



ONE FLOW

Catalyst Cascade Reactions in 'One-Flow'
within a Compartmentalized, Green-Solvent
'Digital Synthesis Machinery' – End-to-End
Green Process Design for Pharmaceuticals

Flow Chemistry Programs in the Ley Group

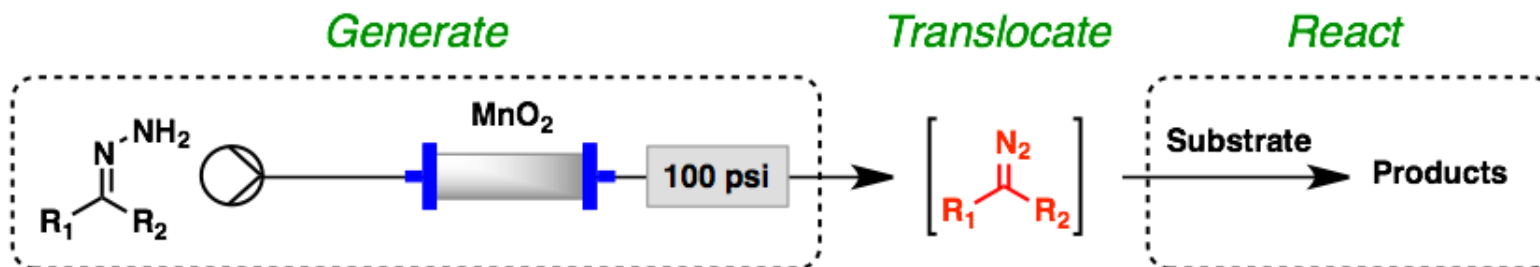
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- ◆ **FET Open Program “One-Flow”** □
- ◆ **New chemistries with diazo compounds** □
(harnessing reactive intermediates)
- ◆ **Iterative chemical processing** □
- ◆ **Integrating batch and flow** □
- ◆ **Microprocessor monitoring and control** □ □
- ◆ **Autonomous self optimization** □
- ◆ **Virtual/augmented reality technique** □
- ◆ **Organic Chemistry Science Gateway program**
- ◆ **Flow API/natural product and prebiotic synthesis**
- ◆ **Photoredox chemistry in flow**
- ◆ **Flowzyme project: multi-enzyme cascades** □
- ◆ **Gas reactions** (currently H_2 , $\text{CH}_2=\text{CH}_2$, N_2O , HCN , CO , previously O_2 , CO_2 , NH_3 , CH_2N_2 , X_2)
- ◆ **New flow electrochemistry methods**
- ◆ **‘Internet of Chemical Things’**
- ◆ **Knowledge transfer activity**

