Highlights from the Flow Chemistry Literature 2015 (Part 2)

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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 April to June 2015 is presented. All the publications are listed and ordered by journal name, with a review article appearing at the end. With a few special issues on flow synthesis that would be appearing in other journals in coming months, the list of publications in this area is expected to grow rapidly towards the end of this year.

Highlighted Articles

"Multistep Continuous-Flow Synthesis of (R)- and (S)-Rolipram Using Heterogeneous Catalysts"
T. Tsubogo, H. Oyamada, S. Kobayashi
Nature **2015**, *520*, 329–332

This paper reports an "eight-step flow synthesis" of important drugs using only columns packed with heterogeneous catalysts. A sequence of four columns maintained at different conditions containing achiral and chiral heterogeneous catalysts and their combinations is used for the synthesis of (*R*)-rolipram, (*S*)-rolipram, and (*R*)-phenibut. Avoiding the isolation of any intermediates and without the separation of any catalysts, coproducts, by-products, and excess reagents, the method shows the future of continuous-flow synthesis.

"Recovery of Artemisinin from a Complex Reaction Mixture Using Continuous Chromatography and Crystallization"
Z. Horváth, E. Horosanskaia, J. W. Lee, H. Lorenz, K. Gilmore, P. H. Seeberger, A. Seidel-Morgenstern
Organic Process Research & Development **2015**, *19*, 624–634

The photocatalytic reaction for the conversion of dihydroartemisinic acid (DHAA) to artemisinin is reported in a tubular reactor. The effluent from the reactor contains the product, unreacted DHHA, the photocatalyst, and several compounds that are structurally similar to artemisinin. This work demonstrates the continuous-flow synthesis as well as recovery and purification of artemisinin by continuous crystallization and multicolumn simulated moving bed (SMB) chromatography. The approach shows an elegant way to synthesize and purify the product and also recover the catalyst.

"Magnetic Droplet Microfluidics as a Platform for the Concentration of $[_{18}F]$Fluoride and Radiosynthesis of Sulfonyl $[_{18}F]$Fluoride"
S. A. Fiel, H. Yang, P. Schaffer, S. Weng, J. A. H. Inkster, M. C. K. Wong, P. C. H. Li
ACS Applied Materials & Interfaces **2015**, *7*, 12923–12929

Aqueous fluorination approaches that offer significant versatility in radiopharmaceutical synthesis with sensitive targeting vectors is reported using magnetic droplet microfluidics (MDM) in two steps. In the first step, the MDM are used to concentrate $[_{18}F]$fluoride from the cyclotron target solution, and it is used for the synthesis of an $_{18}F$-labeled compound on a microfluidic platform. The technique has been used for the synthesis of an arylsulfonyl $[_{18}F]$fluoride compound which can be used as a prosthetic group to label PET targeting ligands.

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"Machines vs Malaria: A Flow-Based Preparation of the Drug Candidate OZ439"
S-H. Lau, A. Galván, R. R. Merchant, C. Battilocchio, J. A. Souto, M. B. Berry, S. V. Ley
Organic Letters **2015**, *17*, 3218–3221

An automated synthesis protocol has been reported for the preparation of the antimalarial drug candidate OZ439. Three key transformations viz. selective partial hydrogenation, acetylation of the phenol group, and Griesbaum coozonolysis are demonstrated in continuous flow synthesis surpassing limitations previously observed batch process.

Organic Synthesis

"High-throughput generation of emulsions and microgels in parallelized microfluidic drop-makers prepared by rapid prototyping"
T. Femmer, A. Jans, R. Eswein, N. Anwar, M. Moeller, M. Wessling, A. J. C. Kuehne
ACS Applied Materials & Interfaces **2015**, *7*, 12635–12638

"Magnetic droplet microfluidics as a platform for the concentration of [18 F]fluoride and radiosynthesis of sulfonyl [18 F]fluoride"
S. A. Fiel, H. Yang, P. Schaffer, S. Weng, J. A. H. Inkster, M. C. K. Wong, P. C. H. Li
ACS Applied Materials & Interfaces **2015**, *7*, 12923–12929

