

Flow Synthesis Online - March 2012

Welcome to a packed spring issue of the Vapourtec newsletter, including:

- A must-read publication from MIT examining in depth the issues of mixing, dispersion and scaleup in continuous flow reactors.
- A new Vapourtec/METTLER TOLEDO joint white paper showing the use of the FlowIR™ system in conjunction with the Vapourtec R Series™ System for real time monitoring of reaction output.
- The unveiling of the new Vapourtec High Pressure flow system.

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- Publications
 - Mixing, dispersion and scaleup in continuous flow reactors
 - Example of scale up to > 2kg
 - Phase Transfer Catalysis in flow
 - Two reviews looking at the flow chemistry world from different perspectives.

You have received this email because you have in the past expressed an interest in Vapourtec Flow Chemistry products. If you'd prefer not to receive this newsletter any more, use the unsubscribe link at the end of the email.

Product Announcements

Vapourtec / METTLER TOLEDO joint white paper

As a result of the recent collaboration between METTLER TOLEDO and Vapourtec (resulting in close integration between the FlowIR™ system and Vapourtec's FlowCommander™ software), a new joint white paper has been prepared.

The study shows how to characterise reaction output in real time for two different reactions, giving instant feedback of conversion with different conditions, and thus facilitating rapid optimization.



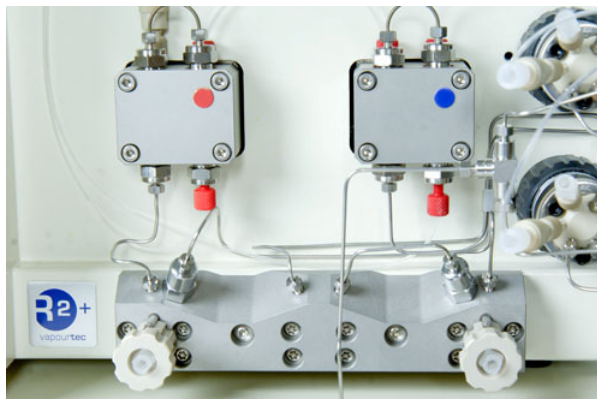
[Click here to request the white paper](#)

The New Vapourtec High Pressure Flow System

There are several specific scenarios where the pressure capability of a standard flow chemistry system is not sufficient.

For example

- high temperatures/very volatile solvents
- Continuous polymerization
- "Flash Chemistry" (very fast reactions)
- Synthesis of ionic liquids at scale



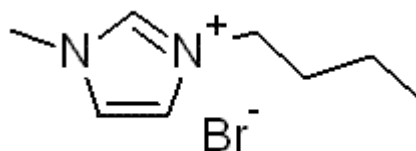
Vapourtec are therefore pleased to announce the development of a new high pressure pump module.

[Click here for more details](#)

Applications

Flow Synthesis of Ionic Liquids

Ionic liquids offer several useful properties and are of growing interest in the push towards greener chemistry. Unfortunately the challenges of batch synthesis make them extremely expensive to obtain.



In continuous flow, however, these challenges are more easily tackled, enabling straightforward and cost effective synthesis of pure ILs at significant scale.

To read more (including an application note showing an ionic liquid synthesis performed on the Vapourtec R Series™ system) click on the link below.

[Click here for more details](#)

Events

Upcoming meetings where you can see the Vapourtec system.

Flow Chemistry Congress

23-24 April 2012
Boston, USA

Please note

Vapourtec newsletter readers get a discount rate. Follow the link below and make sure to use one of the following discount codes.