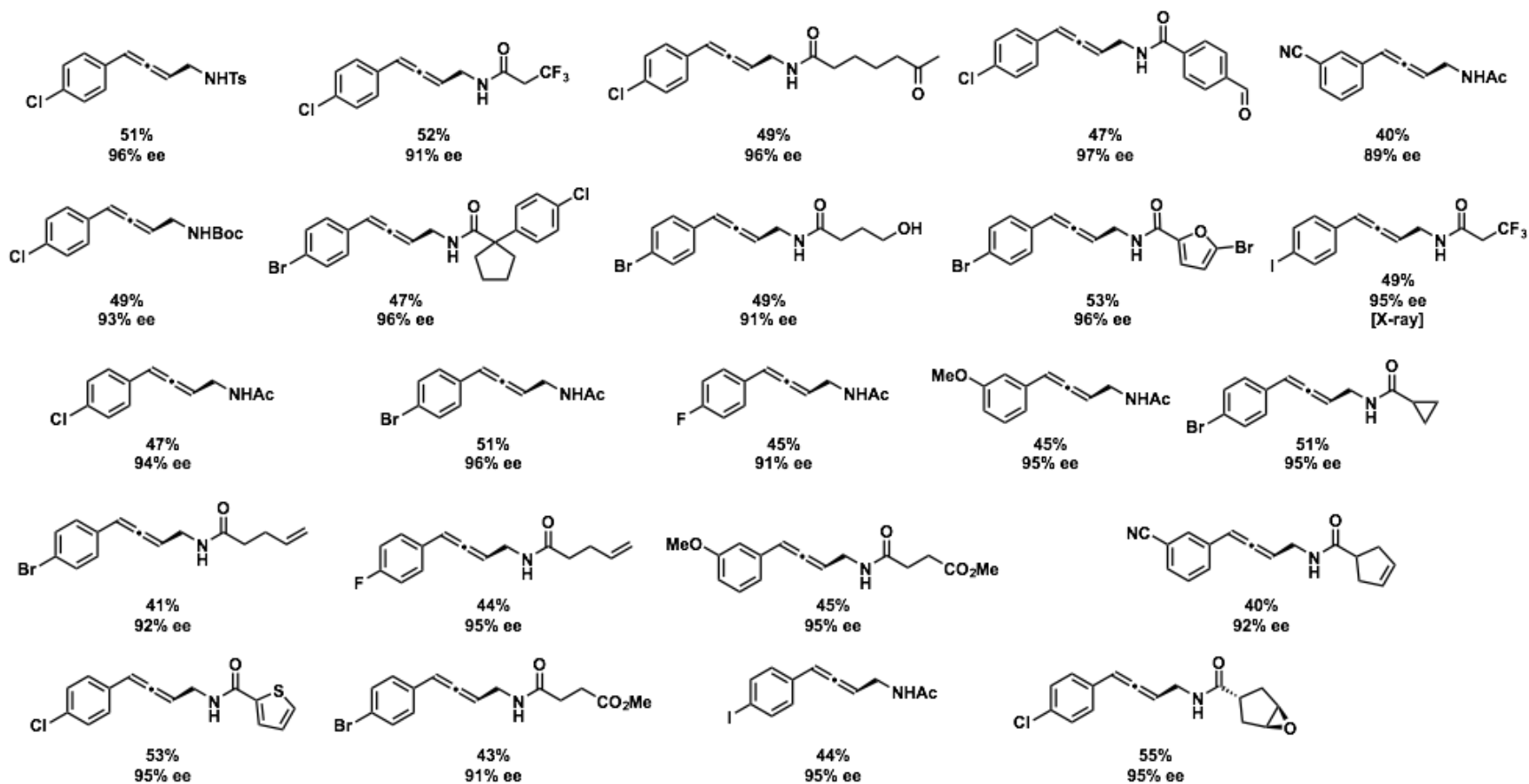
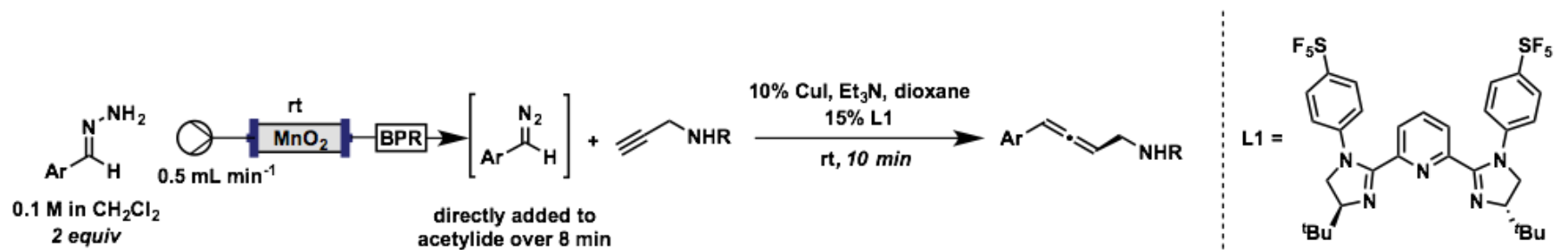


