Flow Synthesis Online - January 2012

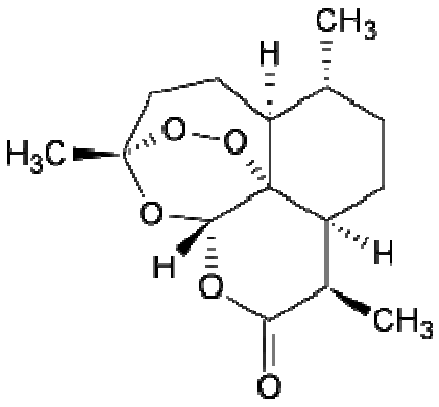
Welcome to the first newsletter of 2012, (and the last one of the Chinese Year of the Rabbit).

Contents

Flow Chemistry In The News

Low cost synthesis of key anti-malarial drug

The laboratory of Peter Seeberger in the Max Planck Institute in Potsdam have just released details of a breakthrough in the synthesis of Artemisinin.



The new low cost route involves a single photochemical step carried out in flow, using the Vapourtec R Series and a photo reactor developed in house.

Read more about the research

The actual publication is the first one in our publications section, see below.

German TV news feature showing the equipment in use (In German)

Product Announcements

Cooled Column

Vapourtec first created their cooled column system in 2010. However, it's mentioned here now as a result of the publication featured below, *Continuous proline catalysis via leaching of solid proline.*
(This paper is free access)

The cooled column is especially useful for work like that mentioned in the paper as it features precise and even control of the column temperature while offering full visibility of the column contents at all time (as shown by the photographs included in the paper)

More details

Announcements

The Vapourtec Flow Chemistry Workshop

In April 2012, Vapourtec will be holding a flow chemistry workshop immediately following the Flow Chemistry Congress conference in Boston. It's a chance to find out more about a range of flow related topics, see reaction demonstrations and get hands on experience of using flow chemistry equipment.

Spaces will be limited, so register your interest soon.

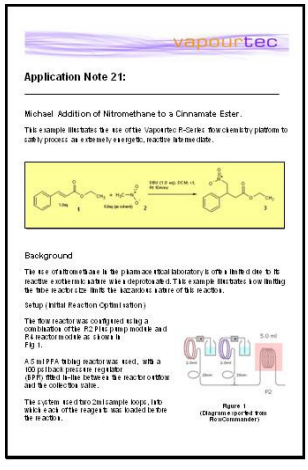
More details

Applications

New Application notes

3 new application notes are now available on the Vapourtec website.

They cover
- Michael Addition of nitromethane to a cinnamate ester
- Reduction of N-Boc Protected amines using lithium aluminium hydride.


vapourtec

Application Note 21:

Michael Addition of Nitromethane to a Cinnamate Ester.

Background

- Optimisation and scale-up of an SNAr using a highly volatile reagent (which would require a pressurised bomb reactor if performed in batch)

Application note page

Events - 2012

Flow Chemistry Europe

13-14 March , 2012
Munich, Germany
More details

RSC Continuous Flow Technology In Industry

19-21 March 2012
York, UK
More details

Flow Chemistry Congress

23-24 April 2012
Boston, USA
More details

Chemspec India

26 - 27 April, 2012
Mumbai, India
More details

Flow Chemistry Asia

25-26 October, 2012
Singapore
More details

Still reading someone else's copy of the newsletter ?

If you like reading the newsletter but tend to get it forwarded by a colleague, why not signup for your own copy ?

It will only take a minute, and your email address won't be used for anything else, ever. Each newsletter contains an "unsubscribe" link in case you should change your mind.

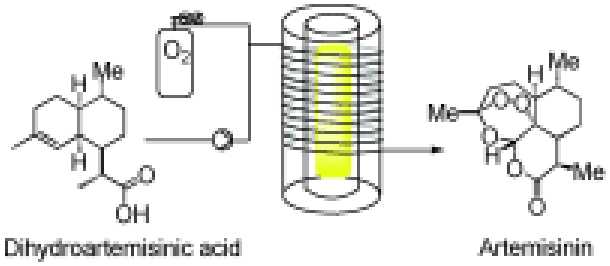
Click here to signup for your own copy

Publications

Continuous-Flow Synthesis of the Anti-Malaria Drug Artemisinin

François Lévesque[1]
Peter H. Seeberger [1 2]

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



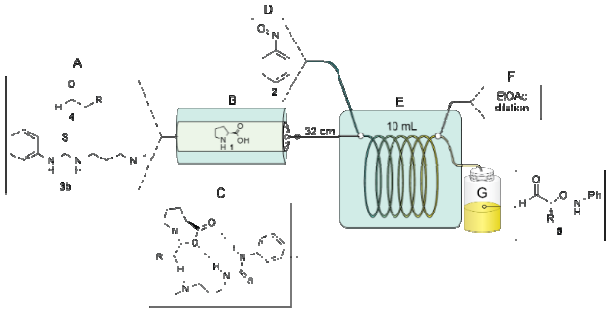
Malaria is a serious global health issue. Artemisinin combination treatments are the first-line drugs, but supplies are limited because artemisinin is obtained solely by extraction from Artemisia annua. A continuous-flow process that converts dihydroartemisinic acid into artemisinin (see scheme) is shown to be an inexpensive and scalable process that can ensure a steady, affordable supply of artemisinin.

