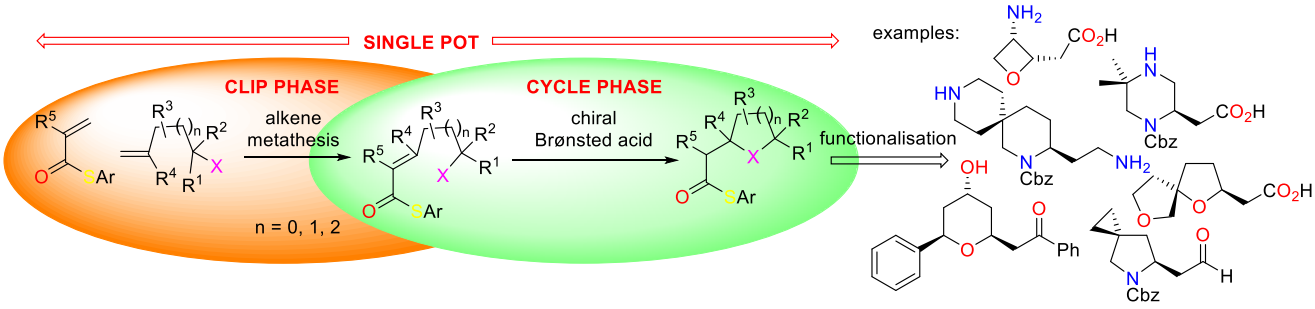
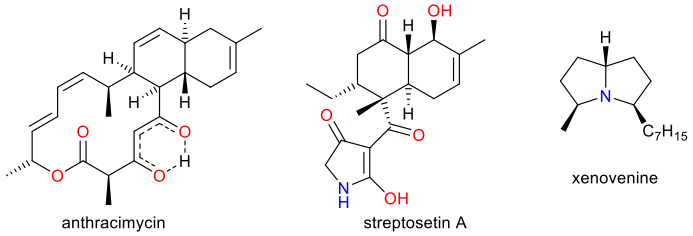
Prof. Paul A. Clarke

Available PhD and MSc Research Projects

Asymmetric 'Clip-Cycle' Synthesis of Cyclic Amines and Ethers: The group has been instrumental in the development of new methods of tetrahydropyran and piperidine synthesis and their application to the total synthesis of natural products, like phorboxazole B and diospongin A and B. Current work in the group is focused on a new asymmetric Brønsted acid-catalysed 'clip-cycle' reaction for the construction of cyclic ethers and cyclic amines. 'Clip-Cycle' provides a new modular, catalytic, and experimentally simple route to functionalised cyclic ethers and amines of different ring sizes. 'Clip-Cycle' uses the robust catalytic alkene metathesis reaction to 'clip' an activating unsaturated thioester group to an unactivated 'allyl' alcohol or amine unit. The 'clip' metathesis reaction is followed, in the same pot, by the 'cycle' hetero-Michael reaction, which is catalysed by a chiral Brønsted acid. The ring size of the heterocycle formed is dependent only on the length of the alkene tether, making this one strategy applicable to the synthesis of different ring sizes. The thioester function which is essential for the 'cycle' step also allows for easy late-stage modification to a range of desirable functional groups. These units are present in many active pharmaceuticals and natural products.

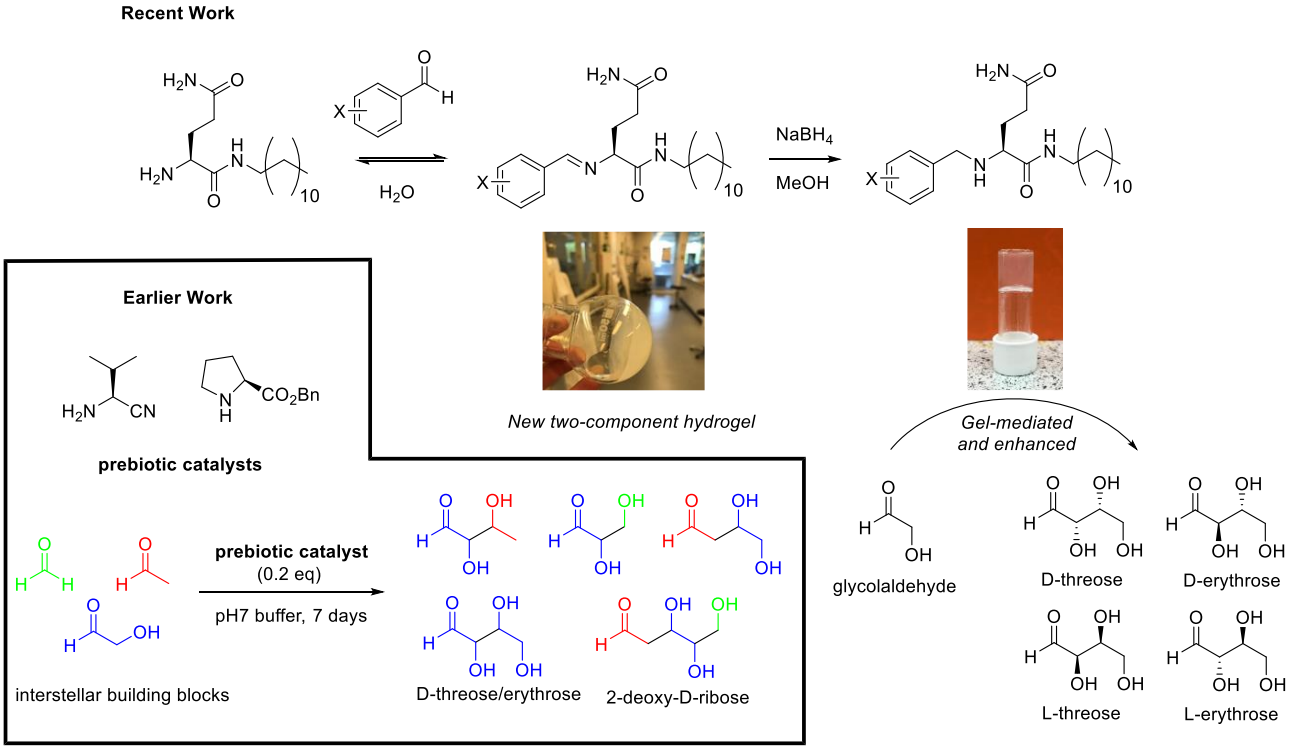


Natural Product Synthesis: Projects are available on the total synthesis of several natural products. Anthracimycin is a potent antimicrobial agent with an unknown mode of action. Streptosetin A exhibits human class III HDAC (SIRT) inhibition, and hence has anticancer properties. Our synthetic strategy for these natural products hinges on asymmetric annulation reactions to set up the decalin rings, followed by efficient functionalisation of the bicyclic structure. Routes to pyrrolizidine alkaloids, exemplified by xenovenine, are under investigation via the application of a desymmetrising 'clip-cycle' reaction.



Prebiotic Genesis of Carbohydrates: We are attempting to answer one of the fundamental questions in science: how the building blocks of life arose on the prebiotic Earth in enantiomerically enriched forms. Specifically, we are investigating the prebiotic genesis of carbohydrates. This exciting research has shown that it is possible to form threose and erythrose in the highest % e.e. to date, and 2-deoxy-D-ribose from interstellar building blocks. Recent studies showed that a simple hydrogel can act as a primitive protocell and catalyse the formation of enantiomerically enriched carbohydrates. We are now focusing on the further development of a hydrogel-based

"living protocell" which can couple the formation of enantiomerically enriched carbohydrates to inorganic phosphate and glycolipids.



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