"A flow-through enzymatic microreactor for the rapid conversion of triacylglycerols into fatty acid ethyl ester and fatty acid methyl ester derivatives for GC analysis"
S. T. Anuar, S. M. Mugo, J. M. Curtis
Analytical Methods **2015**, *7*, 5898–5906

"Making ends meet: flow synthesis as the answer to reproducible high-performance conjugated polymers on the scale that roll-to-roll processing demands"
M. Helgesen, J. E. Carlé, G. A. dos Reis Benatto, R. R. Søndergaard, M. Jørgensen, E. Bundgaard, F. C. Krebs
Advanced Energy Materials **2015**, *5*

"Reactions of difunctional electrophiles with functionalized aryllithium compounds: remarkable chemoselectivity by flash chemistry"
A. Nagaki, K. Imai, S. Ishiuchi, J. Yoshida
Angew. Chem. Int. Ed. **2015**, *54*, 1914–1918

"Continuous synthesis of diethyl carbonate from ethanol and CO2 over Ce–Zr–O catalysts"
I. Prymak, V. N. Kalevaru, S. Wohlrab, A. Martin
Catalysis Science & Technology **2015**, *5*, 2322–2331

"Continuous poly(2-oxazoline) triblock copolymer synthesis in a microfluidic reactor cascade"
E. Baeten, B. Verbraeken, R. Hoogenboom, T. Junkers
Chemical Communications **2015**, *51*, 11701–11704

"Continuous synthesis of methanol: heterogeneous hydrogenation of ethylene carbonate over Cu/HMS catalysts in a fixed bed reactor system"
X. Chen, Y. Cui, C. Wen, B. Wang, W-L. Dai
Chemical Communications **2015**, DOI: 10.1039/C5CC05030H

"Large-scale continuous hydrothermal production and activation of ZIF-8"
A. S. Munn, P. W. Dunne, S. V. Y. Tang, E. H. Lester
Chemical Communications **2015**, *51*, 12811–12814

"Continuous flow of nitroso Diels–Alder reaction"
E. Nakashima, H. Yamamoto
Chemical Communications **2015**, *51*, 12309–12312

"Decarboxylative Reissert type trifluoro- and trichloro-methylation of (iso)quinoline derivatives in batch and continuous flow"
M. Therkelsen, M. T. Rasmussen, A. T. Lindhardt
Chemical Communications **2015**, *51*, 9651–9654

"Continuous metal scavenging and coupling to one-pot copper-catalyzed azide-alkyne cycloaddition click reaction in flow"
I. V. Gürsel, F. Aldiansyah, Q. Wang, T. Noël, V. Hessel
Chemical Engineering Journal **2015**, 270, 468–475

"Rapid and continuous oxidation of organic contaminants with ascorbic acid and a modified ferric/persulfate system"
Y. Lei, H. Zhang, J. Wang, J. Ai
Chemical Engineering Journal **2015**, 270, 73–79

"Nafion-H-catalyzed high-temperature/high-pressure synthesis of a triarylmethane in continuous-flow mode"
S. Hayden, T. Glasnov and C. O. Kappe
Chemical Engineering & Technology **2015**, DOI: 10.1002/ceat.201400581

"Highly selective continuous-flow synthesis of potentially bioactive deuterated chalcone derivatives"
C. T. Hsieh, S. B. Ötvös, Y. C. Wu, I. M. Mándity, F. R. Chang, F. Fülöp
ChemPlusChem **2015**, *80*, 859–864

"Flash chemistry using trichlorovinyllithium: Switching the reaction pathways by high-resolution reaction time control"
A. Nagaki, Y. Takahashi, A. Henseler, C. Matsuo, J. Yoshida
Chemistry Letters, **2015**, *44*, 214–216

"Gas–liquid segmented flow microwave-assisted synthesis of MOF-74(Ni) under moderate pressures"
G. H. Albuquerque, R. C. Fitzmorris, M. Ahmadi, N. Wannenmacher, P. K. Thallapally, B. P. McGrail, G. S. Herman
CrystEngComm **2015**, *17*, 5502–5510

"Enantioselective [small alpha]-amination of 1,3-dicarbonyl compounds in batch and flow with immobilized thiourea organocatalysts"
P. Kasaplar, E. Ozkal, C. Rodriguez-Escrich, M. A. Pericas
Green Chemistry **2015**, *17*, 3122–3129

