iPRD

UNIVERSITY OF LEEDS

Water as A Reaction Medium: Realising Its Green Credentials

Dial-a-molecule Annual meeting 2019

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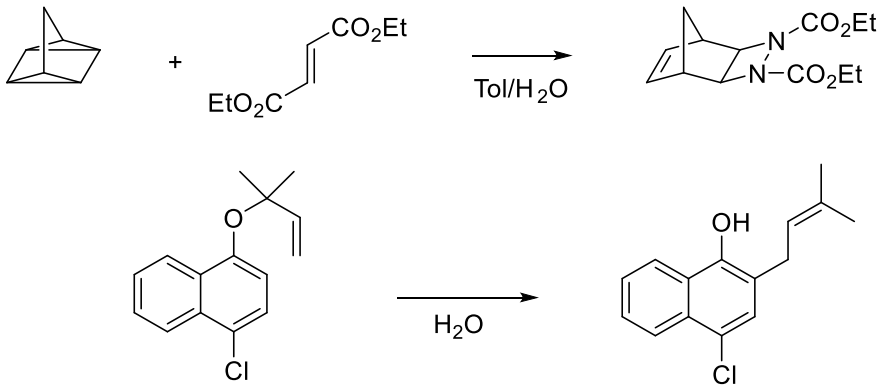
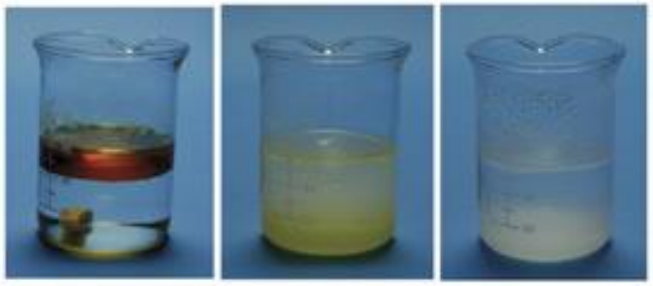
Dial-a-molecule

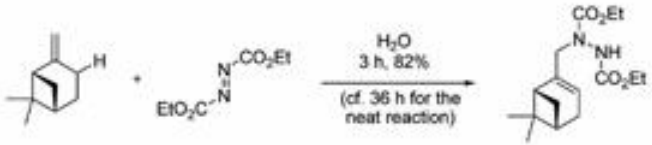
Dial-a-Molecule Grand Challenge - KEY CHALLENGES								
Lab of the Future & Synthetic Route Selection				A Step Change in Molecular Synthesis		Catalytic Paradigms for Efficient Synthesis		
Optimum Reaction and Route Design	The Smart Laboratory	Next Generation Reaction Platforms	Rapid Reaction Analysis	Stepwise Perfections (1000 Click Reactions)	Holistic Approach to Molecular Synthesis	New Reactivity: Target-driven Catalysis	Intervention-free Synthesis	Engineering Control through Under-standing

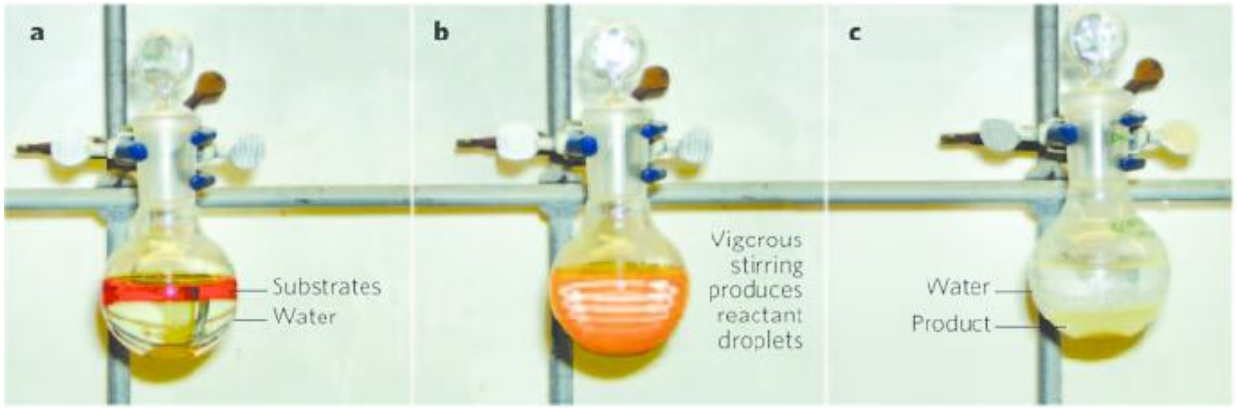
- ‘**Key challenges** documented in the Roadmap are the need to **make synthesis predictable**, developing **smart synthesis by design**, and providing a **sustainable synthesis** to answer the needs of a **sustainable future**.’

