Flow Synthesis Online - Summer 2012

This issue is a big one !

Firstly, there's a brand new flow chemistry system, the E-Series, (right) unveiled. Scroll down for more information.

There are 3 new application notes
- Nitro reduction with iron granules
- Amidocarbonylation with CO using a gas/liquid reactor
- Continuous pumped fluorination with DAST.

And some great flow chemistry publications
- Continuous flow synthesis and inline purification using simulated moving bed (SMB)
- Continuous end group removal of polymers using a RAFT process
- A "Catch-React-Release" Method for the Flow Synthesis of 2-Aminopyrimidines
- Asymmetric Homogeneous Hydrogenation in Flow using a Tube-in-Tube Reactor and more

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New Product Announcement

The New E-Series Flow Chemistry System

Vapourtec are pleased to unveil a completely new flow chemistry system.

The E-Series system is an all in one benchtop system for basic research and teaching, which combines robustness, ease of use and cost effectiveness.

It is available in 3 different configurations, for teaching, medicinal chemistry and polymer and nanoparticle synthesis.

The E-Series offers 2 reaction steps, 2 or 3 reagent pumps, an

easy to use touchscreen interface, and access to the full range of reactors used by the high end Vapourtec R-Series system.

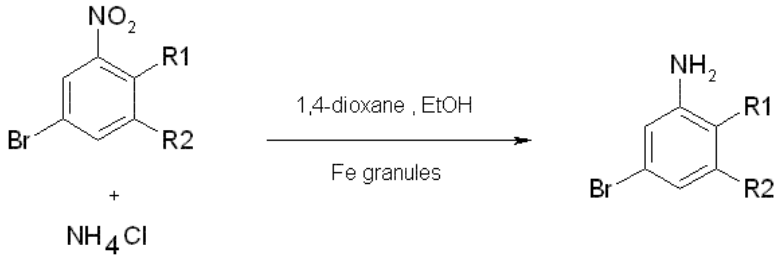
At the heart of the E-Series is the new Vapourtec V3 pump, which offers smooth continuous output, resistance to acids, and even tolerance of particulates.

Click here to find out more

Application Notes

3 new application notes have recently been made available on the Vapourtec website.

Simplified Aromatic Nitro Reduction

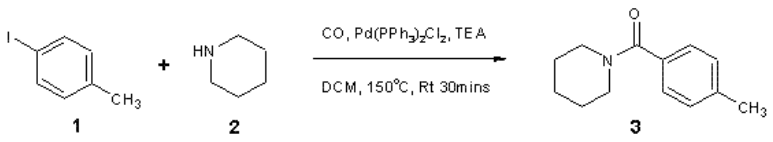


Reduction of aromatic nitro compounds with iron is a facile way to convert an aromatic nitro group to the corresponding amino group in the presence of an aryl halide, but removal of iron oxide afterwards can prove difficult.

In this study a continuous flow process was developed by packing iron granules into an Omnifit column, enabling the author to generate 16g of the desired compound in excellent yield and purity with miniumal work up.

Go to the Vapourtec application note page

Amidocarbonylation using a tube-in-tube membrane reactor



Pd catalysed carboxylation's of aryl halides offer the specific, selective synthesis of a number of carboxylic acid derivatives accessing acids, esters, amides, aldehydes and ketones by reacting the aryl halide, CO and the corresponding nucleophile.

Here the use of the Vapourtec tube-in-tube Gas/Liquid reactor is demonstrated, in an amidocarbonylation of iodotoluene with CO gas. Reaction times are significantly shortened compared with comparable batch methods.

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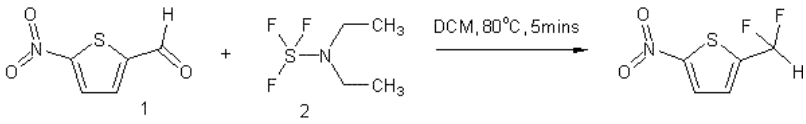
Continuous Fluorination with DAST



1 2

Of the nucleophilic fluorinating regents the most commonly used is Diethylaminosulfur trifluoride (DAST), a reagent derived from SF_4.

