ALMAC

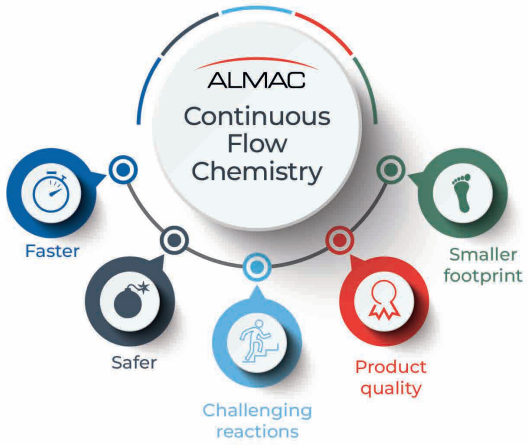
Partnering to Advance Human Health

Brochure

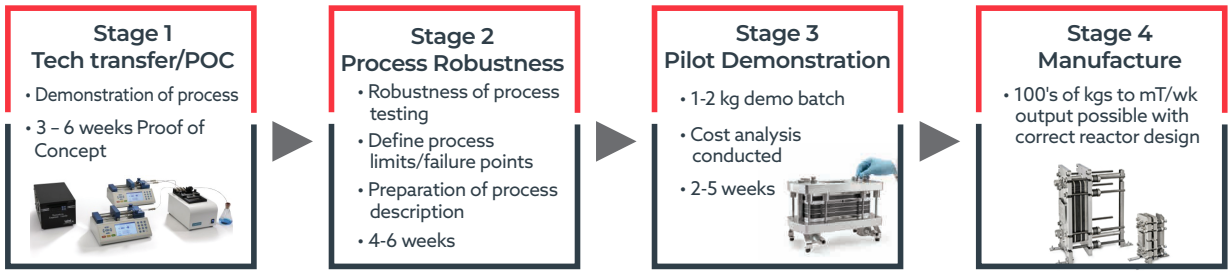
Think Almac...
Integrated Flow Technologies

- An integrated flow enabling technology platform from lab scale to manufacture
- Defined routes from development to manufacture
- Specialist expertise in:
  - High pressure
  - High energy
  - Oxidations
  - Photochemistry

Integrated Flow Technologies



Almac has the expertise and capabilities to deliver flow technologies from proof of concept reaction validity through to manufacture with defined workflows



Stage 1: Proof of concept

Stage 1 involves confirmation of reaction validity under continuous flow including assessment of solubility of starting materials, reagents and products as well as confirmation of product formation. Various parameters will be investigated such as stoichiometry, flow rates, temperature, etc.

Stage 2: Process Robustness

Stage 2 is a test of the process robustness to define safe operating windows for parameters as the process is further developed for scale-up. This stage also includes confirmation of flowability, hazard assessment and preparation of a process description (PD).

Stage 3: Pilot demonstration

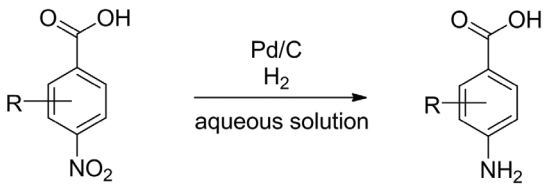
With PD prepared, demo batches of kilograms scale can be carried out on intermediate equipment from lab scale to manufacture. This generates material for customer assessment and critical information for further scale-up if needed.

Stage 4: Manufacture

Manufacture will involve building a suitable flow rig, full safety testing around the process and delivery of the required amount of product with an agreed specification.

At the end of each Stage there is a Go or No Go decision made in agreement with the customer.

Case Study 1 – Aromatic nitroreduction

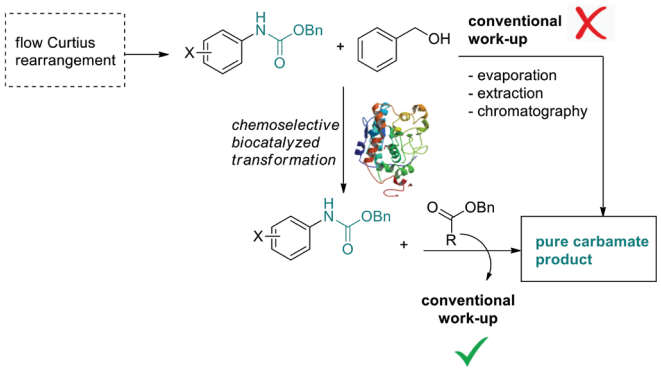


Our client required development of an existing batch transfer hydrogenation to improve downstream processing.

Almac's solution: Packed bed hydrogenation with rapid screening of in-house pelletised catalyst library, process optimisation and delivery of 1 kg for downstream processing assessment.

