Whats included in this newsletter:

- 8 new publications utilising Vapourtec systems
- New suspension/slurry pump module
- Nanoparticle synthesis under flow conditions
- LED continuous flow photochemical reactor
- Further growth in flow chemistry
- Continuous liquid-liquid extraction

CONTENTS

PRODUCT NEWS

Shedding LED light on photochemical research

Vapourtec have launched a second generation LED light source (Gen-2) which increases the range of applications for its innovative, continuous flow UV-150 photochemical reactor.

READ MORE

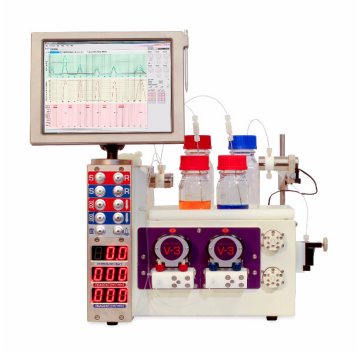
Link with Zaiput delivers liquid - liquid separation

Vapourtec have worked with US-based Zaiput Flow Technologies to add liquid - liquid separation to its product capabilities.

READ MORE

New suspension/light slurry pump module

There has been a significant level of interest in our new suspension / light slurry pump module launched at the end of 2014. Designed to complement our R-Series system, the new pump module offers a number of novel capabilities.



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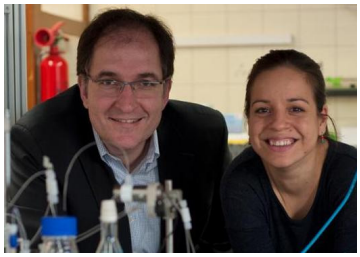
LATEST NEWS

The 'wundermaschine' that makes drugs cheaper!

Our E-Series flow chemistry system has been described in the popular German newspaper Bild as a "Wundermaschine" that dramatically reduces the cost of manufacturing drugs.



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Vapourtec grows the support team with key appointment

We have recently appointed Ian Tanwiar to the position of Service Manager tasked with ensuring that Vapourtec customers get the most from their systems.

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CRO recognises benefits of continuous processing

Regis Technologies, a contract research organisation (CRO) based near Chicago, has just taken delivery of a new R-Series flow chemistry system.

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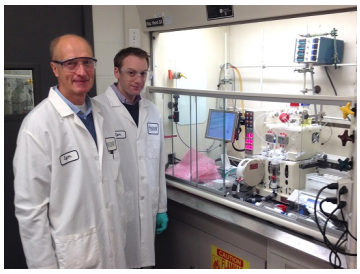


EVENTS

16th April 2015
Dial-a-Molecule Closed Loop Optimisation of Synthesis
Stevenage, UK
Click here for more details

24th-25th June 2015
Chemspec Europe
Cologne, Germany
Click here for more details

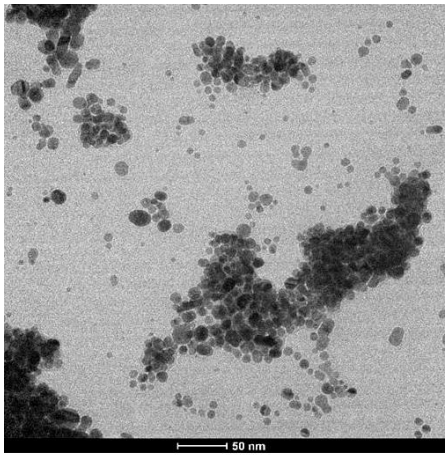
16th-18th August 2015
250th ACS National Meeting & Exposition
Boston, MA, USA
Click here for more details

21st-25th October 2015
5th Conference on Frontiers in Organic Synthesis Technology
Budapest, Hungary
Click here for more details

2nd -4th November 2015
Chemistry in the Oil Industry XIV
Manchester, UK
Click here for more details

APPLICATIONS

Preparation of Silver Nanoparticles under Continuous Flow Conditions

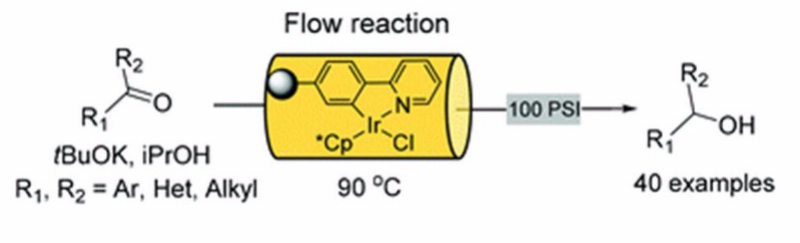


Application Note 40: This Application Note describes the controlled formation of silver nanoparticles in tubular reactors using the Vapourtec E-Series. Control of particle size is shown over the size range 10 to 60 nm. Two classes of nanoparticle are reported.