Harnessing Reactive Intermediates

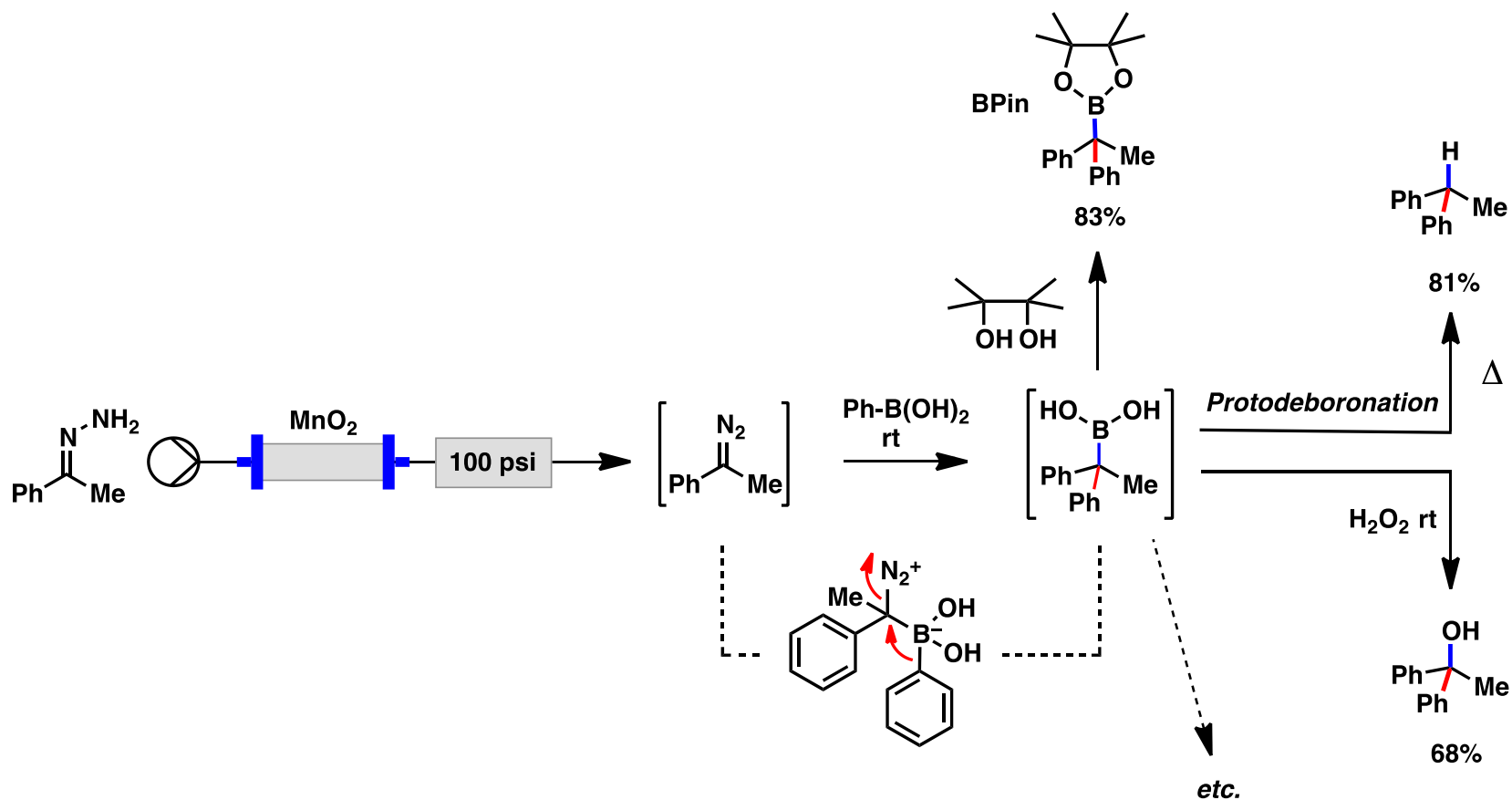
Harnessing Diazo Compounds



Enantioselective Allene Synthesis



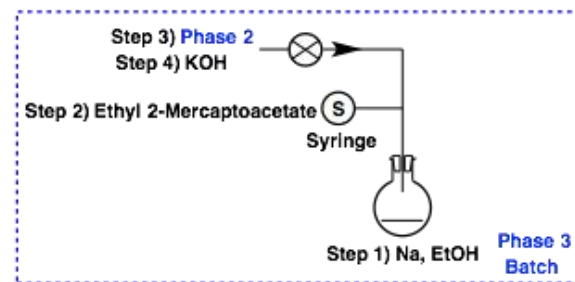
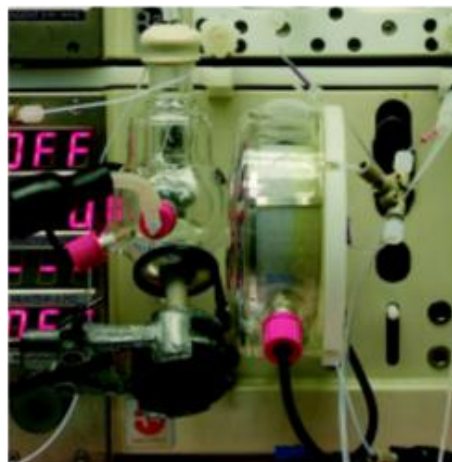