"Catalyst coating on prefabricated capillary microchannels for the direct synthesis of hydrogen peroxide"
V. Paunovic, V. Ordomsky, M. F. N. D'Angelo, J. C. Schouten, T. A. Nijhuis
Industrial & Engineering Chemistry Research **2015**, *54*, 2919–2929

"Continuous photofermentative production of hydrogen by immobilized *Rhodobacter sphaeroides* O.U.001"
R. Zagrodnik, K. Seifert, M. Stodolny, M. Laniecki
International Journal of Hydrogen Energy **2015**, *40*, 5062–5073

"Sorption-enhanced reforming of bioethanol in dual fixed bed reactor for continuous hydrogen production"
A. Lysikov, V. Derevschikov, A. Okunev
International Journal of Hydrogen Energy **2015**, DOI: 10.1016/j.ijhydene.2015.06.029

"Decarbonisation of fossil energy via methane pyrolysis using two reactor concepts: Fluid wall flow reactor and molten metal capillary reactor"
I. Schultz, D. W. Agar
International Journal of Hydrogen Energy **2015**, DOI: 10.1016/j.ijhydene.2015.03.126

"One-step, facile and ultrafast synthesis of phase- and size-controlled Pt–Bi intermetallic nanocatalysts through continuous-flow microfluidics"
D. Zhang, F. Wu, M. Peng, X. Wang, D. Xia, G. Guo
Journal of the American Chemical Society **2015**, *137*, 6263–6269

"Flow alkylation of thiols, phenols, and amines using a heterogenous base in a packed-bed reactor"
A. Baker, M. Graz, R. Saunders, G. J. S. Evans, I. Pitotti, T. Wirth
Journal of Flow Chemistry **2015**, *5*, 65–68

"The use of flow chemistry for two-phase dibromocyclopropanation of alkenes"
R. B. Østby, Y. H. Stenstrøm, T. Didriksen
Journal of Flow Chemistry **2015**, *5*, 69–73

"Multistep continuous-flow synthesis of condensed benzothiazoles"
K. Lövei, I. Greiner, J. Éles, Á. Szigetvári, M. Dékány, S. Lévai, Z. Novák, G. I. Túrós
Journal of Flow Chemistry **2015**, *5*, 74–81

"Two-stage flow synthesis of coumarin via O-acetylation of salicylaldehyde"
X. Li, A. Chen, Y. Zhou, L. Huang, Z. Fang, H. Gan, K. Guo
Journal of Flow Chemistry **2015**, *5*, 82–86

"Influence of support properties on the activity of basic catalysts for aldol condensation of formaldehyde and methyl acetate in a continuous-flow reactor"
Y. Wang, H. Chen, G. Zhao, M. Liu, X. Lang, Z. Zhu
Journal of Flow Chemistry **2015**, *5*, 87–94

"Continuous-flow alcohol protection and deprotection reactions catalyzed by silica-supported sulfonic acid"
S. A. van den Berg, R. A. M. Frijns, T. Wennekes, H. Zuilhof
Journal of Flow Chemistry **2015**, *5*, 95–100

"Active mixing inside double emulsion segments in continuous flow"
V. Misuk, A. Mai, Y. Zhao, J. Heinrich, D. Rauber, K. Giannopoulos, H. Löwe
Journal of Flow Chemistry **2015**, *5*, 101–109

"Scaling up the throughput of synthesis and extraction in droplet microfluidic reactors"
P. M. Korczyk, M. E. Dolega, S. Jakiela, P. Jankowski, S. Makulska, P. Garstecki
Journal of Flow Chemistry **2015**, *5*, 110–118

"3D graphene/nylon rope as a skeleton for noble metal nanocatalysts for highly efficient heterogeneous continuous-flow reactions"
S. Zhang, X. Shen, Z. Zheng, Y. Ma, Y. Qu
Journal of Materials Chemistry A **2015**, *3*, 10504–10511

"Benzyllithiums bearing aldehyde carbonyl groups. A flash chemistry approach"
A. Nagaki, Y. Tsuchihashi, S. Haraki, J. Yoshida
J. Org. Biomol. Chem. **2015**, *13*, 7140–7145

