Welcome to the Feb 2013 issue of Flow Synthesis Online

Welcome to the first newsletter of 2013.

It's a packed issue, with applications, publications, upcoming events and news.

Contents

Product News

Vapourtec E-Series for Organometallic Chemistry

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.

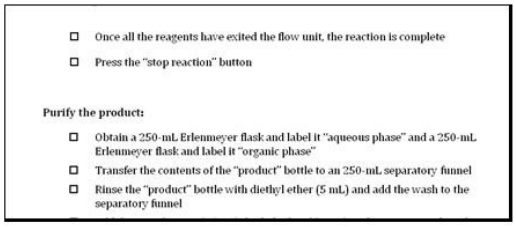
(Scroll down for details of two new application notes showing the system pumping BuLi and Grignard reagents without any drama).

But there are other features besides the pumps that make this system an ideal platform for this kind of work.

Click here for more details

Vapourtec E-Series Undergraduate Teaching materials

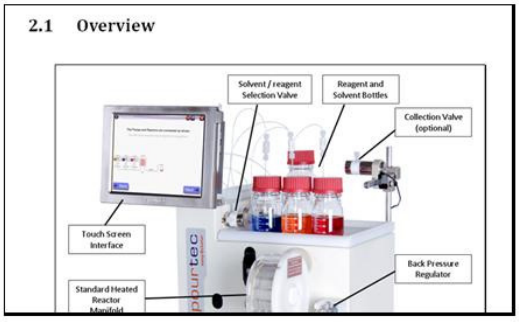
Vapourtec are happy to announce the availability of Undergraduate Laboratory Course materials, enabling the E-Series system to used as part of a hands on introduction to continuous flow chemistry in university chemistry courses.


- Once all the reagents have exited the flow unit, the reaction is complete
- Press the "stop reaction" button

Purify the product:

- Obtain a 250-mL Erlenmeyer flask and label it "aqueous phase" and a 250-mL Erlenmeyer flask and label it "organic phase"
- Transfer the contents of the "product" bottle to an 250-mL separatory funnel
- Rinse the "product" bottle with diethyl ether (5 mL) and add the wash to the separatory funnel

The course materials have been developed with experienced academic partners and have been fully tested on real undergraduates !



These are available free of charge to E-Series system owners.

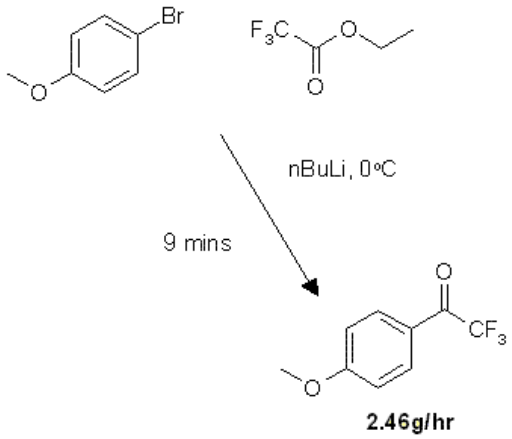
Click here for more details

Applications

Reaction of Organolithium Reagents using Vapourtec E-Series system

This app note shows the use of the E-Series and V-3 pumps to carry out organometallic chemistry, pumping nBuLi, straight from the bottle it was supplied in, for several hours without issue.

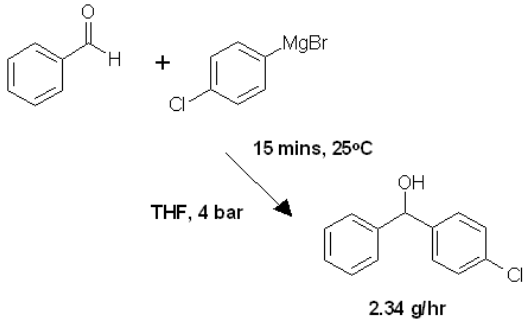
Click here to go to the Application Notes page on the Vapourtec website



Reaction of Grignard Reagents using Vapourtec E-Series system

The Grignard reaction was discovered over a hundred years ago and continues to be an important reaction in the synthetic chemist's tool kit.

Grignard reactions are exothermic, making them a good fit for flow chemistry but the reagents involved can be challenging to pump.



This application note demonstrates the pumping capability of the E-Series in optimizing and delivering a scalable method for the addition of Grignard reagents to aldehydes.

Click here to go to the Application Notes page on the Vapourtec website

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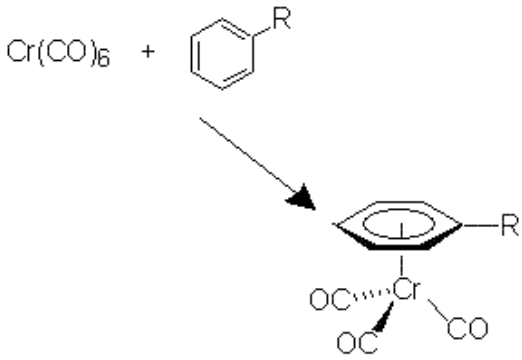
Chromium Arene Synthesis in Flow

Arene chromium tricarbonyl complexes, (arene)Cr(CO)3, have found extensive use in organic synthesis



Their preparation generally involves heating chromium hexacarbonyl under reflux either in the arene as the solvent or in a high boiling solvent containing the arene . Reactions can take in the order of 1-4 days to reach completion and need to be performed under an inert atmosphere.