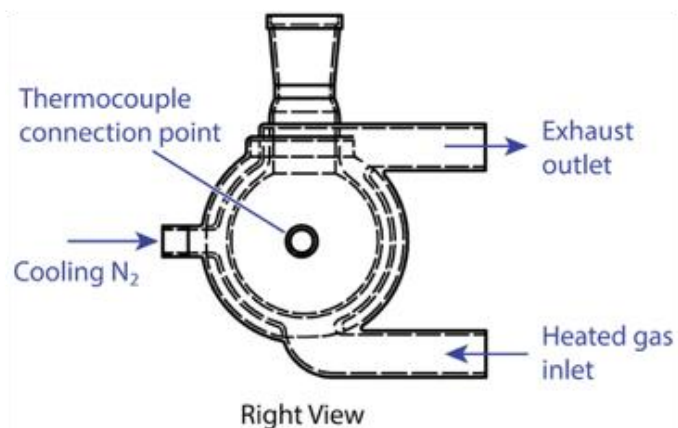
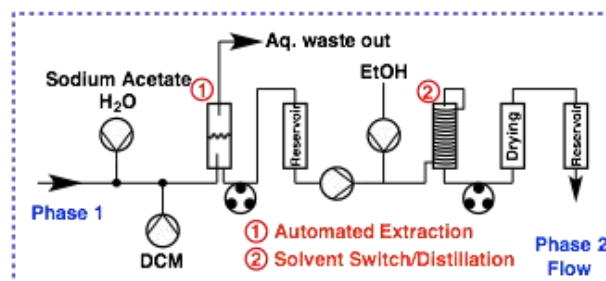
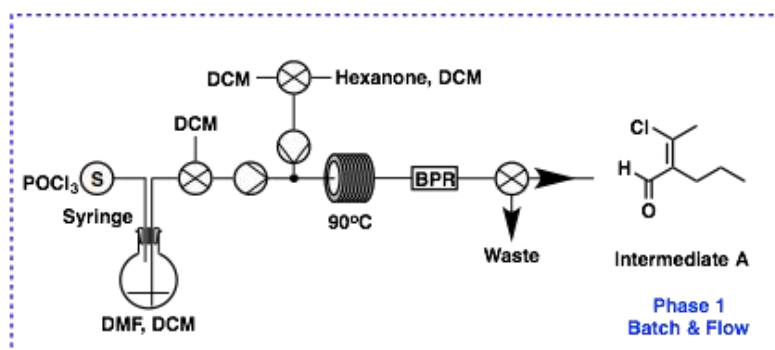
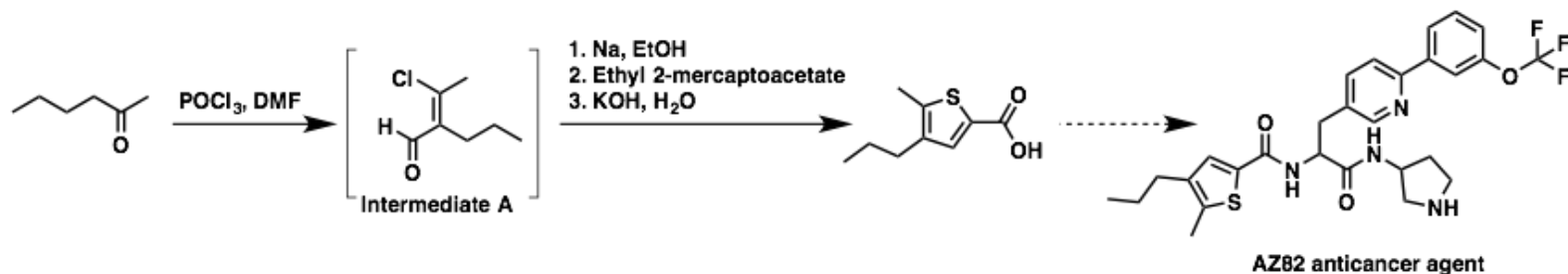
Discovering New Reactions – Cross-Coupling