It is particularly useful for conversion of alcohols to alkyl fluorides, carboxylic acids to acyl fluorides and carbonyl compounds to gem-difluorides.
This sort of reaction lends itself well to a continuous flow approach (more efficient heat transfer to control thermal runaway, the ability to limit reaction volume, the decrease in handling explosive, highly toxic and corrosive reagents and the continuous replenishment of the reactants).
Hence there are a number of publications that demonstrate the use of DAST in microfluidic systems.

The reagent is commonly introduced to the flowing stream after the pumphead via injection loops. but this study describes the use of the Vapourtec R-Series reactor to continuously feed the moisture sensitive fluorinating reagent DAST directly through the acid resistant R2 C Plus pump heads allowing a continuous, scalable reaction.

Go to the Vapourtec application note page

Events - Where to see Vapourtec

A Celebration of Organic Chemistry

Where : AstraZeneca, Alderley Edge, UK
When : 24-25 Sep 2012

More details

Fourth Symposium on Continuous Flow Reactor Technology for Industrial Applications

Where : Lisbon, Portugal
When : 26-27 Sep 2012

More Details

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Publications

Continuous Synthesis and Purification by Direct Coupling of a Flow Reactor with Simulated Moving-Bed Chromatography

Alexander G. O'Brien[1]
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François Lévesque [1]
Ju Weon Lee[3]
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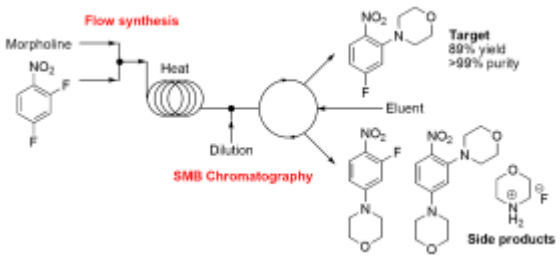

Continuous synthesis meets continuous purification to produce pure products from crude reaction mixtures. In the nucleophilic aromatic substitution of 2,4-difluoronitrobenzene with morpholine the desired monosubstituted product can be continuously separated from the byproducts in a purity of over 99% by coupling a flow reactor to a simulated moving bed (SMB) chromatography module (see scheme).

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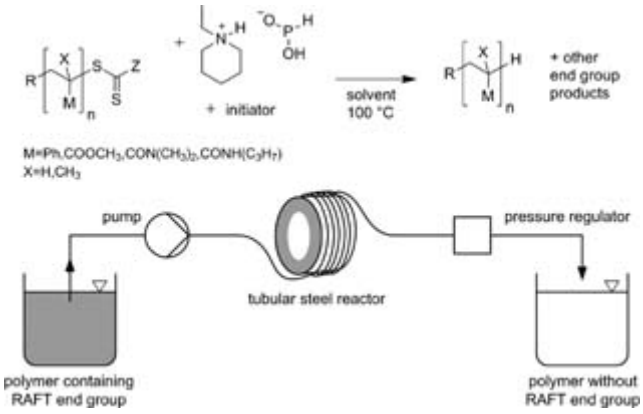
A Continuous Flow Process for the Radical Induced End Group Removal of RAFT Polymers

Christian H. Hornung
Almar Postma
Simon Saubern
John Chiefari

CSIRO Materials Science & Engineering, Victoria Australia



A continuous flow process for the radical-induced end-group removal of polymers made by a RAFT process is described. A series of different monomers, including acrylamides, methacrylate, and styrene are polymerized at 70–100?°C using various different RAFT agents, solvents, and radical initiators. The subsequent end group removal process is carried out in a steel tube flow reactor system at 100?°C in organic solvents or water. After reaction, the polymers exhibit low polydispersities between 1.03 and 1.19, and average molecular weights between 7500 and 22 800?g?·?mol-1. This continuous flow approach provides a facile alternative scale-up route to conventional batch operation and can be integrated into a sequential flow process consisting of RAFT polymerization followed by post-treatment.