‘On water’ reactions





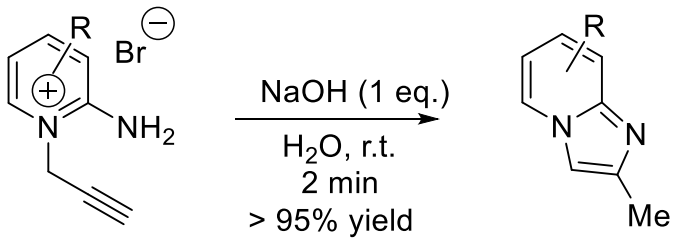


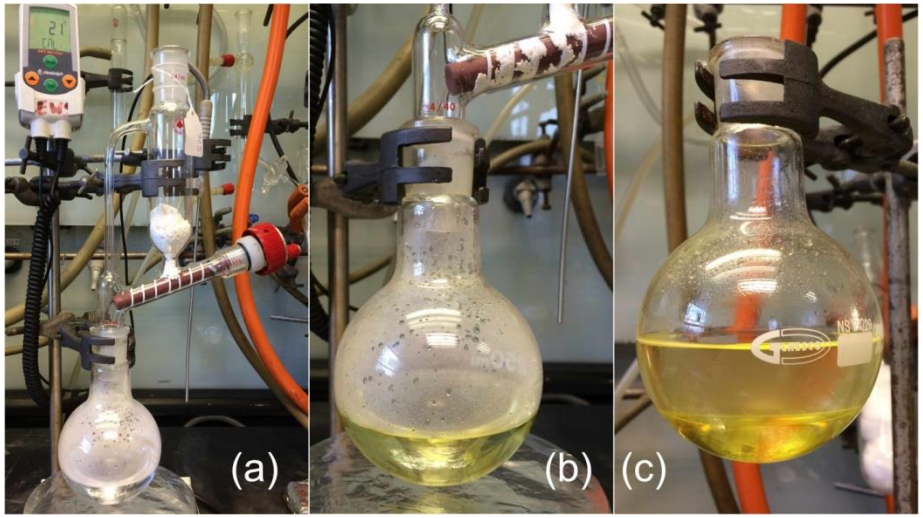


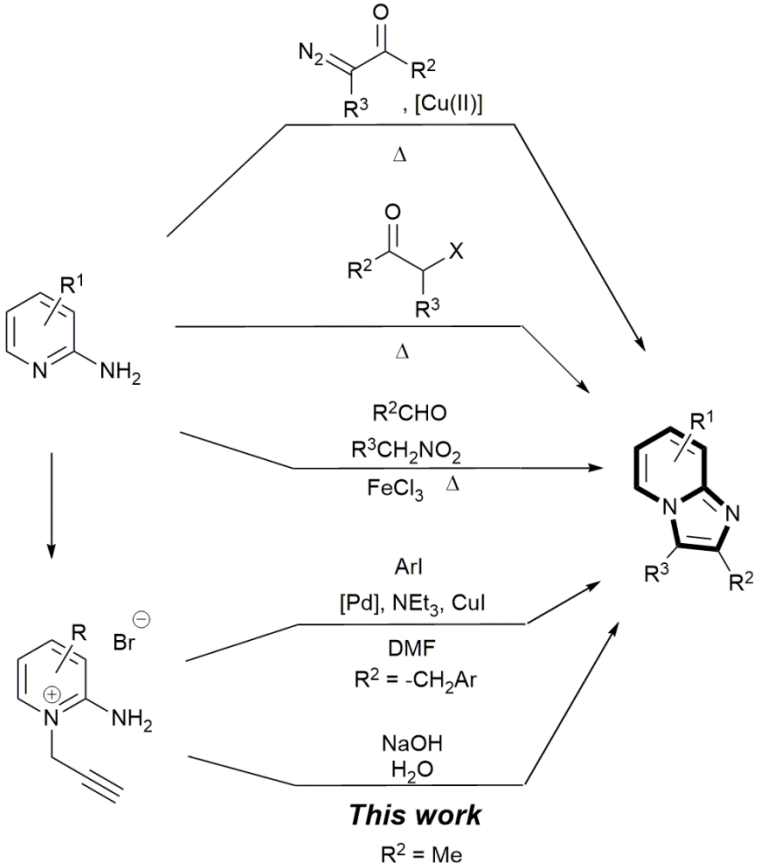
- Accelerated by up to 100s times compared to reactions in organic solvents
- Easy work-up, no organic solvent (in the reaction!)

