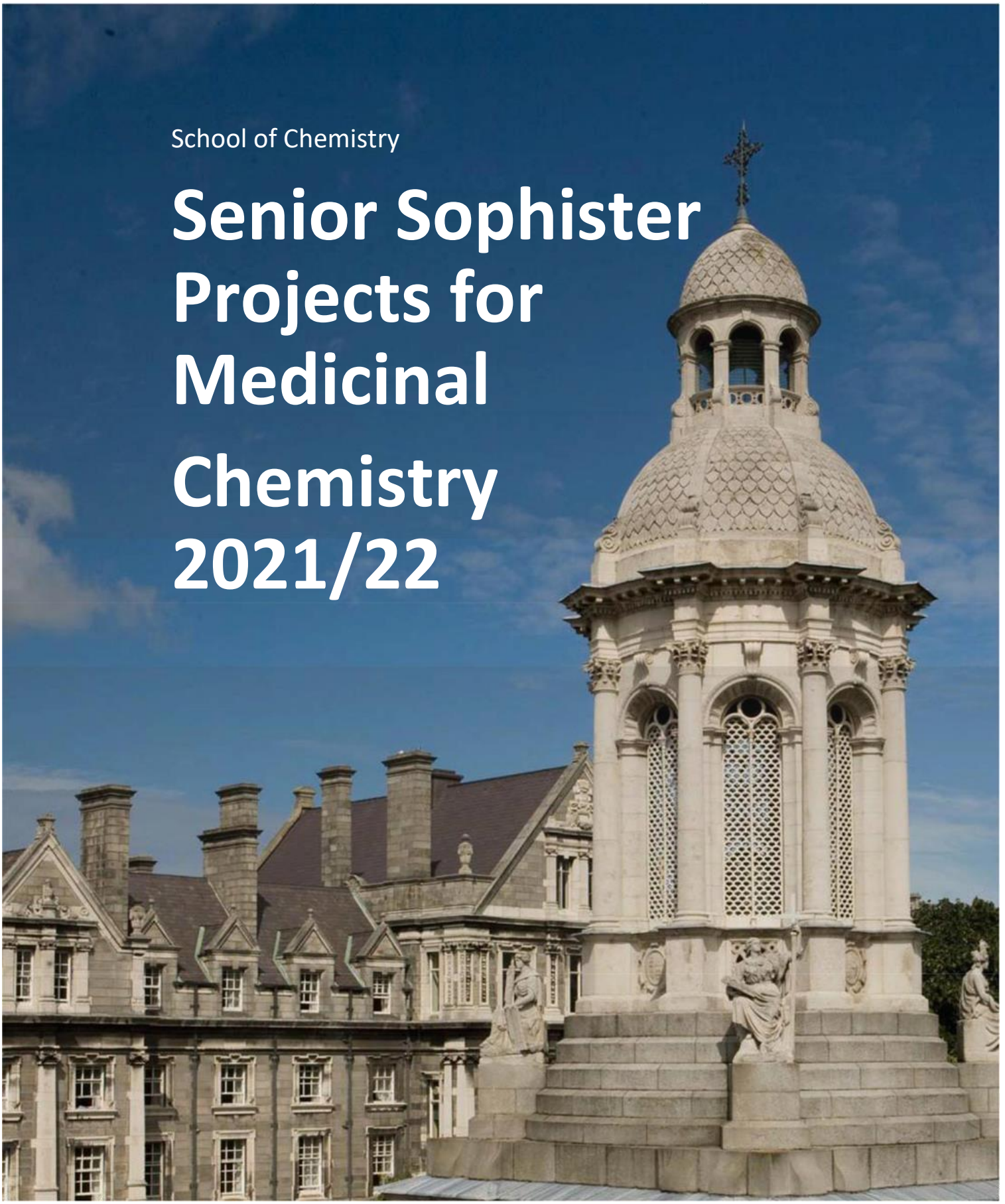
Trinity College Dublin
Coláiste na Tríonóide, Baile Átha Cliath
The University of Dublin

School of Chemistry

Senior Sophister Projects for Medicinal Chemistry 2021/22



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Inorganic and Synthetic Materials Chemistry

School of Chemistry Senior Sophister Research Project 2021

New approaches to WEEE recycling: perfluorinated ligands for lanthanide extraction