Microwave based methods have proved challenging due to the possibility of depositing elemental chrome on the vial walls (leading to catastrophic vial failure).

This application note shows a continuous flow approach to preparation of complexes, and uses it to generate 4 arene chromium tricarbonyl products.

Click here to go to the Application Notes page on the Vapourtec website

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News

University of Montreal Buys further 5 Vapourtec R-Series Systems

Université de Montréal

A major award from the ***Canada Foundation for Innovation*** to Professor André B. Charette has allowed the Department of Chemistry at the Université de Montréal to take delivery of 5 additional fully equipped Vapourtec R-Series systems.

The department is one of the member institutions of the ***Centre for Green Chemistry and Catalysis***, (a consortium drawing members from all the major Quebec universities) which provides analytical and synthesis services to the whole scientific community in Quebec. The Centre was founded in 2009 and now has 52 members who are active in solving the various challenges of sustainable chemistry.

Click here for more details

Webinars

Professor Volker Hessel:
Chemical Intensification in Flow Chemistry and Process Design
25th April 2013 - 9:00 to 10:00

Click here for more details

METTLER TOLEDO :
Continuous Flow Chemistry II
Recent Advances in Organic Chemistry Part 8
On demand:

Click here for more details

Events
(where you can meet Vapourtec and see Vapourtec systems in action)

Flow Chemistry Europe : 19-20 March 2013

Munich, Germany.

Click here for more details

Chemspec Europe : 5-6 June 2013

Munich, Germany.

Click **here** for details of the main event

Click **here** for details of the RSC Symposium ("Practical Continuous Flow Technology ") to be held at the event.

13th ICSN Symposium : 13 June 2013

Click here for more details

Zing Microwave and Flow Conference: 20-23 July 2013

Click here for more details

2nd SCI/RSC Symposium on Continuous Processing and Flow Chemistry : 24-25 September

Click here for more details

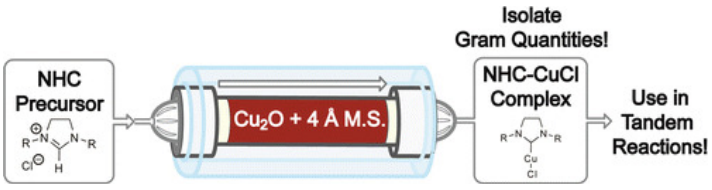
Chemistry in the Oil Industry XIII : 4-5 November

Click here for more details

Publications

Continuous Synthesis and Use of N-Heterocyclic Carbene Copper(I) Complexes from Insoluble Cu_2O

Suzanne M. Opalka [2]
Jin Kyoon Park [3]
Ashley R. Longstreet [1]
D. Tyler McQuade [1]



[1]*Dept of Chemistry and Biochemistry, Florida State University, USA*
[2]*Dept of Chemistry and Chemical Biology, Cornell University, USA*
[3]*Dept of Chemistry and Chemical Institute for Functional Materials, Pusan National University, Korea*

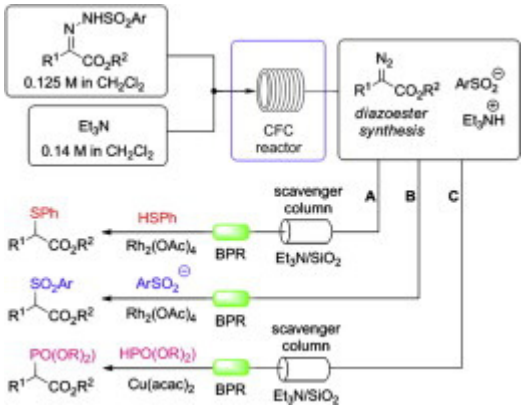
It is demonstrated that homogeneous N-heterocyclic carbene–copper(I)-chloride complexes can be prepared continuously by flowing NHC precursors through a packed bed of solid Cu_2O suspended in molecular sieves. The method enables the synthesis of a wide range of complexes including those that are challenging to prepare using standard approaches. Our strategy enables both sustained output of complex production for long-term catalytic reactions (greater than 5 h) and for generation of gram quantities for storage (greater than 1 g of complex in 16 min).