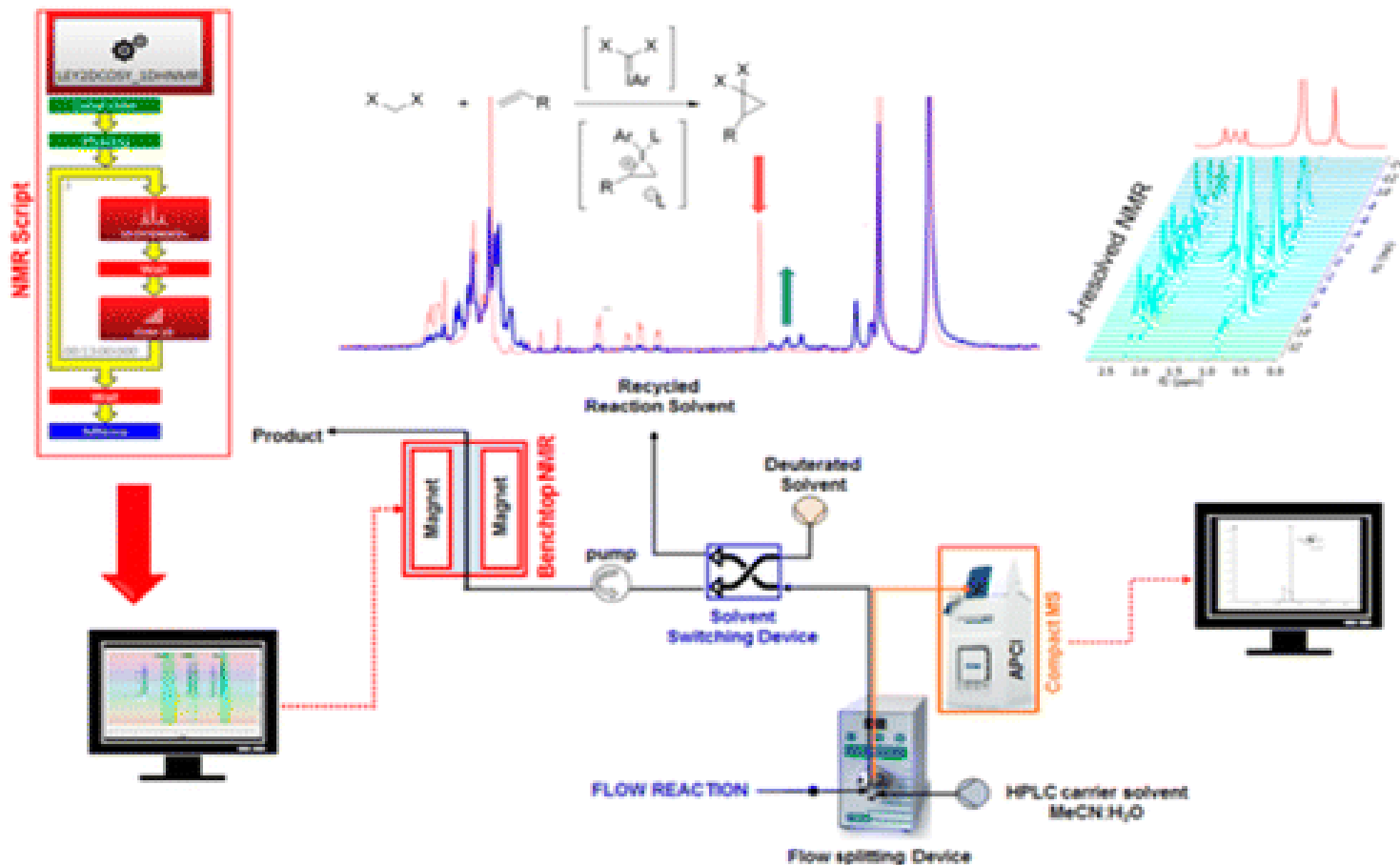
Flow chemistry as a discovery tool to access sp²-sp³ cross-coupling reactions via diazo compounds