Academic attendees coupon code : 465986

Industrial attendees coupon code : 649786

[Click here for discount Registration](#)

Chemspec India

26 - 27 April, 2012

Mumbai, India

[More details](#)

Flow Chemistry Asia

25-26 October, 2012

Singapore

[More details](#)

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Publications

Mixing and Dispersion in Small-Scale Flow Systems

Kevin D. Nagy¹

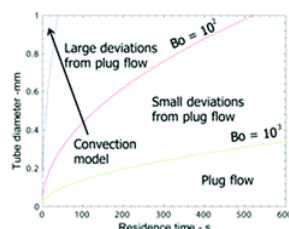
Bo Shen²Klavs F. Jensen¹

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Novartis-MIT Center for Continuous Manufacturing, MIT, USA



Fo_{tubes}	$Fo_{squares}$	Action
< 0.16		use laminar flow reactor model
< 2.1	< 3.3	large deviations from plug flow
< 21	< 33	small deviations from plug flow
> 21	> 33	plug flow behavior
$\chi < Fo$		no premixing necessary
$\chi > Fo$		premixing advised

$$Fo = \frac{4\tau D}{d_t^2}$$

Continuous flow chemistry is being used increasingly; however, without detailed knowledge of reaction engineering, it can be difficult to judge whether dispersion and mixing are important factors on reaction outcome. Understanding these effects can result in improved choices of reactor dimensions and give insight for

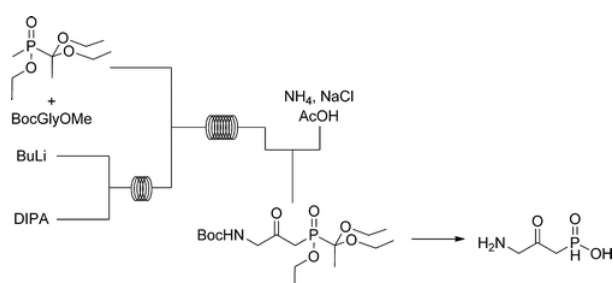
reactor scale-up. We provide an overview of both dispersive and mixing effects in flow systems and present simple relationships for determining whether mixing or dispersion is important for a given flow system. These results are summarized in convenient charts to enable the experimentalist to identify conditions with potential mixing or dispersion problems. The information also expedites design changes, such as inclusion or changes of mixers and changes in reaction tube diameters. As a case study, application of the principles to a glycosylation reaction results in increased throughput and cleaner product profiles compared to previously reported results.

[Click here to go straight to the publication](#)

Development of a Continuous Flow Scale-Up Approach of Reflux Inhibitor AZD6906

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Early scale-up work of a promising reflux inhibitor AZD6906 is described. Two steps of an earlier route were adapted to be performed in continuous flow to avoid issues related to batch procedures, resulting in a robust method with reduced cost of goods and improved product quality. Toxic and reactive reagents and starting materials could be handled in a flow regime, thereby allowing safer and more convenient reaction optimization and production.

[Click here to go straight to the publication](#)

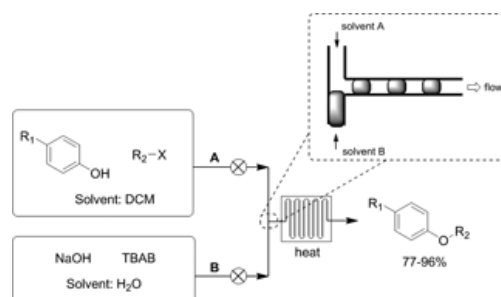
Phase-Transfer Catalysis under Continuous Flow Conditions: An Alternative Approach to the Biphasic Liquid/Liquid O-Alkylation of Phenols

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Italy

O-Alkylation of phenol compounds was performed in a continuous flow apparatus under biphasic liquid/liquid conditions and promoted by tetrabutylammonium bromide (TBAB) as a phase-transfer catalyst. The segmented flow that is generated within the flow system is able to afford the desired ethers in high yield and in very short times.



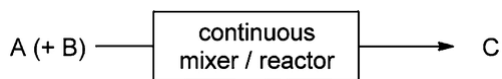
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Reviews

Using Continuous Processes to Increase Production

Neal G. Anderson

Anderson's Process Solutions, Jacksonville, Oregon, United States



Driving forces: safety, yield, quality, economics

Continuous operations have become popular in both academia and the pharmaceutical industry. Continuous operations may be developed to make high-quality material safely, or because continuous operations are the only effective and economical way to make larger quantities of material. This review surveys the area of continuous processes used to make larger quantities of material and discusses the feasibility of developing economical continuous operations.

[Click here to do straight to the publication](#)

Continuous Flow Synthesis. A Pharma Perspective

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