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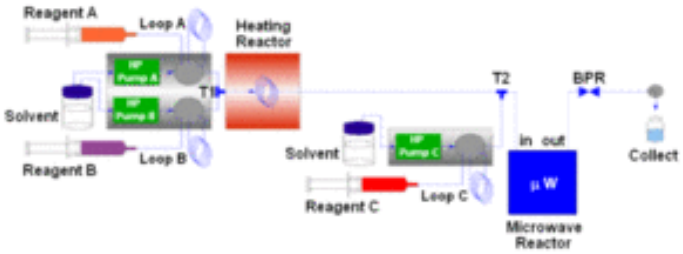
Continuous Flow Synthesis of Secondary Amides by Tandem Azidation- Amidation of Anilines

Christian Spiteri
John E. Moses*

School of Chemistry, University of Nottingham, UK



The continuous flow synthesis of a variety of secondary amides by tandem azidation-amidation of anilines is described. This new procedure benefits from the improved safety feature of generating aromatic azides in flow, thus ensuring low concentrations of any potentially hazardous intermediates. The protocol was amenable to the production of multi-gram quantities of the amide product.

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A "Catch-React-Release" Method for the Flow Synthesis of 2-

Aminopyrimidines and Preparation of the Imatinib Base

Richard J. Ingham
Elena Riva
Nikzad Nikbin
Ian R. Baxendale
Steven V. Ley*

Innovative Technology Centre,
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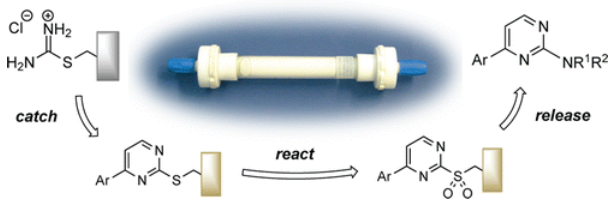

The development of a monolith-supported synthetic procedure is reported, taking advantage of flow processing and the superior flow characteristics of monolithic reagents over gel-phase beads, to allow facile access to an important family of 2-aminopyrimidine derivatives. The process has been successfully applied to a key precursor on route to Imatinib (Ar = 3-pyridyl, R^1 = 2-methyl-5-nitrobenzyl, R^2 = H).

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Sustainable and efficient methodology for CLA synthesis and identification

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Microwave-assisted organic synthesis and continuous-flow techniques have been successfully employed for the preparation of conjugated linoleic acids (CLA), compounds with high health beneficial effects. A good production rate of CLA was obtained. A sustainable methodology for the differentiation of both positional and geometrical CLA isomers (diene), based on the analysis by NMR spectroscopy of the resulting Diels-Alder cycloadducts with an appropriate dienophile, was developed.

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Asymmetric Homogeneous Hydrogenation in Flow using a Tube-in-Tube Reactor

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Eva Casas Arcé[2]

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In this update, the asymmetric homogeneous hydrogenation of a number of trisubstituted olefins utilizing the recently developed tube-in-tube gas-liquid flow reactor is described. A number of chiral iridium- and rhodium-based catalysts and other parameters such as pressure, solvent, temperature and catalyst loading were screened. The advantage of the flow set-up for rapid screening and optimization of reaction parameters is illustrated. Furthermore, a comparative study using batch conditions aided in the optimization of the flow reaction set-up. The set-up was further modified to recycle the catalyst which prolonged catalytic activity.

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Reviews

Micro reactors, flow reactors and continuous flow synthesis

Charlotte Wiles, Paul Watts
University of Hull

This review article explains the advantages of micro reactors and flow reactors as tools for conducting organic synthesis and describes how the technology may be used in research and development as well as production. A selection of examples is taken from the literature to illustrate how micro reactors enables chemists to perform their reactions more efficiently than when using batch processes.

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