Welcome to the **Flow Synthesis Online** newsletter.

This publication is released generally bi-monthly (major holiday periods permitting) and will showcase new applications, events, and equipment in the world of lab scale flow chemistry.

In this issue:

Happy New Year !

Announcements

100th

In January chemistry Copenhagen,

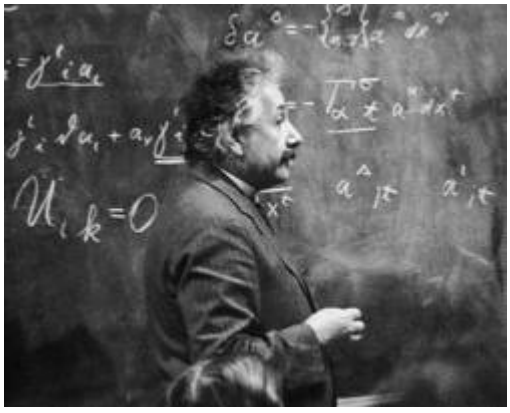
LEO Pharma One will be software whereas the with the open

[Click here to find out about Flow Wizard]

Vapourtec System Installed

2011, Vapourtec installed their 100th flow system, in LEO Pharma in Ballerup near Denmark.

now have two Vapourtec systems. configured with the Flow Commander interface for use by a dedicated user, other will be configured for walk up use, access "Flow Wizard" interface.



New Academic Collaborations

Vapourtec is proud to announce several new collaborations with key academic groups in Europe and North America to help further the field of flow chemistry.

The collaborations are aimed at addressing a number of areas, including the safe use of particular highly reactive

intermediates in multi step reactions, transfer of known batch methodologies to flow, generation of novel organometallic species, and the use of cleaner, greener solvents in a variety of chemical situations.

Click here for more details

Vapourtec to open Asian office

In March 2011 Vapourtec will officially open a new office in Kuala Lumpur, Malaysia.

The creation of the Malaysian office is part of an ongoing program to provide improved support for Vapourtec customers in Malaysia, Japan, South Korea, Australia and Singapore, and to develop distribution in India and China.

This office will house both support and R&D staff. Full contact details will be available on the Vapourtec website in due course but in the meantime, enquiries should be addressed to asia@vapourtec.com

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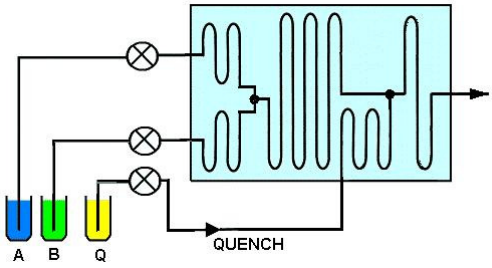
Product News

Tube Reactor with integral heated mixing

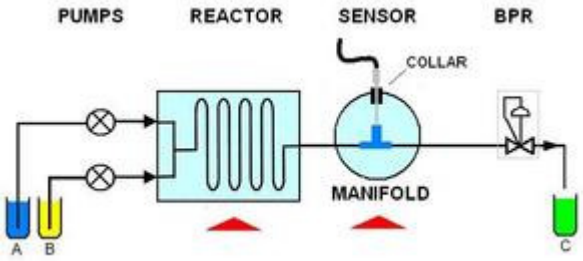


In some cases it is not sufficient to mix reagents and THEN feed the mixture into a reactor at a controlled temperature.

Vapourtec now offer a tube reactor giving more advanced control of the temperature of reagents both before and after the main reactor residence area.

Click here for more details

Controlled Temperature Sensor Manifold



Flow chemistry offers a great platform for inline measurement. However, some sensor technologies require that the sensor itself be kept at a very stable temperature to maintain calibrated accuracy.

The new sensor manifold offers accurate and stable programmable temperature control of any sensor, and plugs straight into any existing Vapourtec R4 reactor heater units.

Click here for more details

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Is it your first time ?

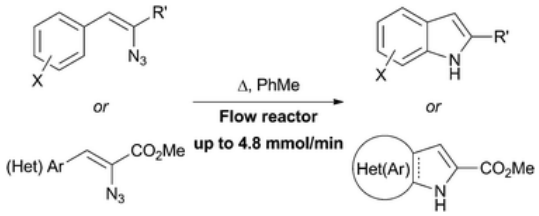
If this is the first issue of the newsletter that you've received, you might like to take a look at what you've missed in some previous issues.

