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 Flow Synthesis world.

In this issue
Applications - *Flow Ozonolysis*
Product News - *The **NEW** Open Access Vapourtec System*
Publications - *Flow chemistry publications from the last few weeks*

Enjoy.

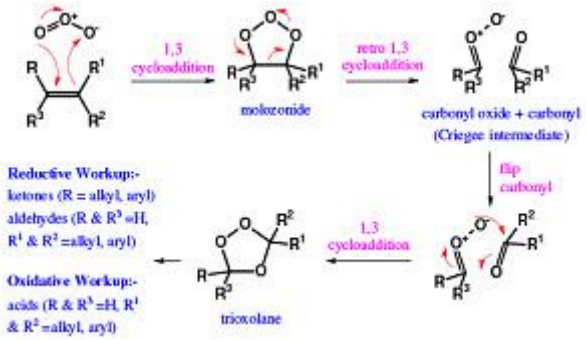
Applications

Ozonolysis in Flow

Earlier this year we briefly described work at University College London using the Vapourtec R Series system for flow ozonolysis.

At the inaugural RSC / SCI Flow Chemistry Symposium in early November, the team from UCL presented this work.

Click here to see the work in detail



Product News

New Vapourtec Brochure available

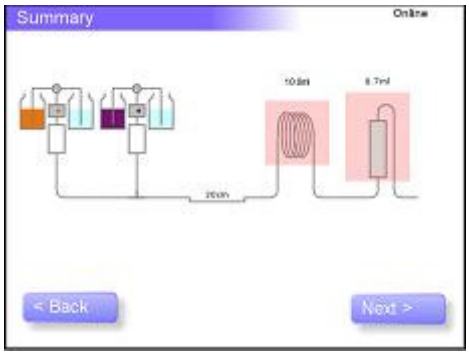
The new Vapourtec brochure shows an up to date list of all the pumping and reactor options available for the highly flexible R Series system.

The 6 page PDF version of the brochure is approximately 1.7MB and can be downloaded using the link below.

Alternatively, reply to this email with full address details to request a printed copy.

Click here to go straight to the brochure

Vapourtec Launch Open Access R Series



Since 2008 the Vapourtec FlowCommander software has offered flexibility, power and control to users of the R Series flow chemistry system.

But increasingly, there is a need for open access to flow chemistry instruments, and it is virtually impossible for one interface to satisfy the needs of both experienced power users and occasional walk up users.

Vapourtec are therefore pleased to announce a new touch screen user interface designed especially for those walk up users.

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.

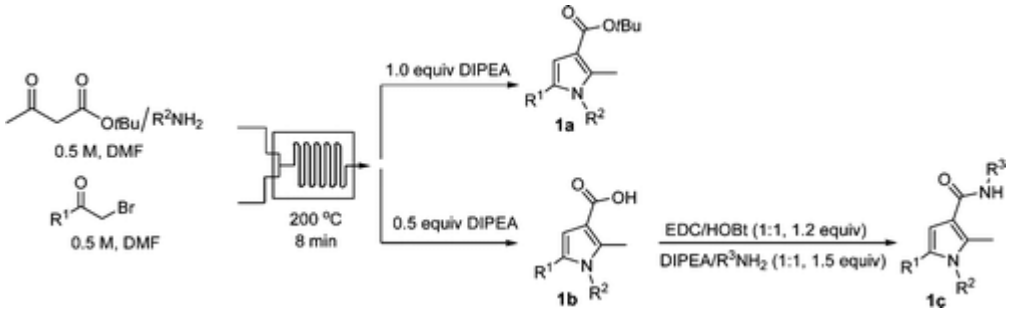
click here to see newsletter archive

Publications

One-Step Continuous Flow Synthesis of Highly Substituted Pyrrole-3-carboxylic Acid Derivatives via in Situ Hydrolysis of tert-Butyl Esters

Ananda Herath and Nicholas D. P. Cosford

Apoptosis and Cell Death Research Program & Conrad Prebys Center for Chemical Genomics, Sanford-Burnham Medical Research Institute, La Jolla, USA



The first one-step, continuous flow synthesis of pyrrole-3-carboxylic acids directly from tert-butyl acetoacetates, amines, and 2-bromoketones is reported. The HBr generated as a byproduct in the Hantzsch reaction was utilized in the flow method to hydrolyze the t-butyl esters in situ to provide the corresponding acids in a single microreactor. The protocol was used in the multistep synthesis of pyrrole-3-carboxamides, including two CB1 inverse agonists, directly from commercially available starting materials in a single continuous process.

