016**, *20*, 495–502

"Application of Continuous Flow for DIBAL-H Reduction and N-Buli Mediated Coupling Reaction in the Synthesis of Eribulin Mesylate"

T. Fukuyama, H. Chiba, H. Kuroda, T. Takigawa, A. Kayano, K. Tagami *Organic Process Research & Development* **2016**, *20*, 503–509

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"A Continuous Process for Buchwald–Hartwig Amination at Micro-, Lab-, and Mesoscale Using a Novel Reactor Concept" S. Falß, G. Tomaiuolo, A. Perazzo et al. *Organic Process Research & Development* **2016**, *20*, 558–567

"Hydrogen Chloride Gas in Solvent-Free Continuous Conversion of Alcohols to Chlorides in Microflow" S. Borukhova, T. Noel, V. Hessel Organic Process Research & Development **2016**, *20*, 568–573

"Design of a Numbering-up System of Monolithic Microreactors and Its Application to Synthesis of a Key Intermediate of Valsartan" A. Nagaki, K. Hirose, O. Tonomura, S. Taniguchi, T. Taga, S. Hasebe, N. Ishizuka, J.-i. Yoshida *Organic Process Research & Development* **2016**, *20*, 687–691

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N. Erdmann, Y. Su, B. Bosmans, V. Hessel, T. Noël Organic Process Research & Development **2016**, 20, 831–835

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T. Martini, C. Chubilleau, O. Poncelet, A. Ricaud, A. Blayo, C. Martin, K. Tarasov *Solar Energy Materials and Solar Cells* **2016**, *144*, 657–663

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