Click here to see newsletter archive

Publications

Continuous flow thermolysis of azidoacrylates for the synthesis of heterocycles and pharmaceutical intermediates

Alexander G. O'Brien,
François Lévesque
Peter H. Seeberger
Department of Biomolecular Systems
Max Planck Institute of Colloids and Interfaces

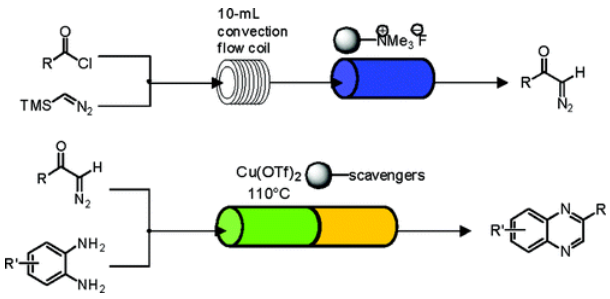


An efficient, safe and scalable procedure for the continuous flow thermolysis of azidoacrylates to yield indoles has been developed and was applied to the synthesis of related heterocycles.
The scalability of the process was demonstrated in the continuous flow synthesis of a precursor to the DAAO inhibitor 4*H*-furo[3,2-*b*]pyrrole-5-carboxylic acid.

Click here to go straight to the publication

Safe and Reliable Synthesis of Diazoketones and Quinoxalines in a Continuous Flow Reactor

Laetitia J. Martin [1],
Andreas L. Marzinzik [1],
Steven V. Ley [2]
Ian R. Baxendale [2]



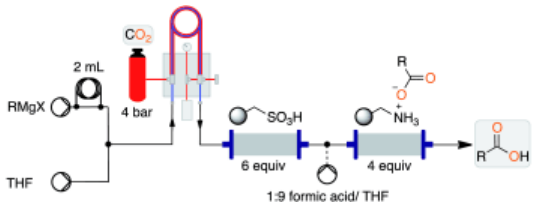
[1] *Novartis Institute for BioMedical Research, Basel, Switzerland*
[2] *Innovative Technology Centre, Department of Chemistry, University of Cambridge, U.K.*

A flow method for the synthesis of aliphatic and aromatic diazoketones from acyl chloride precursors has been developed and used to prepare quinoxalines in a multistep sequence without isolation of the potentially explosive diazoketone. The protocol showcases an efficient in-line purification using supported scavengers with time-saving and safety benefits and in particular a reduction in the operator's exposure to carcinogenic phenylenediamines.

Click here to go straight to the publication

The Continuous-Flow Synthesis of Carboxylic Acids using CO_2

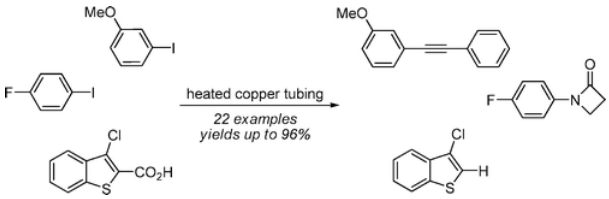
Dr. Anastasios Polyzos,
Dr. Matthew O'Brien,
Trine P. Petersen,
Dr. Ian R. Baxendale,
Prof. Steven V. Ley



Innovative Technology Centre, Department of Chemistry, University of Cambridge, U.K
Keep it simple: A gas–liquid flow reactor has been developed based on a gas permeable tube-in-tube configuration which effectively delivers gas to a liquid substrate stream in a safe, continuous fashion. A series of carboxylic acids were prepared from the reaction of CO_2 with a range of Grignard reagents (see picture).

Click here to go straight to the publication

Continuous Flow Coupling and Decarboxylation Reactions Promoted by Copper Tubing



Yun Zhang [1],
Timothy F. Jamison [2],
Sejal Patel [1],
Nello Mainolfi [1]

[1] *Novartis Institutes for Biomedical Research Inc., Cambridge, United States,*
[2] *Department of Chemistry, MIT, Cambridge, United States*

A convenient and efficient flow method for Ullmann condensations, Sonogashira couplings, and decarboxylation reactions using a commercially available copper tube flow reactor (CTFR) is described. The heated CTFR effects these transformations without added metals (e.g., Pd), ligands, or reagents, and in greater than 90% yield in most cases examined.

