**N-Heterocyclic Carbene Organocatalysis in Sustainable Media**

**Supervisors:** Prof. Sharon Cooper, Prof. Phil Dyer and Prof. AnnMarie O’Donoghue (Department of Chemistry, Durham University)

Organocatalysis, the use of non-metal containing organic molecules as catalysts, has many benefits for sustainable chemistry: high atom economy, non-hazardous chemical syntheses, and energy efficiency. As demonstrated by the award of the 2021 Nobel Prize in Chemistry in this area, Organocatalysis will play a key role towards ensuring a sustainable (bio)chemical future. However, there remains significant scope for improvement regarding solvent usage. The most employed solvents for organocatalysis include dichloromethane, THF and toluene with limited exploration of more sustainable options. The drive towards organocatalysis in alternative media is predominantly dictated by sustainability drivers, however, there are also opportunities for diversifying chemical scope via alternative chemo- and product selectivity. The broader benefits of a move towards catalysis in solvents with ‘greener’ credentials in life-cycle assessment, health and safety descriptors are clear.

N-Heterocyclic carbenes (NHCs) are one of the largest and most diverse class of organocatalysts, providing access to unique chemical reactivity and complex molecular architectures. There are few examples of NHC catalysis in water, mostly limited to the archetypal benzoin condensation (*via* d1 synthon generation). Problems include the poor aqueous solubility of NHC pre-catalysts, substrates, and minimal acid dissociation within the aqueous pH scale. In moving to new solvent systems, all aspects of chemical organocatalysis require re-investigation, including reaction rates, catalyst p*K*as, mechanisms and substrate/product selectivity.

In this PhD project you will explore the application of alternative solvents systems for NHC organocatalysis. Specifically, we will investigate three solvent systems: 1) Structured Ternary Fluids (STFs); 2) High Temperature Water (HTW) and 3) Co-Solvents from Sustainable Origins. In all cases a range of NHC-catalysed synthetic transformations will be explored including challenging C-C bond forming reactions. We will initially explore the benzoin condensation (well-established NHC d1-synthon chemistry) before moving to more diverse transformations including NHC homoenolate-catalysed annulations to heterocyclic products, aldehyde C-H arylation and hydroacylation of unactivated alkenes. This project will suit an applicant with interests in synthetic chemistry and mechanism evaluation.

This interdisciplinary project will involve training in the following areas:

* Synthesis of NHC pre-catalysts and substrates (O’Donoghue)
* Preparation and physicochemical evaluation of STFs (Cooper)
* Generation and safe manipulation of HTW and DES (Dyer)
* Data evaluation, kinetic evaluation, p*K*a determination (O’Donoghue)
* Reaction monitoring using multinuclear NMR and mass spectrometric analysis (O’Donoghue, Dyer).

**Keywords**: organocatalysis, sustainable chemistry, N-heterocyclic carbene, structured ternary fluid, high temperature water, mechanism