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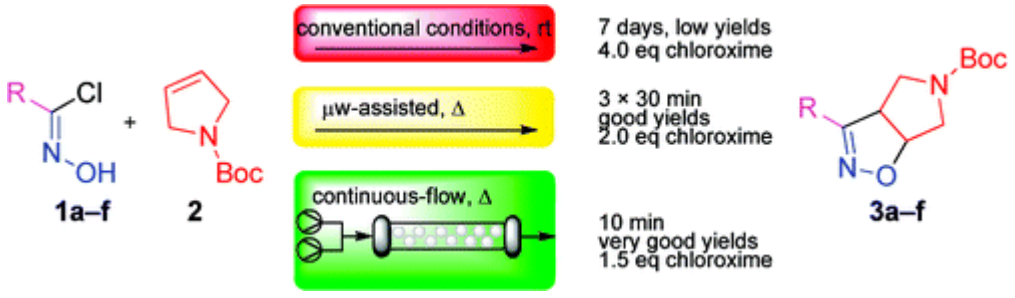
Synthesis of 3-Aryl/benzyl-4,5,6,6a-tetrahydro-3aH-pyrrolo[3,4-d]isoxazole Derivatives: A Comparison between Conventional, Microwave-Assisted and Flow-Based Methodologies

Sabrina Castellano[1], Lucia Tamborini[2], Monica Viviano[1], Andrea Pinto[2], Gianluca Sbardella[1], Paola Conti[2]



[1] *Dipartimento di Scienze Farmaceutiche, Universit degli Studi di Salerno, Italy*
[2] *Dipartimento di Scienze Farmaceutiche "Pietro Pratesi", Universit degli Studi di Milano, Italy*

Two modern synthetic technologies to perform 1,3-dipolar cycloaddition reactions were compared. This study puts in evidence the power of microwave-assisted and flow-based methodologies compared to the conventional one in terms of reaction time and yield, and demonstrates the potential of flow chemistry in terms of time, automation, and scaling up opportunities.

Click here to go straight to the publication

Design and Packaging of Microreactors for High Pressure and High Temperature Applications

Samuel Marre[12], Andrea Adamo[1], Soubir Basak[1], Cyril Aymonier[2], and Klavs F. Jensen*[1]

[1]*Chemical Engineering Department, MIT Cambridge, USA*
[2]*CNRS, Universit de Bordeaux, Pessac , France*

The development of chemically compatible microsystems that can operate across expanded process conditions, such as high pressures (HP) and high temperatures (HT), is of great interest for many applications, including high pressure chemistry and hydrothermal and supercritical fluid processes. We present a methodology for the successful design and use of HP/HT microsystems. Key parameters for the fabrication of microreactors and modular fluidic packaging able to withstand severe pressure and temperature conditions (30 MPa, 400 °C) are described. Applications of these HP/HT plug and play microsystems are illustrated with examples, including multiphase flow visualization through the transition of liquid−liquid immiscible hexane−water segmented flow to homogeneous supercritical flow, on chip supercritical water oxidation, and synthesis of iron oxide nanoparticles.

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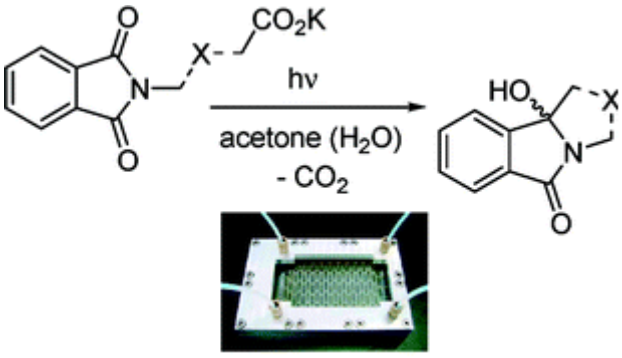
From Conventional to Microphotochemistry: Photodecarboxylation Reactions Involving Phthalimides

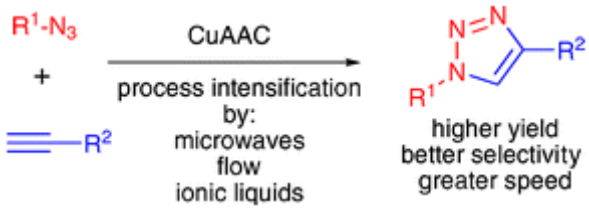


Oksana Shvydkiv[1],
Sonia Gallagher[1],
Kieran Nolan[1],
Michael Oelgemller*[2]

[1]*Dublin City University, School of Chemical Sciences, Ireland,*
[2]*James Cook University, School of Pharmacy and Molecular Sciences, Townsville, Australia*

A series of acetone-sensitized photodecarboxylation reactions involving phthalimides have been investigated using conventional and microphotochemistry. Both, intra- and intermolecular transformations were compared. In all cases examined, the reactions performed in microreactors were superior in terms of conversions or isolated yields. These findings unambiguously prove the advantage of microphotochemistry over conventional photochemical techniques.