Click here **to go straight to the application note**

PUBLICATIONS

A monolith immobilised iridium Cp* catalyst for hydrogen transfer reactions under flow conditions



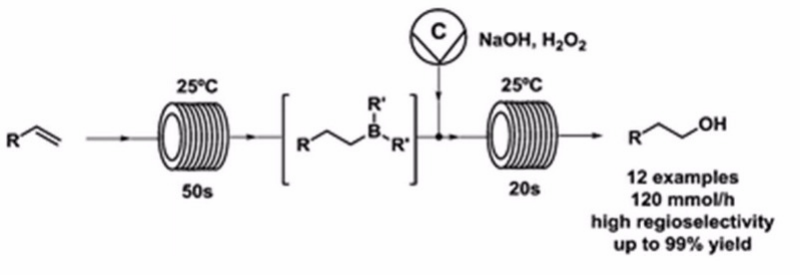
Maria Victoria Rojo,*1
Lucie Guetzoyan1
Ian. R. Baxendale1,2

1. Department of Chemistry, University of Cambridge, Lensfield Road, Cambridge, UK
2. Department of Chemistry, University of Durham, South Road, Durham, UK

An immobilised iridium hydrogen transfer catalyst has been developed for use in flow based processing by incorporation of a ligand into a porous polymeric monolithic flow reactor. The monolithic construct has been used for several redox reductions demonstrating excellent recyclability, good turnover numbers and high chemical stability giving negligible metal leaching over extended periods of use.

Click here **to go straight to the publication**

Development of a flow method for the hydroboration/oxidation of olefins



José A. Souto,*1,2
Robert A. Stockman
Steven V. Ley1

1. Department of Chemistry, University of Cambridge, Lensfield Road, Cambridge CB2 1EW, UK
2. Departamento de Química Orgánica, Universidade de Vigo, Vigo, Spain
3. School of Chemistry, University of Nottingham, Nottingham, UK

A method for the continuous preparation of alcohols by hydroboration/oxidation of olefins using flow techniques is described. The process allows the isolation of up to 120 mmol h−1 of the desired alcohol in a very rapid manner with good functional group tolerance. The flow setup can be modified to perform a continuous extraction of the desired alcohol from the biphasic mixture produced by the reaction.

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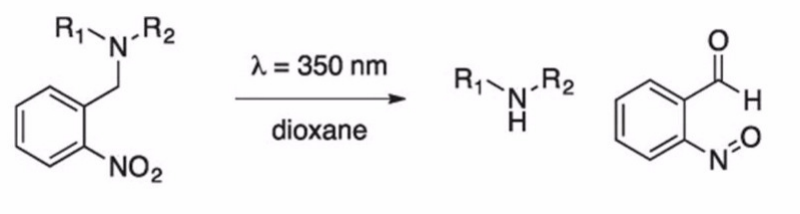
Reevaluation of the 2-nitrobenzyl protecting group for nitrogen containing compounds: an application of flow photochemistry

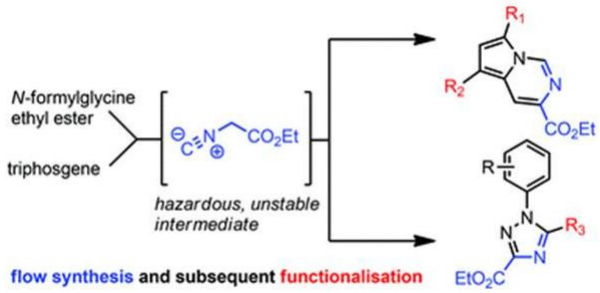


Michael J. Boyd
Chloe I. Wendell
Vertex Pharmaceuticals Inc., 50 Northern Avenue, Boston, MA, United States

Photochemistry under continuous flow conditions has many potential benefits for photochemical reactions that are problematic in batch. The 2-nitrobenzyl moiety is a photolabile protecting group for nitrogen. However, N-deprotection is generally impractical and, therefore, has not been extensively adopted. This Letter reports significant improvements in the N-deprotection of the 2-nitrobenzyl group through the application of continuous flow photolysis. This procedure was applied to a variety of substrates including indoles, indazoles, pyrazoles and secondary amines. Significant improvement in yield, reaction time and scalability was observed under continuous flow conditions.

Click here to go straight to the publication

Flow synthesis of ethyl isocyanoacetate enabling the telescoped synthesis of 1,2,4-triazoles and pyrrolo-[1,2-c]pyrimidines



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The efficient flow synthesis of important heterocyclic building blocks based on the 1,2,4-triazole and pyrrolo[1,2-c]pyrimidine scaffold has been achieved. Crucially, a telescoped continuous flow process was developed based on the reaction of N-formylglycine with triphosgene to deliver a stream of ethyl isocyanoacetate in situ, which subsequently yielded the desired heterocyclic entities in a telescoped reaction. Additionally, the functionalisation of the pyrrolo[1,2-c]pyrimidine core via subsequent SEAr reactions was studied revealing insight into a 'halogen dance' phenomenon associated with these medicinally relevant architectures.