Prof. Robert Baker (BB1)
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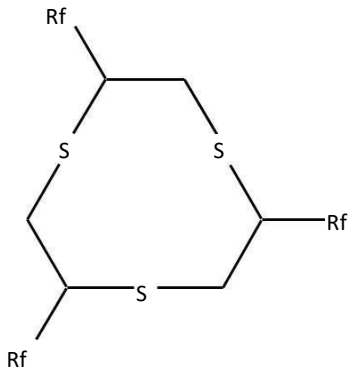
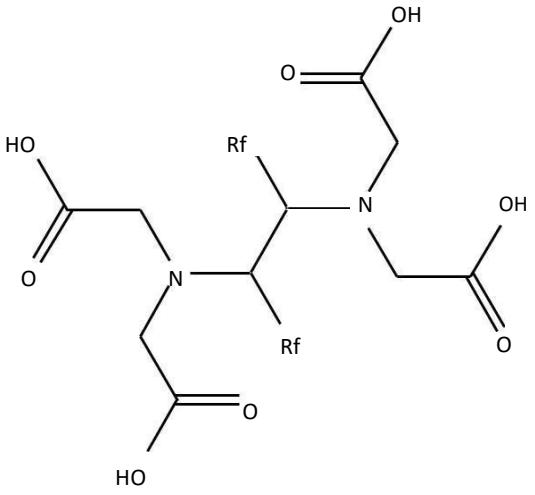
Research Project Description:

Lanthanide ions have been incorporated in an increasing number of technologies due to their unique properties. For example, neodymium is one of the key metals for magnets that are used in applications from wind turbines to hard disc drives. However, the amount of Nd that can be mined from the earth is not enough to continue the expansion of these technologies. This has lead the US, UN and EU to define the lanthanides as "energy critical".[1] If the toxic metals and high value speciality metals could be separated, a sustainable recycling scheme could be implemented ensuring a 'closed loop' system for material use. This idea has recently been highlighted by a UN report that showed that recycling of such electronic equipment is not currently addressed in most developed countries. We have recently designed a number of highly fluorinated ligands for the extraction of toxic metals such as arsenic, tin or mercury or radionuclides such as uranium or plutonium.[2] The advantages of fluorinated ligands is that the ligands and metal complexes are soluble in supercritical carbon dioxide – an excellent solvent for "green" solvent extractions.

In this project you will synthesise a series of perfluorinated ligands and use them to extract the lanthanides europium and neodymium and monitor the extraction using UV-vis and emission spectroscopy. The initial aim of the project is to prepare one of the ligands below and fully characterize it using multinuclear NMR (^{1}H, ^{13}C, ^{19}F) spectroscopy and vibrational spectroscopy.





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School of Chemistry Senior Sophister Research Project 2021

3D printing for catalysis

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Research Project Description:

Immobilising of heterogeneous catalysts is an important topic as it allows the benefits of selectivity with the ability to separate products from the catalyst. With the advent of 3D printing, some work has shown that heterogeneous catalysts can be printed [1], but there are no reports of a homogeneous catalyst being incorporated into 3D printed 'reactionware'. In this project the aim is to immobilise a test catalyst – Wilkinsons Catalyst – into polycaprolactone that can be converted into filament for 3D printing. The advantages are that with the correct choice of polymer, the printing temperature will not decompose the catalyst; any shape reactionware module can be prepared; thereaction is on the solid-liquid interface, so this lends itself to microfluidics approaches where conventional techniques give high catalyst degradation and is the overall goal of this work.

The student will:

- prepare the catalyst,
- dope it into the polymer,
- convert this to a filament using in house equipment.
- Print reactionware using a 3D printer available for this project.
- Conduct test hydrosilylation reactions to evaluate the stability and recyclability of the catalyst.

In each step the catalyst will be characterised by solid-state ^{31}P NMR and thermal methods to ensure no oxidation or thermal decomposition of the catalyst. Wilkinsons catalyst is thermally stable to temperatures above the glass transition point of the polymer and has a convenient NMR probe. Once printed the catalyst will be used in the hydrosilylation reaction to evaluate the recyclability of the product and NMR spectroscopy will be used to see if the catalyst is leaching from the polymer.