Value for Client: Removal of organic solvents from process. Easier product purification due to no catalyst removal issues. Increased control of GTI by-product intermediates.

Case Study 2 – Curtius Rearrangement

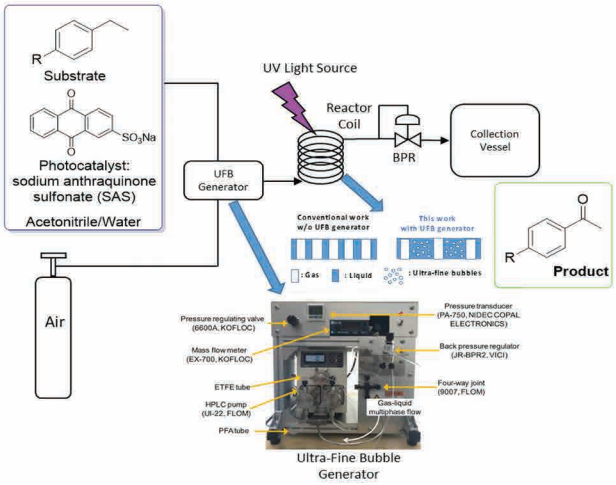


Our client required development of a high energy continuous flow process to access carbamate derivatives.

Almac's solution: Direct activation of carboxylic acids with diphenylphosphoryl azide (DPPA) was a key decision due to the stability and commercial availability of DPPA and acid substrates, and permitted use of a scalable homogeneous liquid-phase system. An excess of nucleophile (benzyl alcohol) was necessary.

Value for Client: Coupling of the Curtius rearrangement with an immobilized enzyme elegantly facilitated chemoselective tagging of the residual reagent, resulting in a facile purification process under continuous flow.

Case Study 3 – Oxidation

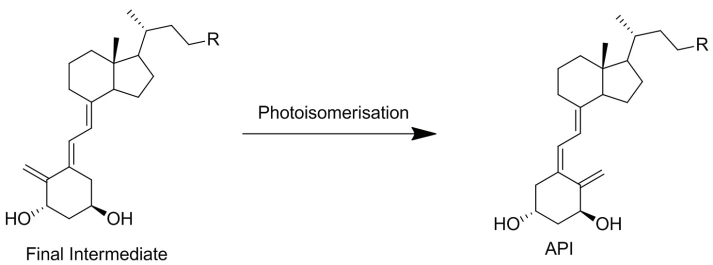


Our client required a selective photooxidation of an alkyl benzene where batch scale-up was limited due to poor gas/liquid mass transfer and light penetration.

Almac's solution: Selective photooxidation of alkyl benzenes was studied in a custom-built continuous flow photochemical reactor equipped with fine bubble generator and a low power UV light source. Fine bubbles of air were used as an oxidizing agent along with water-soluble sodium anthraquinone sulfonate as catalyst.

Value for Client: Due to enhanced mass transfer and greater efficiency, compressed air can be used as oxidant instead of pure O_2, alleviating potential safety concerns and making the process safer and more amenable for scale up.

Case Study 4 – Photoisomerisation



Our client required delivery of 12 kg of a high potency API where the final step was photoisomerisation under cGMP manufacture.

Almac's solution: Development of a full cGMP process with a UV flow through cell to circumvent typical scale up limitations associated with batch photochemistry including screening of filters to set specific wavelengths of light for irradiation.

Value for Client: Delivery of API to cGMP manufacture target specification for clinical trials.

Supporting Capabilities

Almac's integrated flow technology platform can be applied throughout your product lifecycle to guide your synthesis project from conception to manufacture.

We offer the following:

- Route invention using continuous flow technology
- Proof of concept studies and proces demonstration
- Flow as an enabling technology for suitable reactions in multi-step synthetic routes
- Reaction validity in flow and process robustness within microreactors
- Process tech transfer and product delivery
- Lab scale production to low kgs
- UV-photochemical flow cell and LED's
- Development capabilities for both batch and flow and their integration
- Enzyme immobilisation development and associated flow processes
- Suspension polymerisation
- Process Analytical Technologies (PAT)
- Microbubble technology

Meet the Almac experts

Dr Scott Wharry

Scott is the Custom and Flow Chemistry Manager at Almac Sciences. Scott has extensive experience managing multi-disciplinary teams in process development, technology transfer for multi-kg manufacturing and flow projects. He is responsible for continuous processes at Almac.

Dr Megan Smyth

Megan is Team Leader within our Custom and Flow Chemistry Team at Almac Sciences. Megan leads the development of flow capabilities, is responsible for the delivery of projects for customers and has the role of industrial supervisor for a number of academic collaborations. She has additional experience including technology transfer and process scale-up.

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