Welcome to the Autumn issue of Flow Synthesis Online

We're excited to announce that Vapourtec just turned 10 years old.
We'd like to say a big thank you to all our customers, who have moved chemistry forward enormously and helped Vapourtec grow over the years.

We look forward to another decade of working with you.

Contents

Products

- E-Series tools. We take a look at the simple but powerful tools built into every E-Series flow chemistry system, including the ability to run an automated flow experiment with no manual intervention.

Events

- Meetings, conferences or exhibitions where you can see Vapourtec products and talk to Vapourtec staff.

Publications

- A New Publication Showing the Use of the E-Series System for Organometallic Chemistry.
- Alkyl-Aryl Negishi Cross-Coupling in Flow
- Palladium-Catalyzed Decarboxylative Couplings using Oxygen as the Oxidant
- Integrated Synthesis and Testing of Substituted Xanthine Based DPP4 Inhibitors
- Applying Flow Chemistry: Methods, Materials, and Multistep Synthesis
- Rapid Generation of Isothiocyanates in Flow

Product News

Vapourtec E-Series Tools - Get more done, quicker.

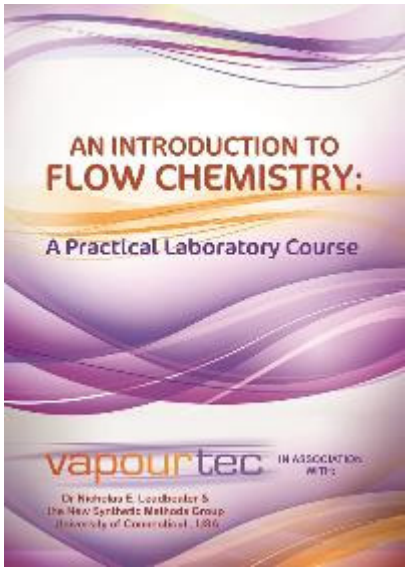
The Vapourtec E-Series (launched late summer 2012) offers unrivalled capabilities for organometallic chemistry. At it's core is the revolutionary new V-3 pump, which has been extensively reviewed in the first publication mentioned in this issue of our newsletter (see below).

The E-Series is especially easy to use, not least because of the simplicity of the user interface. But in addition to the standard flow and temperature settings, the **easy-Scholar** has a number of extra tools available which make the job of running basic day-to-day experiments more straightforward than ever..

Click here for more details

Vapourtec E-Series Undergraduate Teaching materials

All E-Series systems come with a set of Undergraduate Laboratory Course materials, enabling the easy-Scholar system to used as part of a hands on introduction to continuous flow chemistry in university chemistry courses.



These notes and sample reactions are also ideal for any chemist new to flow chemistry to gain an understanding of the technique.

Click here to read more

Events

Events where you can see Vapourtec systems in action:

19-21 September 2013
Chemspec Asia
Bangkok International Trade & Exhibition Centre (BITEC)
Click here for more details

24-25 September
2nd SCI/RSC Symposium on Continuous Processing and Flow Chemistry
Novartis, Horsham, UK

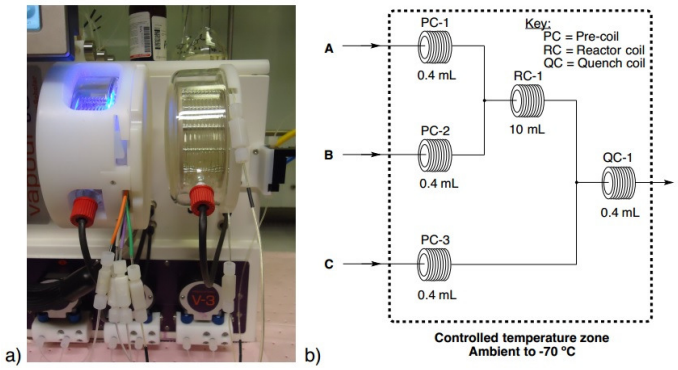
Click here for more details

4-5 November
Chemistry in the Oil Industry XIII
Manchester Conference Centre, UK
Click here for more details