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School of Chemistry Senior Sophister Research Project 2021

Non-innocent ligands for f-block chemistry

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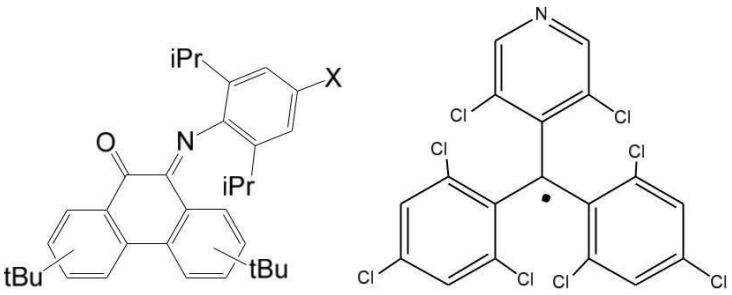
Research Project Description:
The lanthanide ions show intriguing magnetic properties that are only now being fully utilized. In contrast those properties of the actinides are very poorly understood.[1] We have reported on some unusual magnetism and spectroscopic properties of uranium(IV) but wish to expand our studies[2] into ligands that are non-innocent. In this case the ligand can contain one electron that can couple between two metal centers. In this project you will synthesise some ligands based on a semiquinone or aryl[3] type ligand system and explore the coordination chemistry to a number of transition metal and lanthanide complexes.



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School of Chemistry Senior Sophister Research Project 2021

Compound Interest: Heavy Metal Complexes as Photosensitisers

Prof. Sylvia Draper (SMD1)

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Research Project Description: In general, the conversion of energy from one form to another flows downhill, with each step representing an energy loss. Upconversion is a mechanism by which carefully designed molecules can buck this trend by taking in light energy and pooling it so as to emit light of higher energy. This is a valuable phenomenon particularly in the development of next generation solar cells and photovoltaic devices and it has application in photocatalysis and luminescent oxygen sensing. The Draper team have uncovered the potential of some of their systems to engage in triplet-triplet annihilation, the molecular process at the heart of upconversion.[1]

Triplet-triplet annihilation (TTA) works by taking a sensitiser (usually a transition metal complex (Ru(II), Pt(II) or Ir(III)) with accessible triplet excited states) to harvest the exciting light and to transfer the energy by triplet-triplet energy transfer (TTET) to an acceptor. The triplet excited state is annihilated by the collision of two molecules to generate one in the ground state and one in its singlet excited state. The radiative relaxation of the latter produces the upconverted fluorescence. Our work has centred on a series of symmetrical Ir(III) and Ru(II) 1,10-phenanthroline complexes (Figure 1) incorporating aryl acetylene chromophores of increasing size.

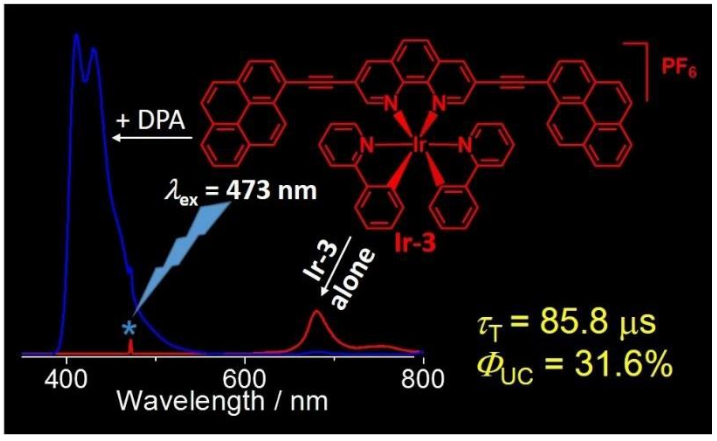

Figure 1: Emission spectra showing the sensitizer emission alone (red) and upconverted emission from DPA (blue) in a donor acceptor mixture (*exciting at 473 nm)

The aim of this project is to build on what is already known and to improve on these features in the next generation of triplet sensitizers.[2,3] The work forms part of on-going collaboration with Prof. Jianzhang Zhao's research group at Dalian University of Technology. To date it has yielded some of the highest known upconversion quantum yields.

The project will involve ligand design and synthesis and the spectroscopic characterisation of the resulting novel metal coordination complexes. The materials will be screened in TCD for their optical properties and lead compounds will be sent to China for further testing with the hope of making further new contributions to the applications of the materials in Photodynamic Therapy and chemical transformations.