Click here to go straight to the publication



Click chemistry under non-classical reaction conditions (Review)

C. Oliver Kappe and Erik Van der Eycken

First described almost a decade ago, "click" reactions such as the Cu(I)-catalyzed azide–alkyne cycloaddition (CuAAC) are widely used today in organic and medicinal chemistry, in the polymer and material science field, and in chemical biology. While most click reactions can be performed at room temperature there are instances where some form of process intensification is required. In this tutorial review, aimed at the synthetic chemistry community, examples of click chemistry carried out under non-classical reaction conditions, such as for example applying microwave heating or continuous flow processing will be highlighted.

Click here to go straight to the publication

Oxidation of Sulfides with a Silica-Supported Peracid in Supercritical Carbon Dioxide under Flow Conditions: Tuning Chemoselectivity with Pressure

Rossella Mello, Andrea Olmos. Ana Alcalde-Aragonés, Alba Díaz-Rodríguez, María Elena González Núñez. Gregorio Asensio

Dep. Quim. Org., Univ. Valencia, Spain

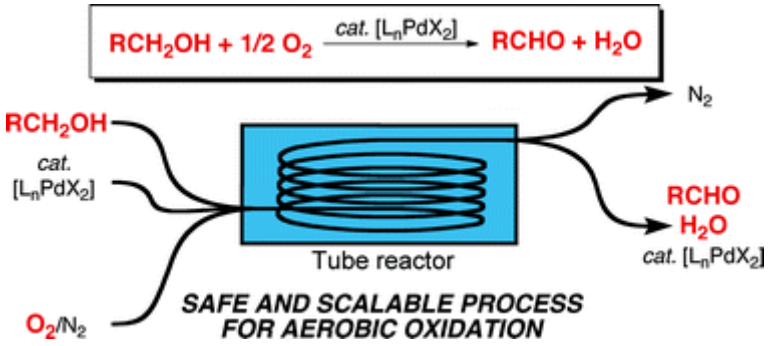
Supercritical carbon dioxide is a convenient medium for performing the selective oxidation of sulfides to either sulfoxides or sulfones with [2-percarboxyethyl]-functionalized silica under flow conditions. The chemoselectivity of the reaction, which results from the different diffusion rates of sulfide and sulfoxide over the reagent bed, can be controlled by adjusting the pressure and the hydration of the silica surface as both the solvating power of the mobile phase and the surface activity of the stationary phase determine the migration rates of sulfide and sulfoxide over the supported peroxide. The results elucidate the impact of surface phenomena on the course of chemical reactions carried out under flow conditions.

Click here to go straight to the publication

Development of safe and scalable continuous-flow methods for palladium-catalyzed aerobic oxidation reactions

Xuan Ye[1], Martin D. Johnson[2], Tianning Diao[1], Matthew H. Yates[2] and Shannon S. Stahl[1]

[1]*University of Wisconsin, USA*
[2]*Eli Lilly & Co*



The synthetic scope and utility of Pd-catalyzed aerobic oxidation reactions has advanced significantly over the past decade, and these reactions have the potential to address important green-chemistry challenges in the pharmaceutical industry. This potential has not been realized, however, because safety concerns and process constraints hinder large-scale applications of this chemistry. These limitations are addressed by the development of a continuous-flow tube reactor, which has been demonstrated on several scales in the aerobic oxidation of alcohols. Use of a dilute oxygen gas source (8% O2 in N2) ensures that the oxygen/organic mixture never enters the explosive regime, and efficient gas-liquid mixing in the reactor minimizes decomposition of the homogeneous catalyst into inactive Pd metal. These results provide the basis for large-scale implementation of palladium-catalyzed (and other) aerobic oxidation reactions for pharmaceutical synthesis.

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Efficient Access to New Chemical Space Through Flow—Construction of Druglike Macrocycles Through Copper-Surface-Catalyzed Azide–Alkyne Cycloaddition Reactions

Keith James & Andrew Bogdan

The Scripps Institute, La Jolla, USA

A series of 12- to 22-membered macrocycles, with druglike functionality and properties, have been generated by using a simple and efficient copper-catalyzed azide–acetylene cycloaddition reaction, conducted in flow in high-temperature copper tubing, under environmentally friendly conditions. The triazole-containing macrocycles have been generated in up to 90 % yield in a 5 min reaction, without resorting to the high-dilution conditions typical of macrocyclization reactions. This approach represents a very efficient method for constructing this important class of molecules, in terms of yield, concentration, and environmental considerations.

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The technical articles above are in PDF form and may be immediately downloaded or read online. No registration is required. Enjoy !

Any 3rd Party publications referred to may require a subscription to download.

About Vapourtec Ltd

Vapourtec develop and manufacture the R Series Flow Chemistry Platform, the leading choice of industrial and academic users worldwide. To find out more about the R Series, or about Flow Chemistry generally, go to

http://www.vapourtec.co.uk

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