"Multistep continuous-flow synthesis of (R)- and (S)-rolipram using heterogeneous catalysts"
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Nature **2015**, *520*, 329–332

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Organic Process Research & Development **2015**, *19*, 624–634

"Continuous-flow process for the synthesis of 2-ethylphenylhydrazine hydrochloride"
Z. Yu, G. Tong, X. Xie, P. Zhou, Y. Lv, W. Su
Organic Process Research & Development **2015**, *19*, 892–896

"Continuous-flow synthesis of meta-substituted phenol derivatives"
J. H. Park, C. Y. Park, M. J. Kim, M. U. Kim, Y. J. Kim, G.-H. Kim, C. P. Park
Organic Process Research & Development **2015**, *19*, 812–818

"The Biginelli reaction under batch and continuous flow conditions: catalysis, mechanism and antitumoral activity"
G. C. O. Silva, J. R. Correa, M. O. Rodrigues, H. G. O. Alvim, B. C. Guido, C. C. Gatto, K. A. Wanderley, M. Fioramonte, F. C. Gozzo, R. O. M. A. de Souza, B. A. D. Neto
RSC Advances **2015**, *5*, 48506–48515

"Continuous-flow hydrogenation of olefins and nitrobenzenes catalyzed by platinum nanoparticles dispersed in an amphiphilic polymer"
T. Osako, K. Torii, A. Tazawa, Y. Uozumi
RSC Advances **2015**, *5*, 45760–45766

"A continuous-flow synthesis of 1,4-benzodiazepin-5-ones, privileged scaffolds for drug discovery"
M. Viviano, C. Milite, D. Rescigno, S. Castellano, G. Sbardella
RSC Advances **2015**, *5*, 1268–1273 (also as *ChemInform* **2015**, *46* (20))

"A sequential Ugi multicomponent/Cu-catalyzed azide–alkyne cycloaddition approach for the continuous flow generation of cyclic peptoids"
C. E. M. Salvador, B. Pieber, P. M. Neu, A. Torvisco, C. K. Z. Andrade, C. O. Kappe
The Journal of Organic Chemistry **2015**, *80*, 4590–4602

"Polymerization of vinyl ethers initiated by dendritic cations using flow microreactors"
A. Nagaki, M. Takumi, Y. Tani, J. Yoshida
Tetrahedron **2015**, *71*, 5973–5978

Nanomaterials

"A versatile and robust microfluidic platform toward high throughput synthesis of homogeneous nanoparticles with tunable properties"
D. Liu, S. Cito, Y. Zhang, C. Wang, T. M. Sikanen, H. A. Santos
Advanced Materials **2015**, *27*, 2298–2304

"Microfluidic synthesis of biodegradable polyethylene-glycol microspheres for controlled delivery of proteins and DNA nanoparticles"
L. Deveza, J. Ashoken, G. Castaneda, X. Tong, M. Keeney, L.-H. Han, F. Yang
ACS Biomaterials Science & Engineering **2015**, 1, 157–165

"Widening synthesis bottlenecks: realization of ultrafast and continuous-flow synthesis of high-silica zeolite SSZ-13 for NOx removal"
Z. Liu, T. Wakihara, K. Oshima, D. Nishioka, Y. Hotta, S. P. Elangovan, Y. Yanaba, T. Yoshikawa, W. Chaikittisilp, T. Matsuo, T. Takewaki, T. Okubo
Angewandte Chemie International Edition **2015**, *54*, 5683–5687

"Production of polymeric nanoparticles by micromixing in a co-flow microfluidic glass capillary device"
R. Othman, G. T. Vladisavljević, H. C. H. Bandulasena, Z. K. Nagy
Chemical Engineering Journal **2015**, 280, 316–329

"Process intensification: nano-carrier formation by a continuous dense gas process"
C. C. Beh, R. Mammucari, N. R. Foster
Chemical Engineering Journal **2015**, 266, 320–328

"Scalable continuous solvo-jet process for ZIF-8 nanoparticles"
H-S. Choi, S-J. Lee, Y-S. Bae, S-J. Choung, S-H. Im, J. Kim
Chemical Engineering Journal **2015**, 266, 56–63