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New membranes for water purification

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Research Project Description:

Introduction

Water for both domestic and industrial use is becoming a scarce and expensive resource requiring careful control and protection. Membrane based separation systems dominate the European market for industrial process water treatment equipment. In particular, recently new nanotechnology-based solutions (nanofiltration) have emerged as potentially superior and cost-effective ways to remove sediments, charged particles, chemical effluents, bacteria and other pathogens in addition to the removal of toxins like arsenic or impurities like oil [1]. However, biofouling of membranes is a severe and common problem. The growth of biomass on the surface of membranes and adsorbents (biofouling) limits both the efficiency (volume treated per unit time) and lifetime of systems and necessitates periodical washing of the membrane equipment with aggressive chemicals. There is, therefore, a pressing need to develop antifouling systems that exhibit active durability and are eco-friendly.

Objectives

The main goal of this project is to develop new nanofiltration approaches and membranes for complex water purification. In this project, biofouling issues and other related problems will be addressed *via* development of a new generation of active membranes with potential anti-fouling properties which will be designed and engineered at low cost. The increasing safety of NMs is of particular importance and we will implement the necessary measures to prevent the occurrence of nanoparticles in treated water, using our membrane design in addition to filtering pre-existing particles from water. New membranes of varying compositions and porosity will be tested to determine the optimal water treatment conditions.

Expected outcomes

The successful realisation of this project will result in the development of new nanostructured adsorbents and membranes with enhanced bactericide and anti-biofouling activity, which will allow removal of various contaminants including bacteria, oils, grease, dyes, detergents, colloidal substances, toxins, pesticides, drugs and antibiotics from water. The special purity water will be particularly important for food industries in Ireland, for example for production of various drinks and dairy products. The exploitation of new membranes will give potential users more reliable, cost efficient treatment that generates high quality water, with a tailored mineral content.

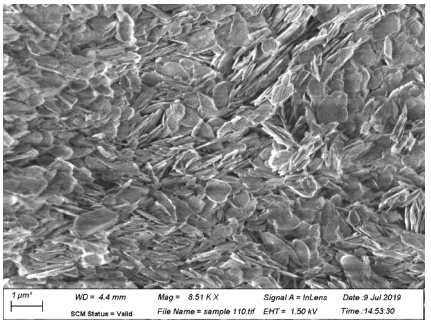

Figure: Cross-section scanning electron microscopy image of new membrane for water purification.

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School of Chemistry Senior Sophister Research Project 2021

Multimodal magnetic core-shell nanoparticles

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Research Project Description:

Introduction

Multimodal magnetic nanoparticles have been used for a broad range of applications including catalysis, cell labeling, drug delivery, hyperthermia treatment and biological imaging (e.g. see Figure below) [1, 2]. The focus of our research is the development of new magnetic nanostructures and their conjugates to be used as potential theranostic tools in cancer research. These structures possess the unique advantage of the large surface area and small size characteristic of nanoparticles, coupled with the magnetic modality required for biological imaging and drug delivery.

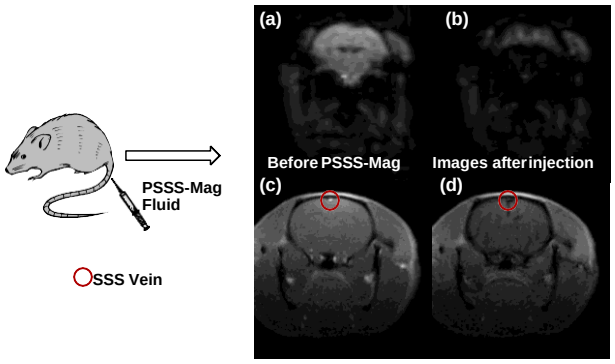

Figure: Echo planar image (EPI) of mouse brain (a) before and (b) as magnetite-based magnetic fluid passes through; Fast Low Angle Shot (FLASH) image of mouse brain (c) before and (d) as our new MRI fluid passes through.

Objectives

The main goal of this work is to develop new multimodal magnetic nanocomposites for biomedical (e.g. MR and CT imaging and cancer therapy) applications. Magnetic oxide core-shell nanostructures will be synthesised using co-precipitation and other processing techniques. The characterization testing and evaluation of new materials will be performed by electron microscopy, FTIR, Raman spectroscopy and magnetization measurements. The nanomaterials will be functionalised with specific biomarkers and drugs and will be tested for potential *in vitro* and *in vivo* cancer diagnostic and therapy.

Expected outcomes

The successful realisation of this project should result in the development of new multimodal magnetic nanomaterials, which could serve as MRI and CT contrast agents and vectors for drug delivery in cancer therapy.