Publications

Continuous Flow-Processing of Organometallic Reagents Using an Advanced Peristaltic Pumping System and the Telescoped Flow Synthesis of (E/Z)-Tamoxifen

Philip R D Murray [1]
Duncan L Browne [1]
Julio C Pastre [1,2]
Chris Butters [3]
Duncan Guthrie [3]
Steven V Ley [1]



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[2] *Instituto de Química, University of Campinas, Brazil.*
[3] *Vapourtec Ltd, UK*

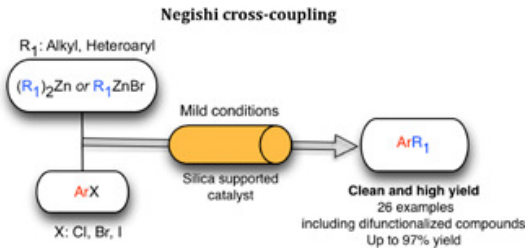
A new enabling-technology for the pumping of organometallic reagents such as n-butyllithium, Grignard reagents and DIBAL-H is reported, which utilizes a newly developed chemically-resistant peristaltic pumping system. Several representative examples of its use in common transformations using these reagents, including metal-halogen exchange, addition, addition-elimination, conjugate addition and partial reduction are reported, along with examples of telescoping of the anionic reaction products. This platform allows for truly continuous pumping of these highly reactive substances and examples are demonstrated over periods of several hours, to generate multi-gram quantities of products. This work culminates in an approach to the telescoped synthesis of (E/Z)-Tamoxifen using continuous-flow organometallic reagent mediated transformations.

Click here to go straight to the publication (free access)

Click here for more details about the E-Series and usage of organometallic reagents

First Example of Alkyl-Aryl Negishi Cross-Coupling in Flow: Mild, Efficient and Clean Introduction of Functionalized Alkyl Groups

Brecht Egle[2],
Juan M. Muñoz[1],
Nerea Alonso[1],
Wim M. Borggraeve[2],
Antonio Hoz3,
Angel Díaz-Ortiz[3],
Jesús Alcázar[1]



[1]*Janssen Research and Development Department of Medicinal Chemistry, Janssen-Cilag, Spain*
[2]*Department of Chemistry, Molecular Design and Synthesis University of Leuven, Belgium*
[3]*Universidad de Castilla-La Mancha Facultad de Ciencias y Tecnologías Químicas, Spain*

The first example of an alkyl–aryl Negishi coupling in a practical, sustainable, and high-yielding process using a silica-supported catalyst in flow is described. Excellent conversions and good functional group compatibility were obtained under very mild conditions. Functionalized alkyl groups were also introduced to provide access to synthetically useful molecules and to demonstrate the versatility of the method. The scalability was assessed, and a throughput of 7.5 mmol/h of processed substrate was achieved. All crude products were free from phosphine derivatives and ready for use in subsequent reaction steps.

Click here to go straight to the publication

Microwave heating and conventionally-heated continuous-flow processing as tools for performing cleaner palladium-catalyzed decarboxylative couplings using oxygen as the oxidant – a proof of principle study

DiAndra Rudzinski
Nicholas Leadbeater

Department of Chemistry, University of Connecticut, USA

A microwave unit interfaced with a gas-loading accessory is used as a tool for facilitating the palladium-catalyzed decarboxylative Heck reaction of 2,6-dimethoxybenzoic acid and methyl acrylate using molecular oxygen as the oxidant. The reaction is complete in less time and at a lower catalyst loading than when using conventional approaches. The reaction is scaled up using continuous-flow processing employing a reactor in which both gas input and heating can be performed simultaneously. An 86% isolated product yield is

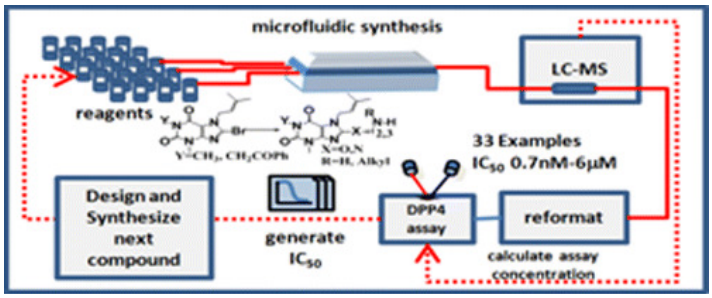
obtained. This proof-of-principle study paves the way for the technology to be used in other cases of these increasingly popular decarboxylative coupling reactions.