"Continuous synthesis of hierarchical porous ZnO microspheres in supercritical methanol and their enhanced electrochemical performance in lithium ion batteries"
J. Kim, S-A. Hong, J. Yoo
Chemical Engineering Journal **2015**, 266, 179–188

"Segmented flow-based multistep synthesis of cadmium selenide quantum dots with narrow particle size distribution"
V. Misuk, M. Schmidt, S. Braukmann, K. Giannopoulos, D. Karl, H. Loewe
Chemical Engineering & Technology **2015**, *38*, 1150–1153

"Segmented flow-based multistep synthesis of cadmium selenide quantum dots with narrow particle size distribution"
V. Misuk, M. Schmidt, S. Braukmann, K. Giannopoulos, D. Karl, H. Loewe
Chemical Engineering & Technology **2015**, *38*, 1150–1153

"Gas slug microfluidics: a unique tool for ultrafast, highly controlled growth of iron oxide nanostructures"
A. Larrea, V. Sebastian, A. Ibarra, M. Arruebo, J. Santamaria
Chemistry of Materials **2015**, *27*, 4254–4260

"Generation of alginate nanoparticles through microfluidics-aided polyelectrolyte complexation"
K. Kim, D. Kang, M. Kim, K. Kim, K. Park, S. Hong, P. Chang, H. Jung
Colloids and Surfaces A: Physicochemical and Engineering Aspects **2015**, 471, 86–92

"The continuous synthesis and application of graphene supported palladium nanoparticles: a highly effective catalyst for Suzuki–Miyaura cross-coupling reactions"
K. W. Brinkley, M. Burkholder, A. R. Siamaki, K. Belecki, B. F. Gupton
Green Processing and Synthesis **2015**, *4*, 241–246

"Changing the size and surface roughness of polymer nanospheres formed using a microfluidic technique"
I. Kucuk, M. Edirisinghe
Journal of Minerals, Metals and Materials Society **2015**, *67*, 811–817

"Soft chemistry synthesis route toward Bi2Te3 hierarchical hollow spheres"
J. Fouineau, J. Peron, S. Nowak, M. Giraud, M. Sicard, S. Ammar-Merah, L. Sicard
Journal of Nanoparticle Research **2015**, *17*, 166

"The influence of stabilizers on the production of gold nanoparticles by direct current atmospheric pressure glow microdischarge generated in contact with liquid flowing cathode"
A. Dzimitrowicz, P. Jamroz, K. Greda, P. Nowak, M. Nyk, P. Pohl
Journal of Nanoparticle Research **2015**, *17*, 185

"On-demand one-step synthesis of monodisperse functional polymeric microspheres with droplet microfluidics"
X. Yu, G. Cheng, M. Zhou, S. Zheng
Langmuir **2015**, *31*, 3982–3992

"Role of self-polarization in a single-step controlled synthesis of linear and branched polymer nanoparticles"
N. Visaveliya, J. M. Koehler
Macromolecular Chemistry and Physics **2015**, *216*, 1212–1219

"Controlled synthesis of layered double hydroxide nanoplates driven by screw dislocations"
A. Forticaux, L. Dang, H. Liang, S. Jin
Nano Letters **2015**, *15*, 3403–3409

"Continuous preparation of Fe3O4 nanoparticles using a rotating packed bed: dependence of size and magnetic property on temperature"
C. Lin, J. Ho, M. Wu,
Powder Technology **2015**, *274*, 441–445

"One-step, facile and ultrafast synthesis of phase- and size-controlled Pt–Bi intermetallic nanocatalysts through continuous-flow microfluidics"
D. Zhang, F. Wu, M. Peng, X. Wang, D. Xia, G. Guo
Journal of the American Chemical Society **2015**, *137*, 6263–6269

"Semi-automated nanoprecipitation-system—an option for operator independent, scalable and size adjustable nanoparticle synthesis"
R. Rietscher, C. Thum, C. Lehr, M. Schneider
Pharmaceutical Research **2015**, *32*, 1859–1863

Reviews

"Liquid phase oxidation chemistry in continuous-flow microreactors"
H. P. L. Gemoets, Y. Su, M. Shang, V. Hessel, R. Luque, T. Noel
Chemical Society Reviews **2015**, DOI: 10.1039/C5CS00447K