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School of Chemistry Senior Sophister Research Project 2021

Mimicking Class Ib Dimanganese Ribonucleotide Reductases

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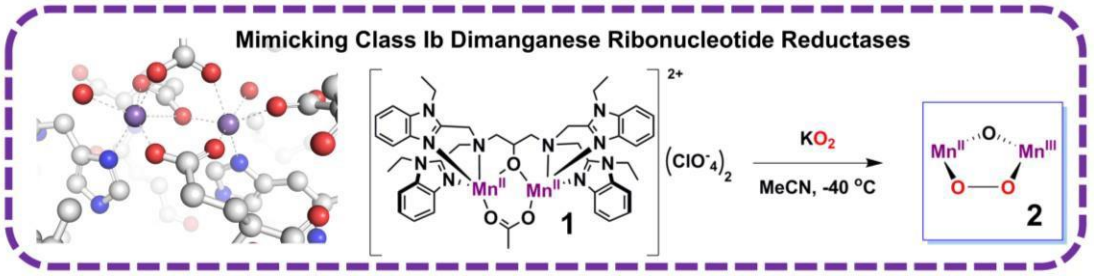
Research Project Description:
The research proposed herein will address the Chemistry of a family of enzymes that play a pivotal role in human health. You will perform a project in the area of Bioinorganic Chemistry. You will explore the natural Chemistry of a family of enzymes called Ribonucleotide Reductases (RNRs). RNRs employ dioxygen and manganese for the biosynthesis of deoxyribonucleotides, precursors to DNA.

You will attempt to gain an understanding of the mechanism and intermediates of the reactions these enzymes catalyse. This will help us to understand their biochemistry, and develop treatments where these metal-containing enzymes are performing adversely. You will develop synthetic small-molecule analogues of the active site of these enzymes. These small-molecule compounds will display the same physical properties as the enzymatic active site.

You will focus on a single aspect of the postulated reaction mechanism, that is the reaction of a derivative of dioxygen, called superoxide, with dimanganese (and other bimetallic) complexes. Superoxide interacts with the metal site in these enzymes producing a so-called metal-peroxide intermediate. You will synthesise metal-superoxide complexes and investigate their reactivity properties. In investigating these model compounds, we will probe the kinetics of these reactions, identify the products of reactions, and try to verify the postulated reaction mechanism for the RNRs. The outcome of these investigations will be particularly exciting, because it will provide the first and the only experimental investigations into certain biochemistries of this large family of metalloproteins. You will utilise organic and inorganic synthetic methods in this project, learn how to perform reactions under exclusively anaerobic conditions, as well as gaining skills in a variety of spectroscopic techniques.



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School of Chemistry Senior Sophister Research Project 2021

High-Valent Metal-Halide Oxidants

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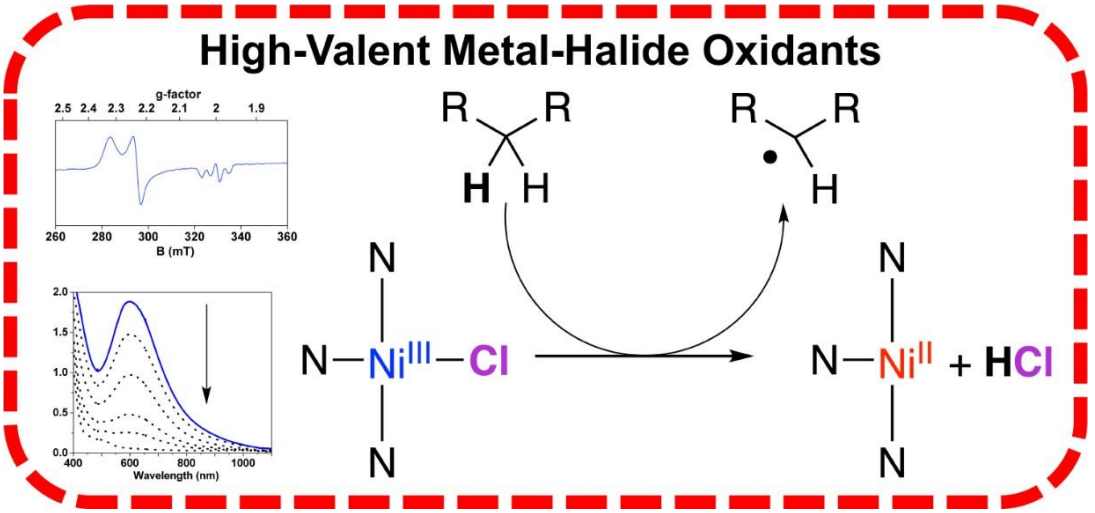
Research Project Description:
The oxidative functionalization of inert C–H bonds in hydrocarbons is an important transformation in biological systems as well as industrial catalysis. A large number of Fe- and Cu-containing metalloenzymes perform such hydrocarbon oxidations, forming hydroxylated, halogenated, or desaturated hydrocarbons. It has been proposed that such reactions involve hydrogen atom transfer (HAT) from an inert C–H bond to a high valent metal-based oxidants such as metal-oxo (M=O) and M-OX (OX = OH, OR, O_2C-R, ONO_2). However, the HAT reactivity of the metal-bound halide in C–H/O-H activation has rarely been studied, although we postulate there will be a very high driving force for such oxidations.