D.N. Tran, C. Battilocchio, S. Lou, J. M. Hawkins, S.V. Ley Chem. Sci. 2015, 6, 1120-1125

Integrating Batch and Flow



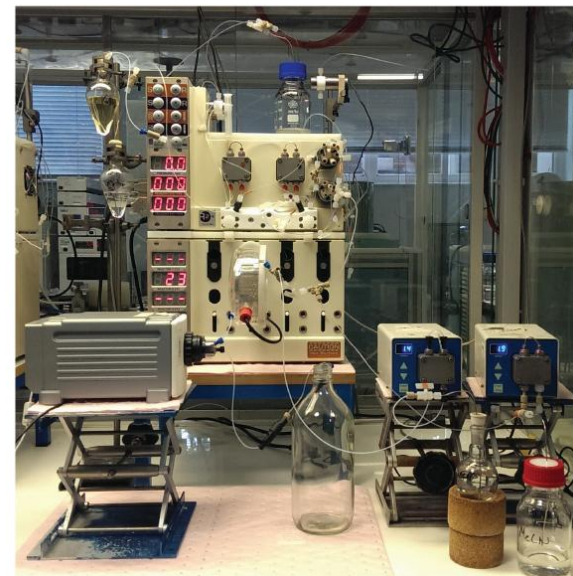
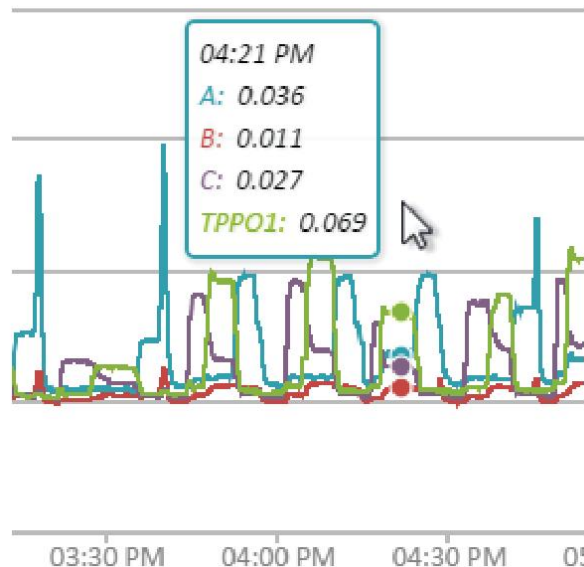
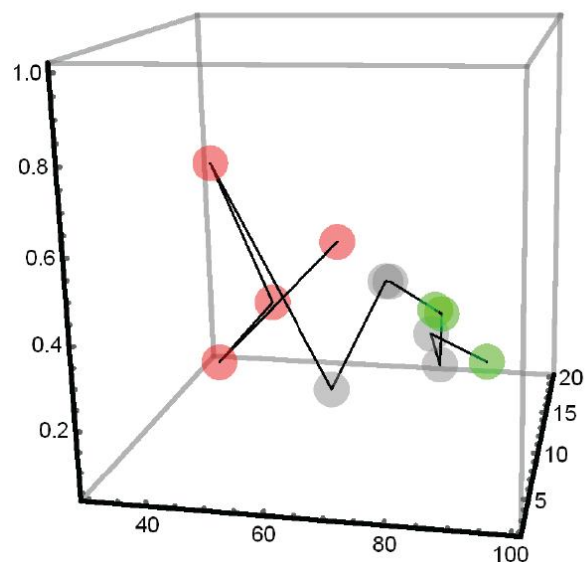
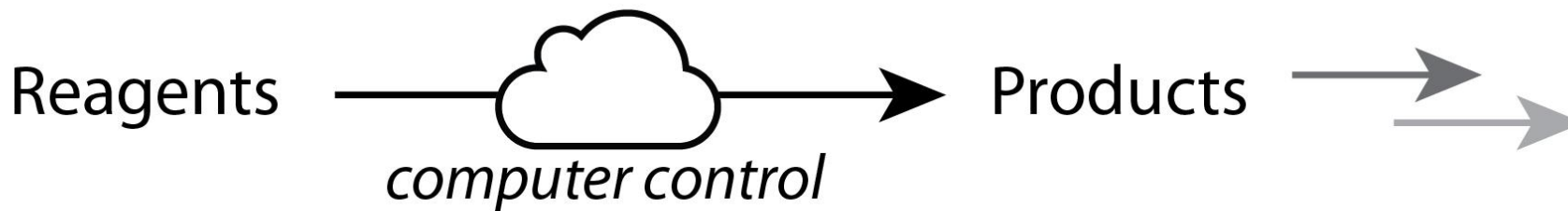
NMR Monitoring in Flow