Angew. Chem. Int. Ed. **2005**, *44*, 3275

‘On water’ reactions



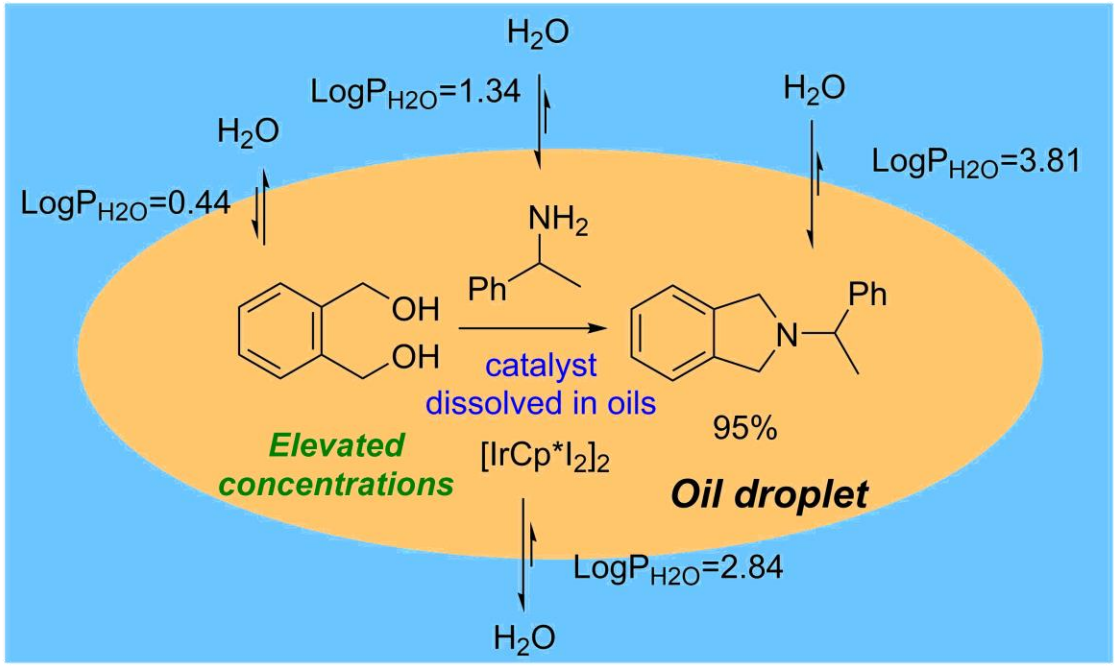




- The product can be solidified/filtered/washed with cooling or separated with a separation funnel giving >95% purity