The major objective of this project will be to prepare a series of metal-halide (Ni, Cu) complexes supported by stable and robust ligands. You will prepare high-valent derivatives of these complexes and subsequently investigate the reactivity of the corresponding high valent metal halide complexes towards hydrocarbons. It will also be a goal to explore the oxidative halogenation of hydrocarbons using such compounds. You will utilise organic and inorganic synthetic methods in this project, learn how to perform reactions under exclusively anaerobic conditions, as well as gaining skills in a variety of spectroscopic techniques.



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Functionalisation of 2D Nanomaterials for Catalysis

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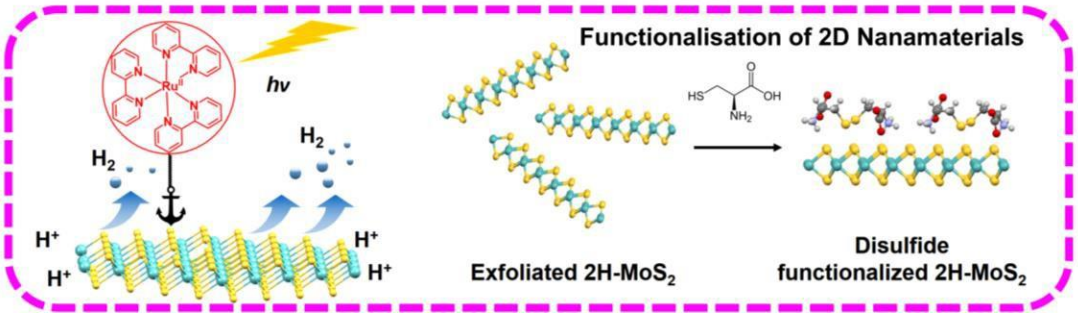
Research Project Description:
Molybdenum disulfide (MoS_2) is a widely used catalyst for important industrial processes like hydrodesulfurisation and hydrocracking of pertroleums (it is used to remove sulfur containing molecules from fuels, limiting emission of SO_2 gas). Furthermore, MoS_2 is a highly reactive hydrogen evolution catalyst. We explore the reactivity properties of two-dimensional (2D, analogous to graphene) MoS_2 nanosheets for applications in hydrodesulfurisation and hydrogen evolution catalysis. We expect exceptional enhancement in catalytic efficiency when moving from bulk MoS_2 to 2D MoS_2 nanosheets. We attribute this to the increase in S vacancy defects and Mo free sites present at the edges in the delaminated (2D) nanomaterials. These sites are known to facilitate adsorption of reactive molecules onto the catalyst surface, and therefore may enhance reaction rates.

This project will focus on the exploration of the reactivity properties of 2D MoS_2 (and functionalised derivatives thereof) in hydrodesulfurisation and hydrogen evolution reactions. You will prepare 2D $_{MoS2}$ nanomaterials, characterise them using an array of spectroscopic probes (UV-vis, FT-IR, TGA, XRD, XPS, Raman). You will then optimise the reactivity properties of the 2D nanomaterials.