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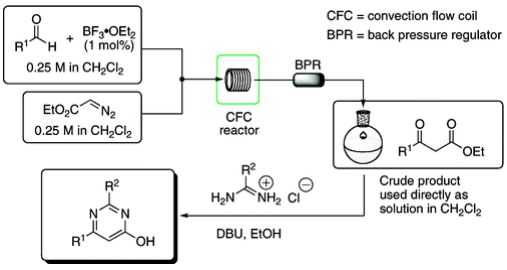
Synthesis of ß-Keto Esters In Flow and Rapid Access to Substituted Pyrimidines

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 Global Research and Development, Sandwich, UK*

An in-flow process has been developed for the synthesis of ß-keto esters via the BF_3OEt_2-catalyzed formal C-H insertion of ethyl diazoacetate into aldehydes. The ß-keto esters were then condensed with a range of amidines to give a variety of 2,6-substituted pyrimidin-4-ols.!

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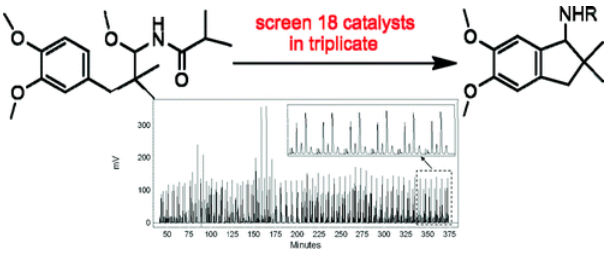
Rapid Catalyst Screening by a Continuous-Flow Microreactor Interfaced with Ultra-High-Pressure Liquid Chromatography



Hui Fang,
Qing Xiao,
Fanghui Wu,
Paul E. Floreancig
Stephen G. Weber
Department of Chemistry, University of Pittsburgh, USA

A high-throughput screening system for homogeneous catalyst discovery has been developed by integrating a continuous-flow capillary-based microreactor with ultra-high-pressure liquid chromatography (UHPLC) for fast online analysis. Reactions are conducted in distinct and stable zones in a flow stream that allows for time and temperature regulation. UHPLC detection at high temperature allows high throughput online determination of substrate, product, and byproduct concentrations. We evaluated the efficacies of a series of soluble acid catalysts for an intramolecular Friedel-Crafts addition into an acyliminium ion intermediate within 1 day and with minimal material investment. The effects of catalyst loading, reaction time, and reaction temperature were also screened. This system exhibited high reproducibility for high-throughput catalyst screening and allowed several acid catalysts for the reaction to be identified. Major side products from the reactions were determined through off-line mass spectrometric detection. $Er(OTf)_3$, the catalyst that showed optimal efficiency in the screening, was shown to be effective at promoting the cyclization reaction on a preparative scale.

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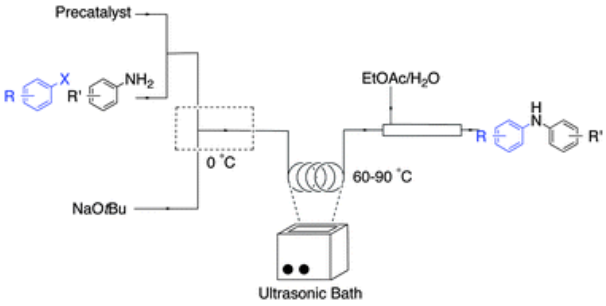
Palladium-catalyzed amination reactions in flow: overcoming the challenges of clogging via acoustic irradiation



Timothy Noël,
John R. Naber,
Ryan L. Hartman,
Jonathan P. McMullen,
Klavs F. Jensen
Stephen L. Buchwald
Massachussetts Institute of Technology, USA

A continuous-flow palladium-catalyzed amination reaction was made possible through efficient handling of solids via acoustic irradiation. Various

diarylamines were obtained with reaction times ranging from 20 s to 10 min.

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