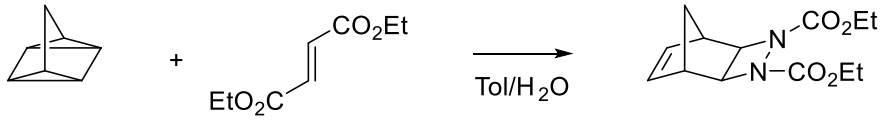
Green Chem. **2016**, *18*, 4623

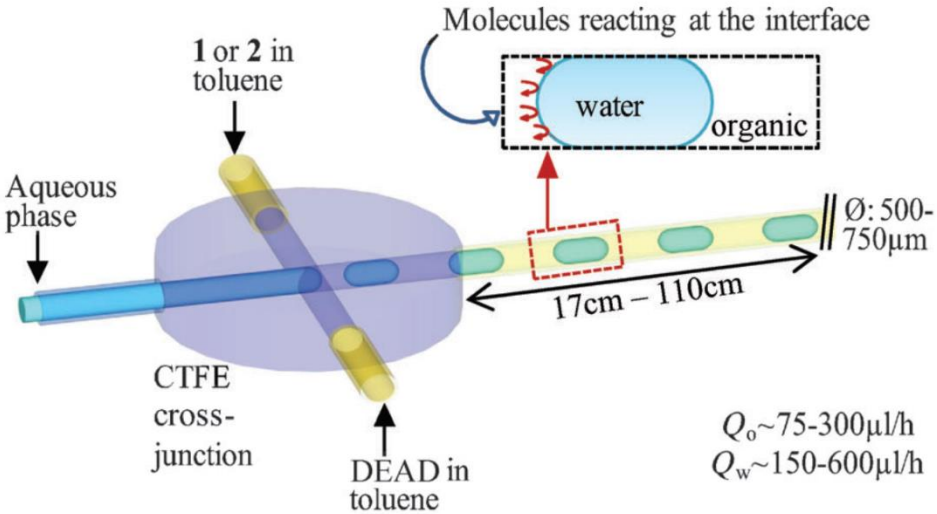
‘On water’ reactions

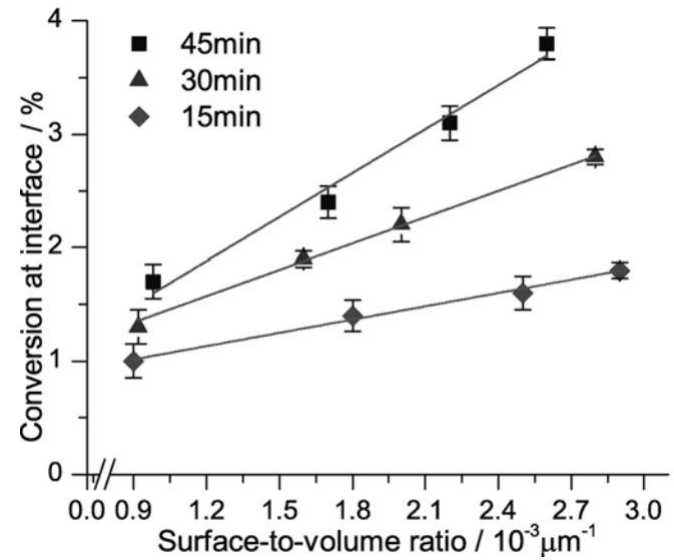


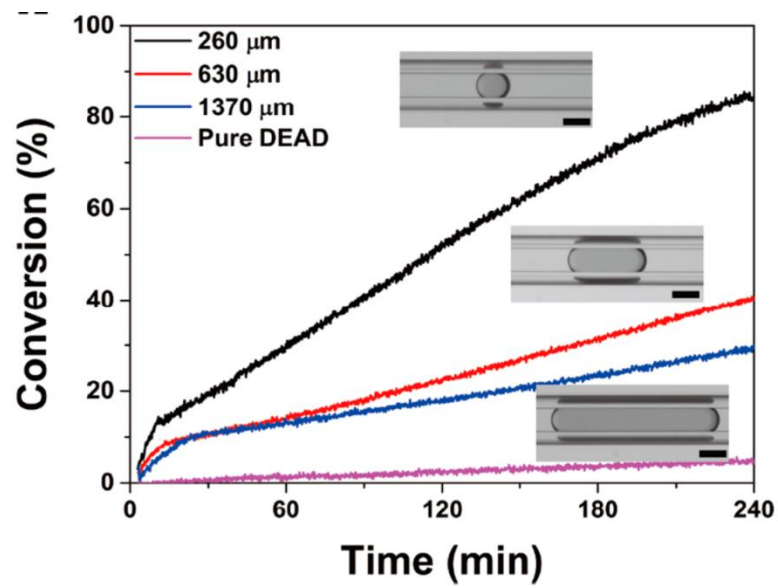
- Water-accelerated catalytic N-alkylation in Leeds
- Water is pushed out of the organic drolets, driving the reaction forward