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Towards Artificial Enzymes: Bio-inspired Oxidations in Metal-Organic Frameworks

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Metal-organic frameworks (MOFs) are important crystalline materials consisting of clusters or metal ions linked through organic ligands and resulting in microporous networks. MOFs are regarded as key compounds related to energy storage and conversion, as their unprecedented surface areas make them promising materials for gas storage and catalysis purposes. This project addresses the question of how MOFs whose functionalities may relate to those of biological enzymes can be constructed and exploited for sustainable energy, 'solar-fuel'-related applications. In order to design efficient oxidation catalysts, our proposed activities take inspiration from the oxygen-evolving complex (OEC) of photosystem II (PS-II) that catalyses the highly endergonic - H_2O oxidation half-equation to produce O_2. The energy demand of this latter reaction and the lack of cost-effective catalysts currently hampers the Technological breakthroughs towards sustainable H_2 economies. A scientific breakthrough would be one of the greatest scientific achievements with unprecedented impact to future generations. The Senior Sophister project will be assisted by a postgraduate/postdoctoral researcher and will involve the following key aspects:

a) **Synthesis and characterisation of organic ligands of new catalytically-active MOFs:** The student will synthesise new organic ligands which give rise to the formation of highly porous MOFs. The ligands will be reacted with a series of transition metal ions to form new MOFs whose building units resemble the active Mn site in PS-II. Depending on the project, ligands may comprise of light-harvesting ligands including polyaromatic carboxylates, porphyrins, etc. which will be synthesised in multi-step organic synthesis and characterised by NMR and IR spectroscopy.
b) **Structural and physico-chemical characterisation of the MOFs:** The X-ray structures, the thermal stability, the porosity and the surface area of the MOFs will be investigated.
c) **Investigation of the catalytic properties of the MOF:** The photo- and/or the electrocatalytic activity of the MOFs towards H_2O oxidation to produce O_2 or the formation of H_2 will be investigated.

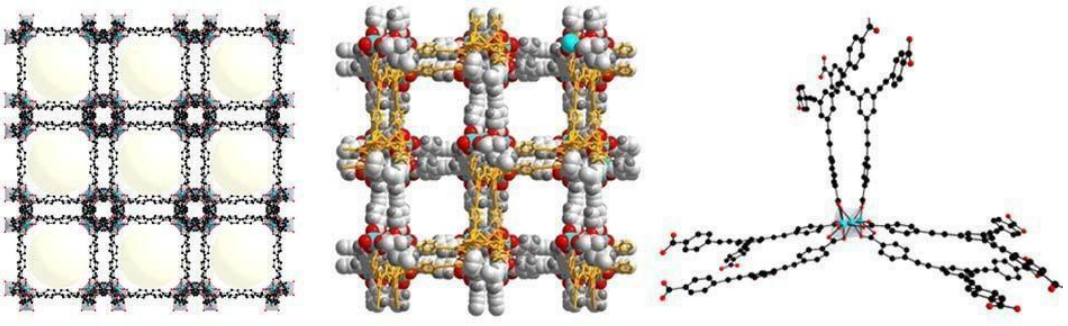

Figure: Crystal structure of a novel MOF that gives rise to porosity and ultra-high surface areas and high catalytic activity for the oxidation of H_2O.

Representative Publications:

(•) ***Nature Communications*, 2017**, DOI:10.1038/ncomms15268. *"Ultra-large supramolecular coordination cages composed of endohedral Archimedean and Platonic bodies"* (•) ***Eur. J. Inorg. Chem*, 2018**, DOI:10.1002/ejic.201800217. *"CO_2 Adsorption in SIFSIX-14-Cu-i: High Performance, Inflected Isotherms, and Water-Triggered Release via Reversible Structural Transformation".* (•) ***Chem. Commun.*, 2015**, *51*, 13313-13316, "*Towards multifunctional lanthanide-based metal–organic frameworks".* (•) ***Chem.- Eur. J.* 2014**, DOI: 10.1002/chem.201304856. *"Hetero-Epitaxial Approach by Using Labile Coordination Sites to Prepare Catenated Metal–Organic Frameworks with High Surface Areas"*

Supramolecular Coordination Cages for Bio-Inspired Catalysis and Bio-Medical Applications

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Coordination cages represent metallo-supramolecular species in which metal ions or small polynuclear complexes are connected through organic ligands to produce compounds with well-defined cavities. Over the last decades, extensive synthetic approaches focused on the preparation of new cage topologies whose structural, constitutional and electronic characteristics can give rise to attributes with potential applications in **catalysis**,[1-4] **drug delivery**,[5] **sensing**[6,7] and others.[8] Most commonly applied synthetic approaches to functional capsular entities use the formation of kinetically stable binding geometries or coordination complexes with defined ligand-accessible sites and which direct the assembly into capsular entities. Amongst the most remarkable cage systems, are examples that exemplify **enzyme-type reaction characteristics**,[9,10] whereby confined host-guest environments influence the transition states and catalytic performances.