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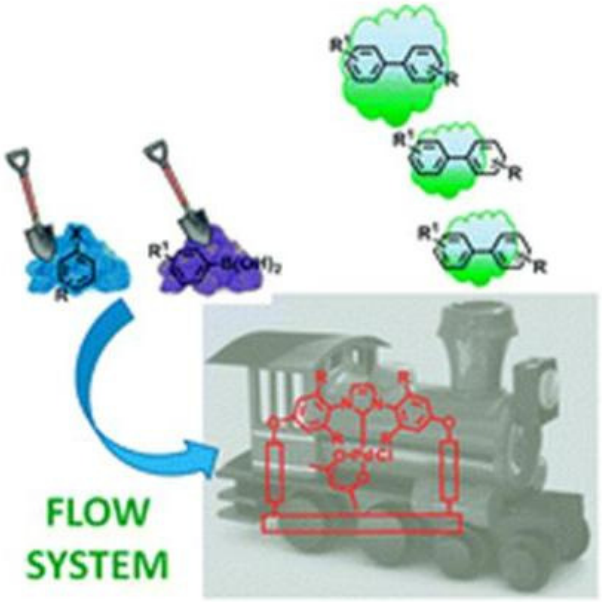
Heterogenization of Pd-NHC complexes onto a silica support and their application in Suzuki-Miyaura coupling under batch and continuous flow conditions

Alberto Martínez,[1] Jamin L. Krinsky,[1] Itziar Peñafiel,[1] Sergio Castillón,[2] Konstantin Loponov,[3] Alexei Lapkin,[3] Cyril Godard*[1] Carmen Claver*[1]



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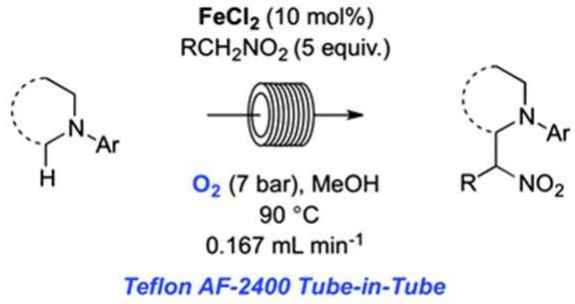
The heterogenisation of a new family of Pd-NHC complexes is reported via a straightforward and efficient synthetic procedure. These silica-immobilised materials were successfully applied as catalysts in the Suzuki-Miyaura coupling of aryl chlorides and bromides under mild conditions. The materials exhibited improved stability when the catalytic reaction was run under anhydrous conditions and could be recycled up to five times without significant loss of activity. When the reaction was run within a continuous flow microreactor, these catalysts showed good activity after at least two hours on stream.

Click here **to go straight to the publication**

The direct α-C(sp3)-H functionalisation of N-aryl tetrahydroisoquinolines via an iron-catalysed aerobic nitro-Mannich reaction and continuous flow processing



Martin Brzozowski

Jose A. Forni
G. Paul Savage
Anastasios Polyzos

CSIRO Manufacturing Flagship, Bayview Avenue, Clayton 3168, Australia

An efficient nitro-Mannich type direct α-C(sp3)-H functionalisation of N-aryl-1,2,3,4-tetrahydroisoquinolines catalysed by simple iron salts in combination with O2 as the terminal oxidant is described. The use of a Teflon AF-2400 membrane Tube-in-Tube reactor under continuous flow conditions allowed for considerable process intensification to be achieved relative to previous batch methods.

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Generation and Trapping of Ketenes in Flow

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Bogdan Ibanescu1,
Sally Bloodworth1,
David C. Harrowven1,
Xunli Zhang2,
Andy Craven3,
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Richard J. Whitby1,*

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3. GlaxoSmithKline R&D Ltd., Medicines Research Centre, Gunnels Wood Road, Stevenage, HERTS, SG1 2NY, UK

Ketenes were generated by the thermolysis of alkoxyalkynes under flow conditions, and then trapped with amines and alcohols to cleanly give amides and esters. For a 10 min reaction time, temperatures of 180, 160, and 140 °C were required for >95% conversion of EtO, iPrO, and tBuO alkoxyalkynes, respectively. Variation of the temperature and flow rate with inline monitoring of the output by IR spectroscopy allowed the kinetic parameters for the conversion of 1-ethoxy-1-octyne to be easily estimated (Ea = 105.4 kJ/mol). Trapping of the in-situ-generated ketenes by alcohols to give esters required the addition of a tertiary amine catalyst to prevent competitive [2+2] addition of the ketene to the alkoxyalkyne precursor.

Click here to go straight to the publication

A Concise Flow Synthesis of Efavirenz

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Dr. Kerry Gilmore1,
Prof. Dr. D. Tyler McQuade3 and
Prof. Dr. Peter H. Seeberger1,2,*

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2. Institute for Chemistry and Biochemistry, Freie Universität Berlin, Arnimallee 22, 14195 Berlin (Germany)
3. Department of Chemistry and Biochemistry, Florida State University, Tallahassee, FL 32306 (USA)

Efavirenz is an essential medicine for the treatment of HIV, which is still inaccessible to millions of people worldwide. A novel, semi-continuous process provides rac-Efavirenz with an overall yield of 45%. This streamlined proof-of-principle synthesis relies on the efficient copper-catalyzed formation of an aryl isocyanate and a subsequent intramolecular cyclization to install the carbamate core of Efavirenz in one step. The three-step method represents the shortest synthesis of this life-saving drug to date.

Click here **to go straight to the publication**

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