Click here to go straight to the publication

Integrated Synthesis and Testing of Substituted Xanthine Based DPP4 Inhibitors: Application to Drug Discovery

Werngard Czechtizky [1],
Jüergen Dedio [1],
Bimbisar Desai [2],
Karen Dixon [2],
Elizabeth Farrant [2],
Qixing Feng [2],
Trevor Morgan [2],
David M. Parry [2],
Manoj K. Ramjee [2],
Christopher N. Selway [2],
Thorsten Schmidt [1],
Gary J. Tarver *[2],
Adrian G. Wright [2]

[1] *Sanofi-Aventis, Frankfurt, Germany*
[2] *Cyclofluidic Ltd., U.K.*



A novel integrated discovery platform has been used to synthesize and biologically assay a series of xanthine-derived dipeptidyl peptidase 4 (DPP4) antagonists. Design, synthesis, purification, quantitation, dilution, and bioassay have all been fully integrated to allow continuous automated operation. The system has been validated against a set of known DPP4 inhibitors and shown to give excellent correlation between traditional medicinal chemistry generated biological data and platform data. Each iterative loop of synthesis through biological assay took two hours in total, demonstrating rapid iterative structure–activity relationship generation.

Click here to go straight to the publication

Applying Flow Chemistry: Methods, Materials, and Multistep Synthesis

D. Tyler McQuade *[13]
Peter H. Seeberger [12]

[1] *Department of Biomolecular Systems, Max Planck Institute of Colloids and Interfaces, Potsdam, Germany*
[2] *Institute for Chemistry and Biochemistry, Freie Universität Berlin, Germany*
[3] *Department of Chemistry and Biochemistry, Florida State University, United States*

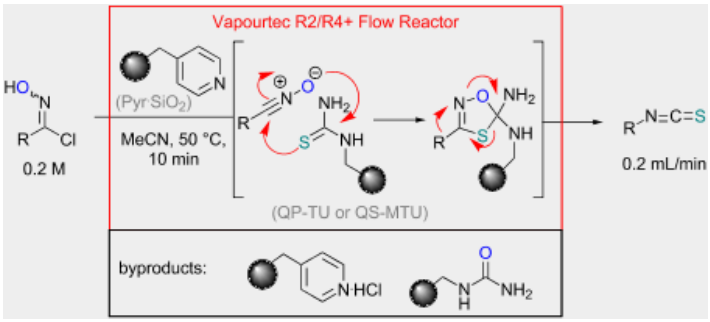
The synthesis of complex molecules requires control over both chemical reactivity and reaction conditions. While reactivity drives the majority of chemical discovery, advances in reaction condition control have accelerated method development/discovery. Recent tools include automated synthesizers and flow reactors. In this Synopsis, we describe how flow reactors have enabled chemical advances in our groups in the areas of single-stage reactions, materials synthesis, and multistep reactions. In each section, we detail the lessons learned and propose future directions.

Click here to go straight to the publication

The rapid generation of isothiocyanates in flow

Marcus Baumann
Ian R. Baxendale

Department of Chemistry,
University of Durham,
U.K.



Isothiocyanates are versatile starting materials for a wide range of chemical reactions. However, their high nucleophilic susceptibility means they are best prepared and used immediately. We report here on a flow platform for the fast and efficient formation of isothiocyanates by the direct conversion of easily prepared chloroximes. To expedite this chemistry a flow insert cartridge containing two immobilised reagents is used to affect the chemical transformation which typically eliminates the requirements for any conventional work-up or purification of the reaction stream.

Click here to go straight to the publication

Thanks for reading.

See you again next time.