Click here to go straight to the publication

Continuous-flow generation of diazoesters and their direct use in S-H and P-H insertion reactions: synthesis of α-sulfanyl, α-sulfonyl, and α-phosphono carboxylates

Hannah E. Bartrum [1]
David C. Blakemore [2]
Christopher J. Moody [1]
Christopher J. Hayes [1]

[1] *School of Chemistry, University of Nottingham, UK*
[2] *Pfizer Neusentis, Cambridge, UK*



The synthesis of α-sulfanyl, α-sulfonyl, and α-phosphono carboxylates has been achieved using a two-step procedure involving the in-flow generation of diazoesters from sulfonylhydrazones, via Bamford–Stevens elimination, and then subsequent S–H, sulfinate, and P–H carbene insertion reactions. The method for α-sulfonyl ester is particularly

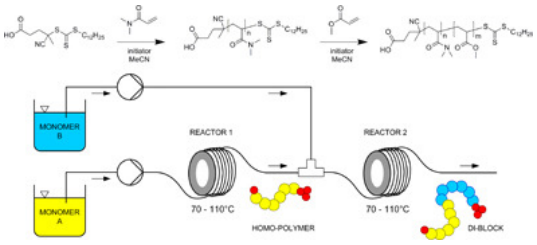
noteworthy as it represents a very atom economic (‘green’) way to access the products, and it completely avoids the use of alkyl halides.

Click here to go straight to the publication

Synthesis of RAFT Block Copolymers in a Multi-Stage Continuous Flow Process Inside a Tubular Reactor

Christian H. Hornung
Xuan Nguyen
Stella Kyi
John Chiefari
Simon Saubern

CSIRO Materials Science & Engineering,
Victoria, Australia



This work describes a multi-stage continuous flow polymerisation process for the synthesis of block copolymers using the RAFT polymerization method. The process retains all the benefits and versatility of the RAFT method and has been adapted for a series of monomer combinations, including acrylates, acrylamides, and vinyl monomers. It resulted in polymers with molecular weights between 13500 and 34100 g mol^{-1}, and dispersities typically between 1.21 and 1.58. Different architectures were prepared (including combinations of hydrophilic and hydrophobic blocks) which are soluble in a range of different solvents including aqueous and organic media.

Click here to go straight to the publication

Synthesis of Carbohydrate-Functionalised Sequence-Defined Oligo(amidoamine)s by Photochemical ThiolEne Coupling in a Continuous Flow Reactor

Felix Wojcik [1,2]
Dr. Alexander G. O'Brien[1,2]
Sebastian Götze [1,2]
Prof. Dr. Peter H. Seeberger [1,2]
Dr. Laura Hartmann [1,2]

[1] *Department of Biomolecular Systems, Max Planck Institute of Colloids and Interfaces, Potsdam (Germany)*
[2] *Institute for Chemistry and Biochemistry, Freie Universität Berlin, Berlin (Germany)*

Poly/oligo(amidoamine)s (PAAs) have recently been recognised for their potential as well-defined scaffolds for multiple carbohydrate presentation and as multivalent ligands. Herein, we report two complimentary strategies for the preparation of such sequence-defined carbohydrate-functionalised PAAs that use photochemical thiolene coupling (TEC)

as an alternative to the established azide–alkyne cycloaddition (“click”) reaction.

These developments enable the synthesis of sequence-defined carbohydrate-functionalised PAAs with potential biological applications.

Click here to go straight to the publication

Ozonolysis of Some Complex Organic Substrates in Flow

Mark David Roydhouse [1]
W B Motherwell [1]
A Constantinou [2]
Asterios Gavriilidis [2]
Rob C Wheeler[3]
Kenneth D Down[3]
Ian B Campbell[1]

[1] *Department of Chemistry, University College London, UK*
[2] *Department of Chemical Engineering, University College London, UK*
[3] *GlaxoSmithKline, Stevenage, UK*

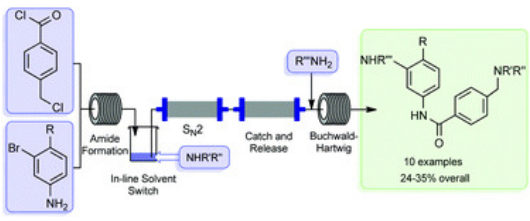
The ozonolyis of several organic substrates to give carbonyl compounds, carboxylic acids and nicotinic acids in flow using a standard lab-scale flow system equipped with a cooled flow cell was examined. Alkyl and aryl alkenes showed good conversion (49-99%) to the corresponding aldehydes and ketones utilising an "in flow" quench of triphenylphosphine. The ozonolysis of either 2 or 3-substituted furans obtained furnished a variety of carboxylic acids including the pharmaceutically important oxetane-3-carboxylic acids in two steps from furan and oxetan-3-one. Substituted benzoic acids were generated with high yields in two steps from aryl iodides. The non-selective ozonolysis of quinolines is known to give 2,3-dicarbonyl substituted pyridines, herein we report the selective ozonolysis of 8-hydroquinoline to give 3-[(1E)-3-oxoprop-1-en-1-yl]pyridine-2-carboxylic acid using flow techniques.

Click here to go straight to the publication

An expeditious synthesis of Imatinib and analogues utilising flow chemistry methods

Mark D Hopkin,
Ian Baxendale,
Steven.V.Ley

Dept of Chemistry, University of Cambridge, UK



A flow-based route to imatinib, the API of Gleevec, was developed and the general

procedure then used to generate a number of analogues which were screened for biological activity against Abl1. The flow synthesis required minimal manual intervention and was achieved despite the poor solubility of many of the reaction components.

Click here to go straight to the publication
