Centre for **Sustainable** Chemical Technologies

MONASH University

UNIVERSITY OF BATH

Bath Monash Global PhD Programme in Sustainable Chemical Technologies

Project Title:	Addressing puzzles of enantioselective organocatalysis: A computational and physical organic chemistry approach.
Supervisor at Bath:	Dr Matthew Grayson
Supervisor at Monash:	Prof. David W. Lupton (lead)
Home Institution:	Monash University
Indicative period at Host Institution:	12 months with exact dates to be confirmed

Project Summary

Enantioselective organocatalysis has evolved rapidly and now provides access to a dizzying array of functional materials. Beyond the academic lab organocatalysis being exploited to solve problems in industry. For example, Merck recently employed an amine catalysed Michael addition in the penultimate step of the commercial route to Letermovir, an approved antiviral for cytomegalovirus infections.

Despite significant attention a range of fundamental questions in this field remain. Drawing from recent experiences from the Lupton lab (Monash University) this collaborative project aims to exploit advanced theoretical computational approaches (Grayson, University of Bath), combined with physical organic chemistry to address a series of puzzles common to the field. It is envisaged that based on the interests of the student studies in this project can be focused from fundamental theoretical chemistry, through to physical organic chemistry, and enantioselective reaction discovery. For the computational studies, no prior molecular modelling experience is required. Training can be provided in the use of computational methods to model chemical reactions, a skill useful across all areas of the chemical sciences in both academic and industrial settings. Training in Python, a broadly used and general-purpose programming language, will also be provided for those interested though no programming is necessary for the project.

Specifically, we will focus on two significant problems:

(1) *Entropy controlled enantioselective transformations.* While enantiodetermining transition states of many reactions are thought to be largely controlled by enthalpy in a number of cases they appear to be entropically controlled, resulting in reactions that are more enantioselective at higher reaction temperatures. While conceptually this can be rationalised, the detail regarding why this is the case, and indeed how this can be exploited to deliver improvements in synthesis, are yet to be developed. Computational methods will be used to calculate the structure and free energy of the transition states of such reactions which will provide a detailed insight into the entropic and enthalpic contributions to the observed selectivity. These insights will then enable rational design of new reactions.

(2) Electronic sensitivity of enantioselective transformations. The impact of the electronic demand of substrates on enantioselectivity is not fully appreciated. In this topic, we will examine a number of reactions that show profound sensitivity to electronic demand. Does an enhanced understanding on this phenomenon allow the design of new catalysts to overcome these limitations? Computational methods will again be used to understand these observations and to make predictions about the likely selectivity that can be achieved with new generation catalysts.

Features of the programme

- PhD researchers will be registered at both institutions and will be awarded a joint PhD degree.
- PhD researchers will be jointly supervised by academics from both Monash and Bath Universities.
- All PhD researchers in the joint programme will also undertake a bespoke advanced training plan covering a range of topics focusing on sustainability.
- Applicants can apply to either Monash University or the University of Bath as their nominated home institution.
- PhD researchers will undertake a period of no less than 12 months at the partner institution.
- Up to four scholarships/studentships will be offered. Additional and suitably qualified applicants who can access a scholarship/studentship from other sources will be also considered. Evidence of funding must be provided.
- The scholarships/studentships include:
  - a *full tuition fee sponsorship* provided by Bath (home or EU students only) or Monash for the course duration (up to a maximum 42 months)
  - *a living allowance (stipend)* provided by Monash or Bath Universities. Note: Overseas Student Health Cover (OSHC) must be paid by the student, unless covered by the university.

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How to apply

Please express interest for up to three projects in order of preference. Please submit your application at the Home institution of your preferred project. However, please note that you are applying for a joint PhD programme and applications will be processed as such.

The deadline to submit applications is Sunday 12 May.

Monash University

Expressions of interest (EoI) can be lodged through https://forms.gle/XkC1TKpqVQh4B4N1A. The EoI should provide the following information:

CV including details of citizenship, full transcripts of academic records, evidence of English language level (IELTS or TOEFL), nominate your host institution (ie Bath or Monash), two referees and contact details, indication of which projects are of interest.

University of Bath

Please submit an application through the following link:
https://samis.bath.ac.uk/urd/sits.urd/run/siw_ipp_lgn.login?process=siw_ipp_app&code1=RDUCH-MO01&code2=0001

Please make sure to mention in the “finance” section of your application that you are applying for funding through the joint Bath/Monash PhD programme for your specified projects.

In the “research interests” section of your application, please name up to three projects you are interested in and rank them in order of preference. Please also include the names of the Bath lead supervisors.