Critical process parameters









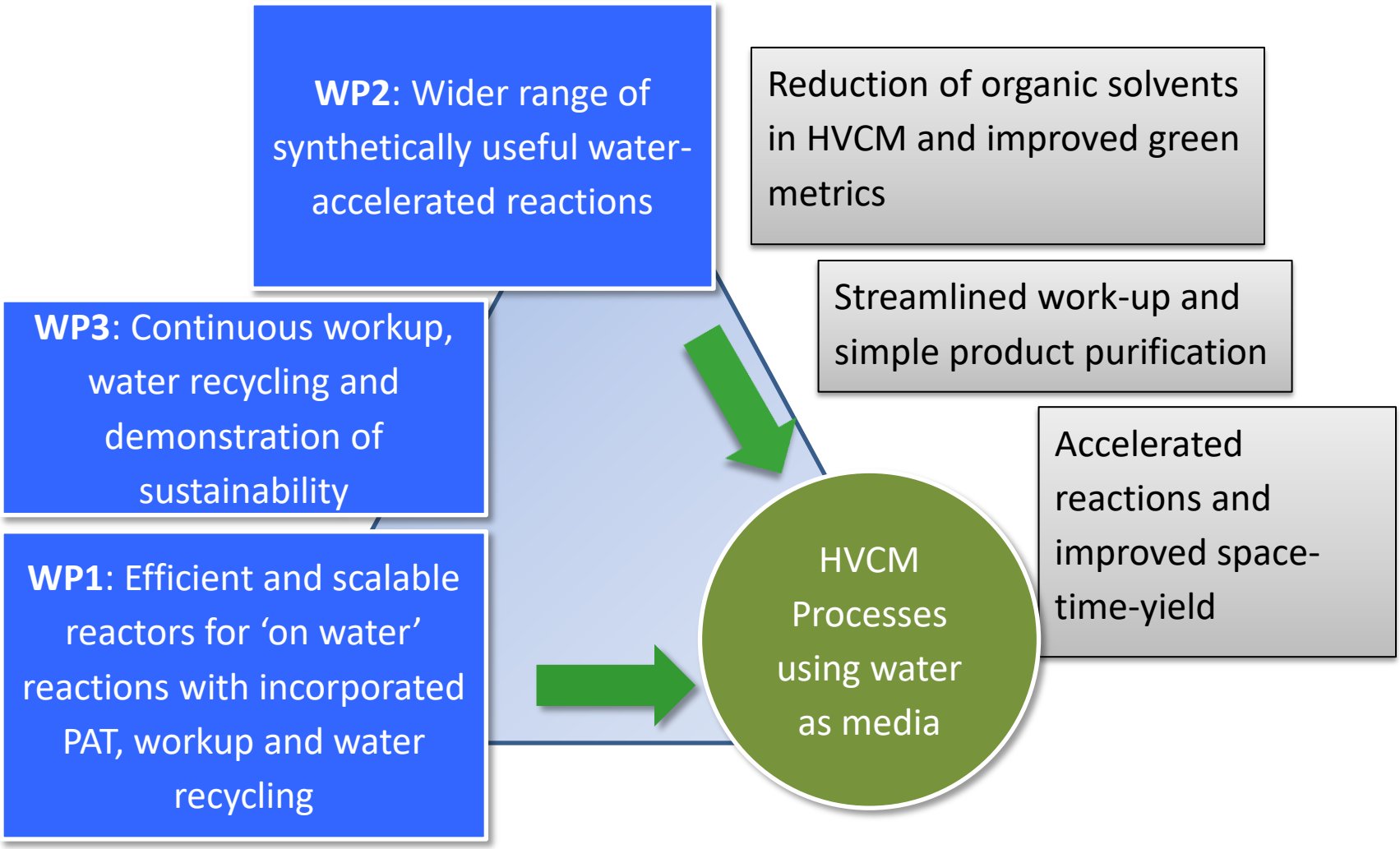
- Acceleration is related to interface area
- Microfluidic system has limited mass transfer rate