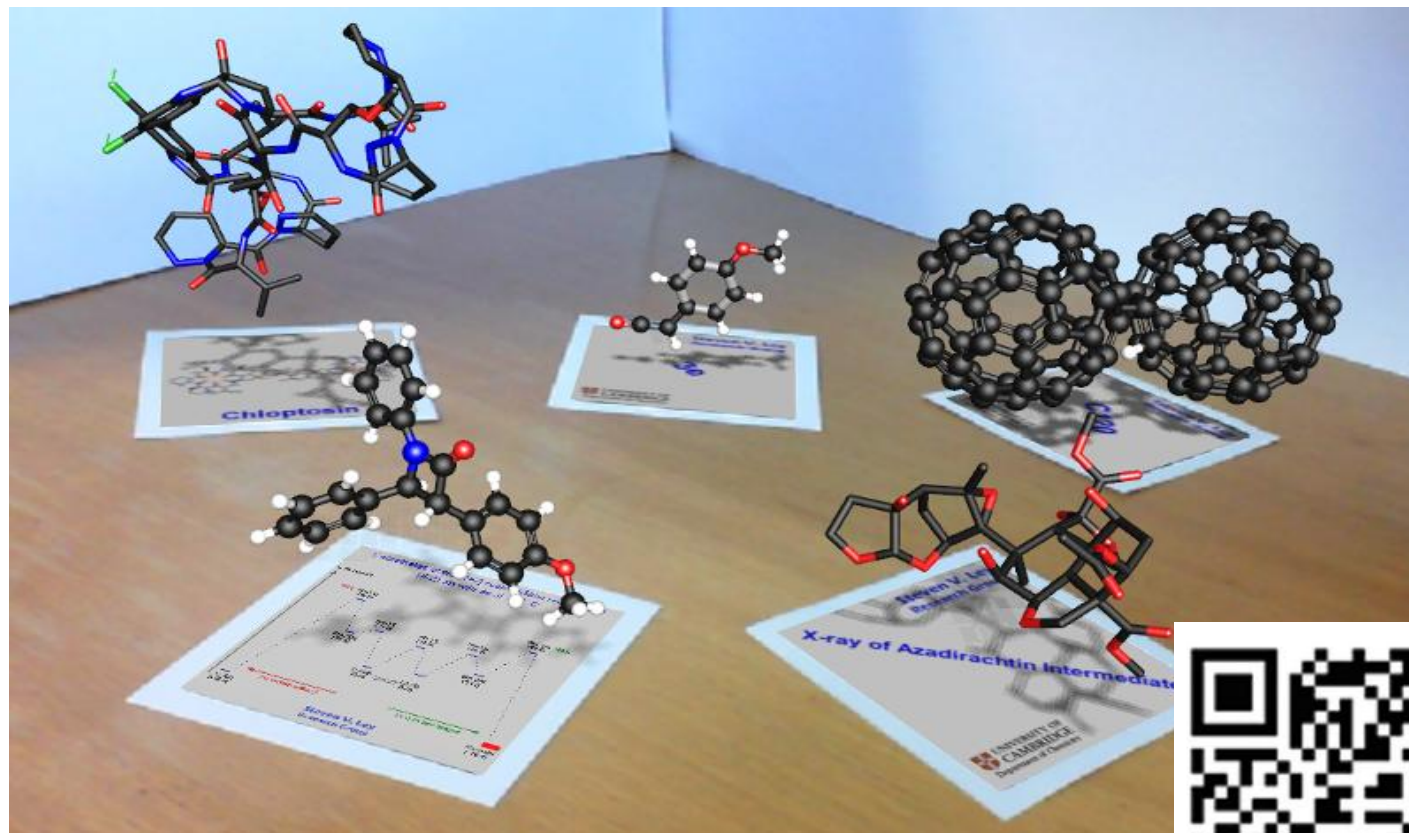
Continuous processing and efficient *in situ* reaction monitoring of hypervalent iodine(III) mediated cyclopropanation using benchtop NMR spectroscopy