Click here to go straight to the publication

Continuous proline catalysis via leaching of solid proline

Suzanne M. Opalka[1]
Ashley R. Longstreet[2]
D. Tyler McQuade[2]

[1]Department of Chemistry and Chemical Biology, Cornell University, USA
[2]Department of Chemistry and Biochemistry, Florida State University, USA



Herein, we demonstrate that a homogeneous catalyst can be prepared continuously via reaction with a packed-bed of a catalyst precursor. Specifically, we perform continuous proline catalyzed a-aminoxylations using a packed-bed of L-proline. The system relies on a multistep sequence in which an aldehyde and thiourea additive are passed through a column of solid proline, presumably forming a soluble oxazolidinone intermediate. This transports a catalytic amount of proline from the packed-bed into the reactor coil for subsequent combination with a solution of nitrosobenzene, affording the desired optically active a-aminooxy alcohol after reduction. To our knowledge, this is the first example in which a homogeneous catalyst is produced continuously using a packed-bed. We predict that the method will not only be useful for other L-proline catalyzed reactions, but we also foresee that it could be used to produce other catalytic species in flow.

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

Application of Flow Chemistry to the Selective Reduction of Esters to Aldehydes

Juan de M. Muñoz[1]
Jesús Alcázarv
Antonio de la Hoz[2]
Angel Díaz-Ortiz[2]
[1]*Janssen, Toledo, Spain*
[2]*Facultad de Ciencias Químicas, Universidad de Castilla-La Mancha, Spain*

The reduction of esters to aldehydes is an important transformation in organic chemistry and several reducing agents have been described. However, the use of this reaction in medicinal and natural product chemistry is limited due to the instability of the intermediates and the high reactivity of the reaction products. In the current article, the general and selective reduction of esters with diisobutyl-tert-butoxyaluminum hydride in flow is reported. This reagent allows esters to be reduced in the presence of different functional groups, including those considered to be of similar or higher reactivity.

Click here to go straight to the publication

Synthesis of Annulated Pyridines by Intramolecular Inverse-Electron-Demand Hetero-Diels-Alder Reaction under Superheated Continuous Flow Conditions

Rainer E. Martin [1]
Falk Morawitz [1]
Christoph Kuratli [1]
André M. Alker [2]
Alexander I. Alanine[1]

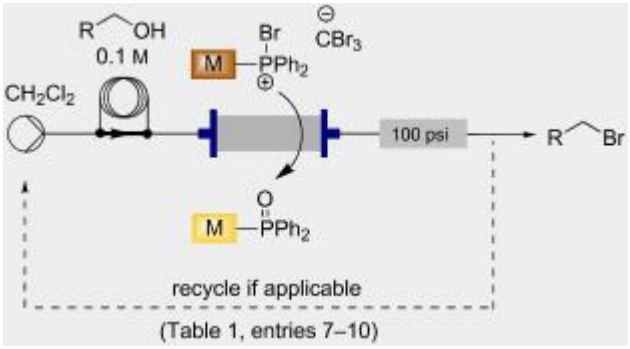
[1]*Chemistry Technology and Innovation, F. Hoffmann-La Roche Ltd, Basel, Switzerland*
[2]*Biostructure Section, F. Hoffmann-La Roche Ltd,Basel, Switzerland*

Pyrimidine alkynes can be transformed into the corresponding annulated pyridines efficiently in flow. The superheating of organic solvents far beyond their boiling point enables toxic and difficult to workup solvents such as nitrobenzene or chlorobenzene, which are usually employed for these reactions, to be replaced by less harmful ones like toluene. The relative rate of reactivity for a series of structurally close starting materials was investigated and a scalable flow process was developed, providing facile access to a series of novel annulated pyridine building blocks.

Click here to go straight to the publication

The application of a monolithic triphenylphosphine reagent for conducting Appel reactions in flow microreactors

Kimberley A. Roper[1]
Heiko Lange[1]
Anastasios Polyzos[1]
Malcolm B. Berry[2]
Ian R. Baxendale[1]
Steven V. Ley[1]
[1]Innovative Technology Centre, University of Cambridge, UK
[2]GlaxoSmithKline, Stevenage, UK



Herein we describe the application of a monolithic triphenylphosphine reagent to the Appel reaction in flow-chemistry processing, to generate various brominated products with high purity and in excellent yields, and with no requirement for further off-line purification.

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

Reviews

Flow Chemistry - A Key Enabling Technology for (Multistep) Organic Synthesis

Jens Wegner
Sascha Ceylan
Andreas Kirschning

Institut für Organische Chemie and Biomolekulares Wirkstoffzentrum (BMWZ), Leibniz Universität Hannover, Germany

Laboratory scaled flow-through processes have seen an explosive development over the past decade and have become an enabling technology for improving synthetic efficiency through automation and process optimization. Practically, flow devices are a crucial link between bench chemists and process engineers. The present review focuses on two unique aspects of modern flow chemistry where substantial advantages over the corresponding batch processes have become evident. Flow chemistry being one out of several enabling technologies can ideally be combined with other enabling technologies such as energy input. This may be achieved in form of heat to create supercritical conditions. Here, indirect methods such as microwave irradiation and inductive heating have seen widespread applications. Also radiation can efficiently be used to carry out photochemical reactions in a highly practical and scalable manner. A second unique aspect of flow chemistry compared to batch chemistry is associated with the option to carry out multistep synthesis by designing a flow set-up composed of several flow reactors. Besides their role as chemical reactors these can act as elements for purification or solvent switch.

Click here to go straight to the publication

Technical articles are in PDF form. Publications may require a subscription to access.

See you in March (in the Chinese New Year of the Dragon).

Vapourtec Ltd
Park Farm Business Centre
Fornham St Genevieve
Bury St Edmunds, England IP28 6TS
UK