Angew. Chem. Int. Ed. **2012**, *51*, 7981; *Langmuir* **2015**, *31*, 13759

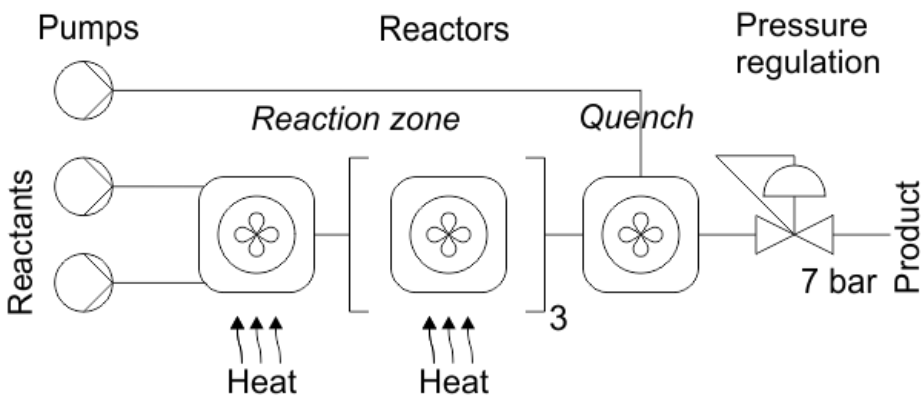
Challenges

- Lack of process knowledge and suitable reactors
- Known reactions are not very synthetically useful
- Still need organic solvents at work-up stage; waste water is contaminated.

Project vision



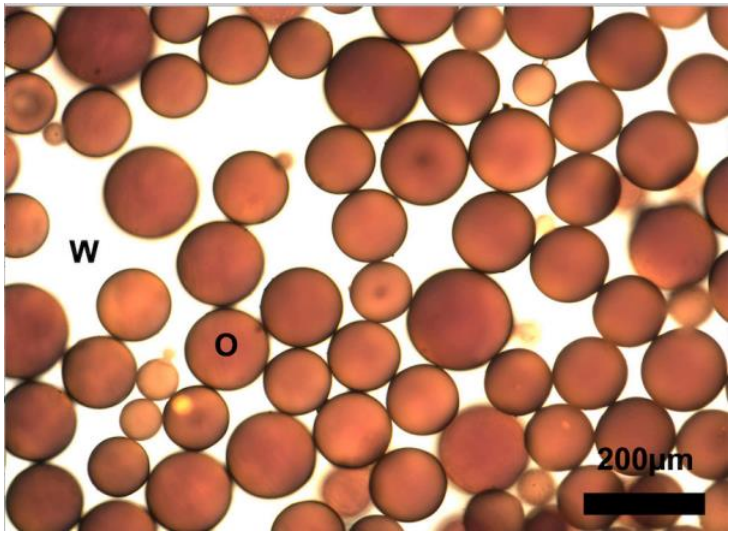
Reactor for water-accelerated processes

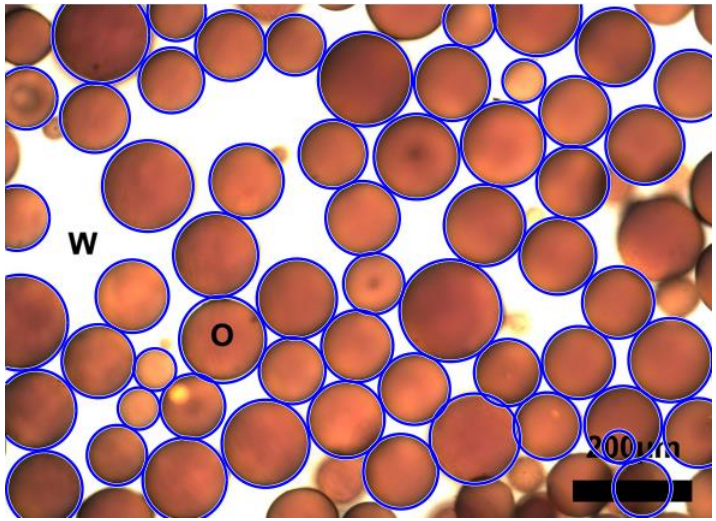


- Multiphasic flow reactors (mini-CSTRs), which accommodate longer reaction time, with excellent mass transfer
- Perfect starting point for water-accelerated reactions
- A study of reactions used by Lonza showed 63% of them are multiphase