B. Ahmed-Omer, E. Sliwinski, J.P. Cerroti and S.V. Ley, *Org. Process Res. Dev.*, 2016, 20, 1603-1614

Self Optimisation in Flow



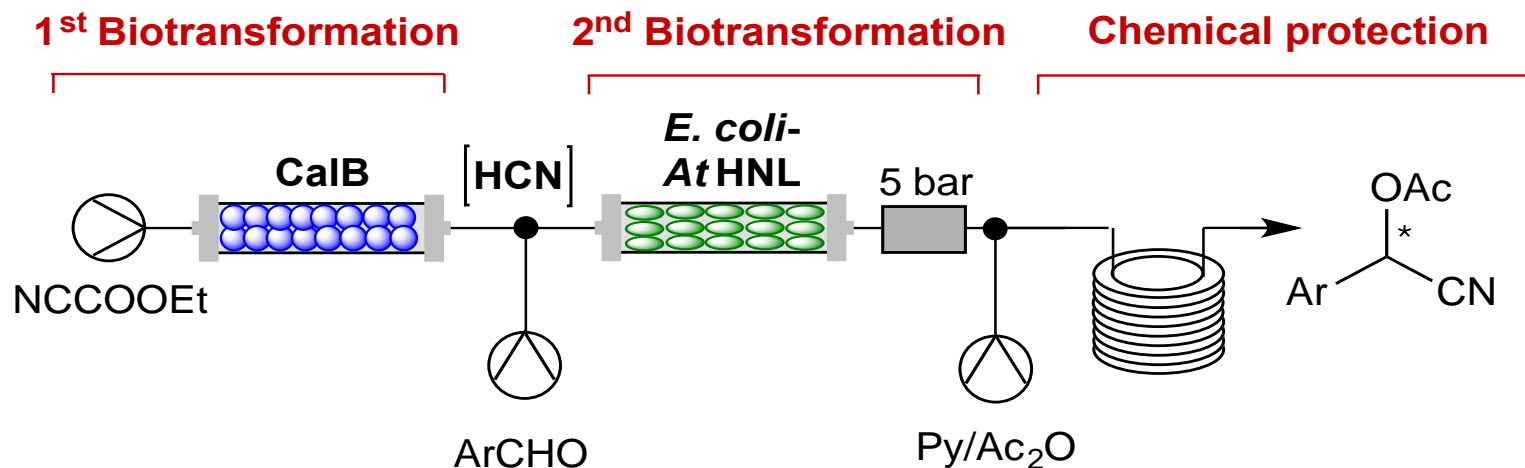
Augmented Reality Technique



Combination of enabling technologies to improve and describe the stereoselectivity of Wolff–Staudinger cascade reaction

B. Musio, F. Mariani, E.P. Sliwinski, M.A. Kabeshov, H. Odajima and S.V. Ley, *Synthesis*, 2016, 48, 3515-352

Flowzyme Project: Multi-Enzyme Cascades



An orthogonal biocatalytic approach for the safe generation and use of HCN in a multistep continuous preparation of chiral O-acetylcyanohydrins

A. Brahma, B. Musio, U. Ismayilova, N. Nikbin, S.B. Kamptmann, P. Siegert, G.E. Jeromin, S.V. Ley, M. Pohl *Synlett* 2016, 27, 262-266