Research cluster potential projects: Organic and Biomolecular Chemistry

Supervisors

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Projects

Project Title: Biocatalysis for Sustainable Chemistry

Supervisor(s): Dr Andrew Carnell

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The use of enzyme biotransformations in synthetic chemistry is now well established, particularly in the production of high value intermediates for the pharmaceutical industry. However, there is ever increasing interest in using efficient sustainable catalytic methods for biomass conversion. In order to realise this, there are many challenges that lie ahead. This project will aim to identify new biocatalysts and develop biotransformations for transforming key platform chemicals that result from processing of biomass.

Project Title: Design and Synthesis of inhibitors of alpha-methylacyl CoA racemase (AMACR) – a new therapeutic target for prostate cancer

Supervisor(s): Dr Andrew Carnell

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The enzyme alpha-methylacyl CoA racemase (AMACR) is involved in the metabolism of branched-chain fatty acids and is overexpressed in prostate cancer. Genetic knockdown of this enzyme in cancer cell lines has been used to validate this as a therapeutic target. So far we have developed a series of substrate-like CoA containing inhibitors. This project will involve the design and synthesis of novel inhibitors of the enzyme with a rational approach to deliver more drug-like non-CoA containing compounds. You will be involved in current collaborations with structural biologists and biomedical scientists.

Project Title: Modelling and Synthesis of Small Molecule Modulators of Protein:Protein Interactions (PPIs)

Supervisor(s): Dr Andrew Carnell & Dr Neil Berry

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Modulating protein-protein interactions (PPIs) with small molecules represents a significant contemporary challenge since protein surfaces are often large with non-contiguous binding
regions. In an interdisciplinary collaboration between the Department of Chemistry and the Institute of Integrative Biology at Liverpool we are developing a new approach for the design of molecules to inhibit or stabilise PPIs that are potential targets for cancer therapy. In this project, we will use computational screening and docking methods, synthetic organic chemistry and protein NMR to design, synthesize and test small molecule inhibitors of PPIs.

**Project Title: Characterization of Supramolecular Complexes in Cooperative Catalysis**

Supervisor(s): Dr J A Iggo (Catalysis), Prof. J L Xiao (Catalysis) and Dr N Berry

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The unification of organometallic with organic catalysis creates an exciting new reaction space – cooperative catalysis – in which the substrates of a reaction are activated simultaneously by electronic and steric interactions with the metal and by non-covalent interactions, such as hydrogen bonding, electrostatic, π-π, CH-π and hydrophobic forces, enabling reactivity and selectivity patterns inaccessible within each of catalysis field alone. This project will use NMR methods (nOe, PFGSE diffusion measurements, etc) to explore the mechanisms by which the two catalysts interact cooperatively through a supramolecular assembly of catalysts and substrate, bound together by non-covalent interactions.

**Project Title: The synthesis of novel β-turn mimetics**

Supervisor(s): Dr Ian O’Neil

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β-Turn mimetics are drug like molecules which resemble a β-turn structure in proteins. There is considerable interest in the synthesis of such compounds as new drugs. This project involves the synthesis of a new morpholine based β-turn mimic using a reverse-Cope cycloaddition. This highly novel chemistry allows for the rapid synthesis of a wide range of morpholine variants. The compounds will be tested by the MRC (medical research council) against G-coupled protein receptors (GPCRs), which are involved in many diseases and currently the target of approximately 40% of all modern drugs.

**Project Title: Selective Oxidations Using Chiral Amine Oxides**

Supervisor(s): Dr Ian O’Neil

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The selective oxidation of organic molecules represents is still a major problem in organic synthesis. For example, the anti-ulcer drug nexium™ is a chiral sulfoxide and the synthesis of this compound presents a major synthetic challenge. This project involves the synthesis of chiral tertiary amine oxides derived from prolinol and using them in the presence of iron to generate
high valent iron-oxo species. These will be used in the selective oxidation of a range of organic species including hydrocarbons, alkenes and thioethers. The process will be developed to give products of high optical purity.

**Project Title: Molecular Wires for Bacterial Energy Production**

Supervisor(s): Dr Ian O’Neil and Prof. David Schiffrin

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Geobacter sulfurreducens are a family of anaerobic bacteria, which respire using simple organic feedstocks, such as acetate to produce electrons at their surface. These can be used to generate an electric current under appropriate conditions. This has the potential to produce a renewable source of electricity. The aim of this project is to design and synthesize an “organic molecular wire” which will be used to attach to the surface of the bacteria to a carbon electrode, increasing the current production. Electrochemical techniques will be used to study the efficiency of the “bacterial wiring.”