http://www.freactor.com/; *Org. Process Res. Dev.* **2017**, *21*, 1294

Analytical technology

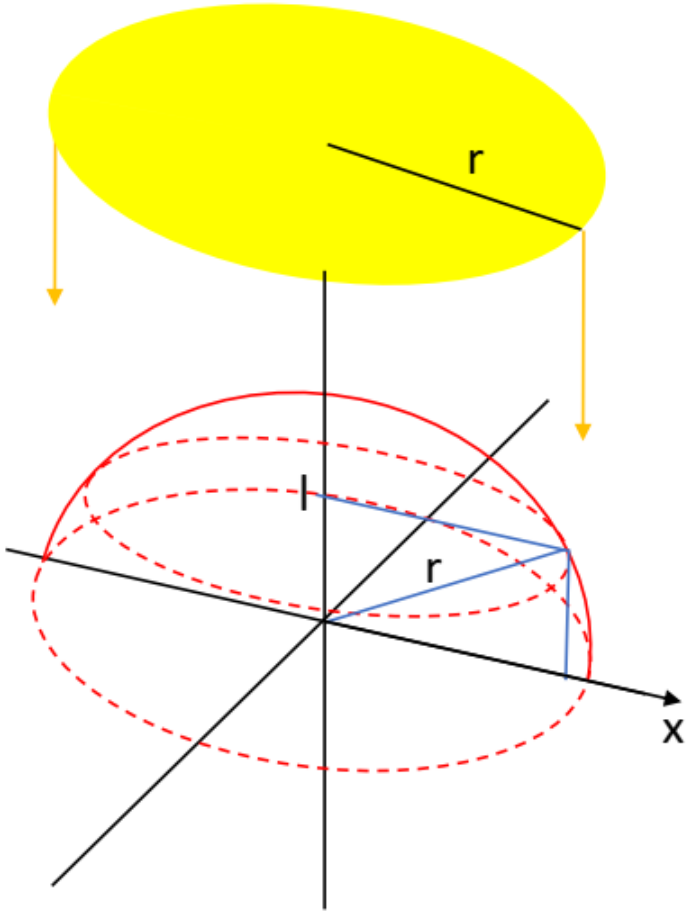


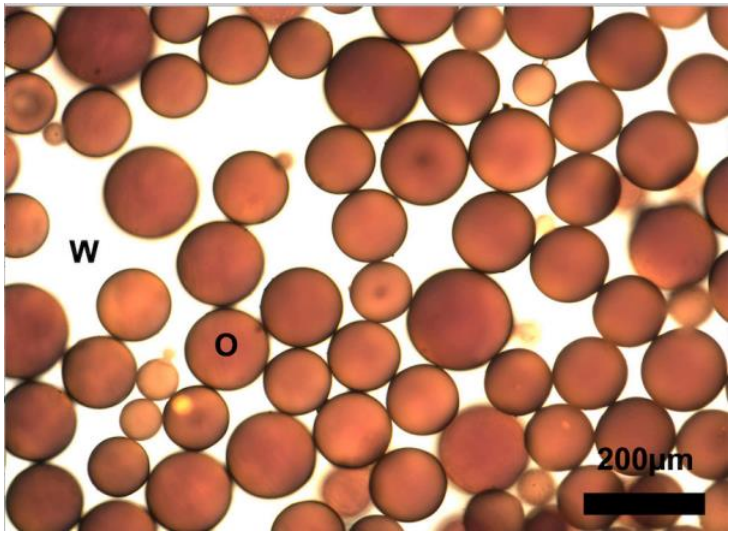


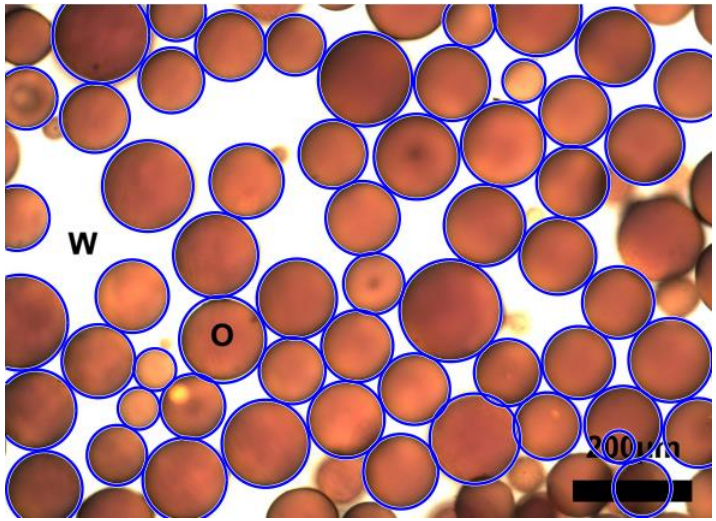
'On water' reactions are:

- Fast
- Multiphase
- Non-trivial to collect data with traditional sampling techniques

Analytical technology

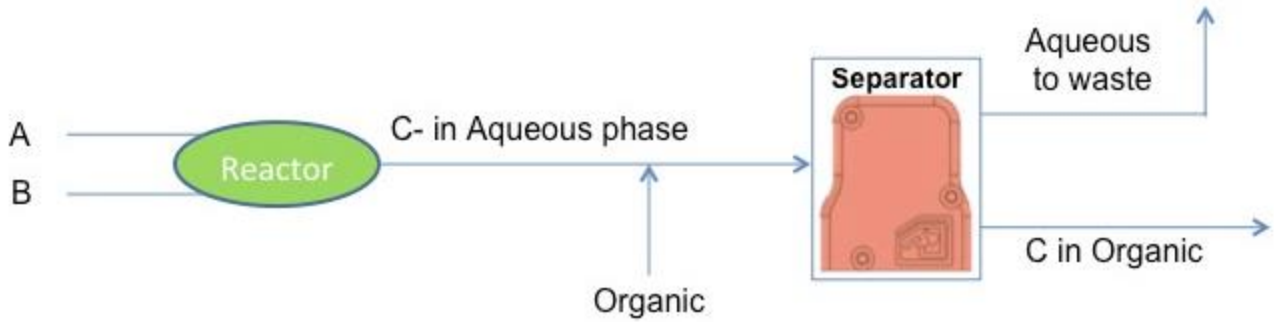


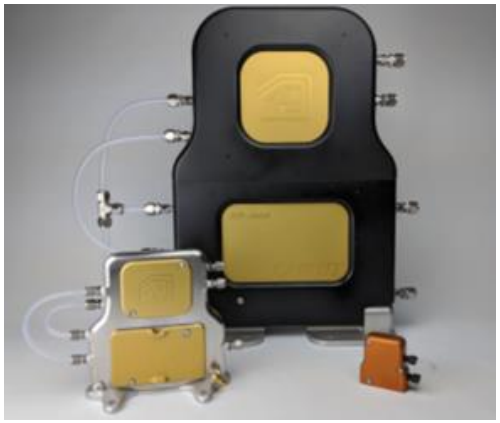


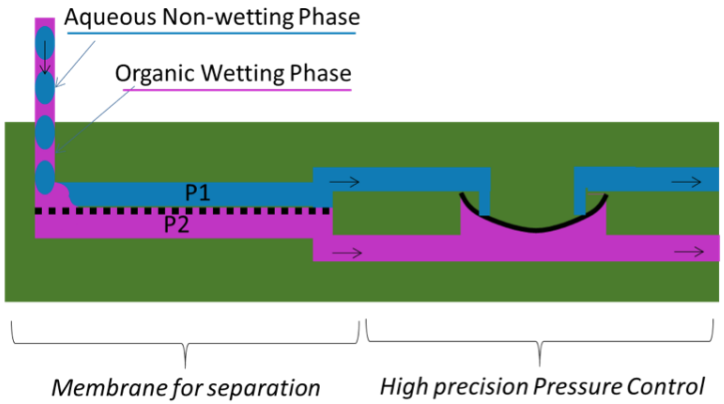


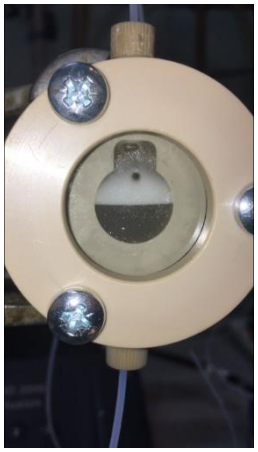
- Droplet size and concentration can be measured at the same time if one reaction component has a visible colour

Work-up and water recycling









- Sustainable use of water requires water recycling
- This is much easier in flow than in batch mode

Project team

iPRD

Bao Nguyen (Physical organic chemistry)

John Blacker (Process chemistry)

Nik Kapur (Fluid dynamics)

EPSRC

Sannia Farooque (PDRA, reactors and analytics)

Sam Boobier (PhD, solubility prediction)

Alison McCorry (PhD, micellar catalysis)

Robin Adderley (MSc, image analysis)

Dr.Reddy's

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ROAR Imperial College London

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