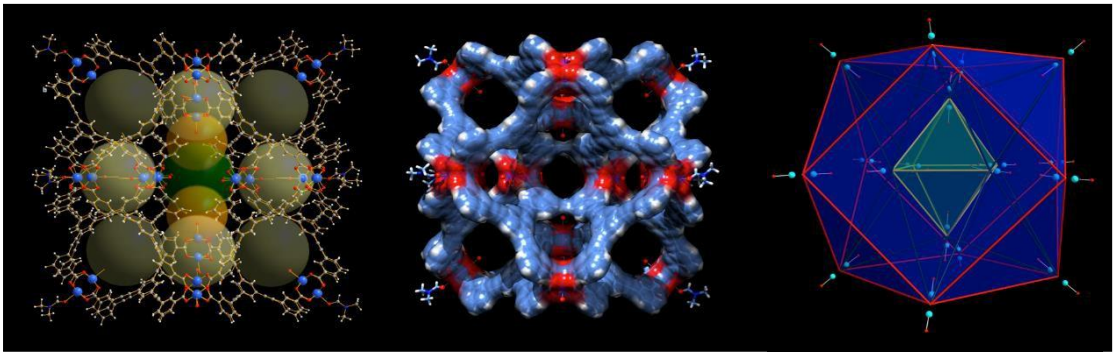

Figure: Structure and topological representations of a coordination cage with exceptional cross-sectional diameters consisting of 36 Cu(II) ions and 24 organic ligands The cage structure is composed of multiple sub-cages providing numerous distinctive binding sites through labile coordination solvent molecules (see. Schmitt et. al. *Nature Communications,* **2017**, DOI:10.1038/ncomms15268).

The Senior Sophister project will be assisted by a postgraduate/postdoctoral researcher and may involve the following key aspects:

a) **Synthesis of new coordination cages involving a combination of organic and inorganic synthetic approaches.** The ligands will be synthesised *via* multi-step organic synthesis and characterised by NMR and IR spectroscopy.
b) **Structural analyses of the coordination compounds using single crystal X-ray diffraction**. Further characterisations may focus on the spectroscopic properties, thermal stability, etc.
c) **Instigation of guest-host chemistry**, e.g. investigation of the incorporation and release of drug molecules (drug delivery), catalysts or photo-active molecules.
d) **Evaluation of properties of the cages/coordination compounds**, e.g. in the areas of bio-inspired oxidation catalysis/enzyme mimetics, or drug-delivery, cell uptake or sensing.

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Organic, Medicinal and Biological Chemistry

Anhydrides as Nucleophiles!

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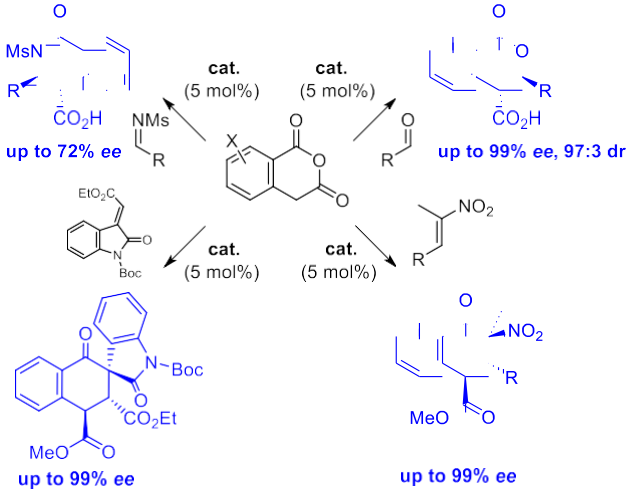
Anhydrides have been used as electrophilic acyl transfer agents for over a century and their chemistry is almost completely dominated by their electrophilicity. We have recently developed a completely new catalytic asymmetric class of reactions in which an anhydride can act as a nucleophile and react with a range of electrophiles to give products of enormous medicinal interest with excellent stereocontrol.

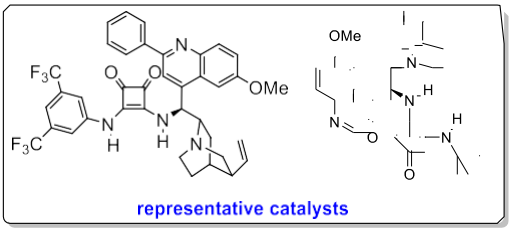
We wish to fully exploit this technology along multiple lines – principally by expanding the substrate scope to include different anhydrides, but also through and innovative catalyst design

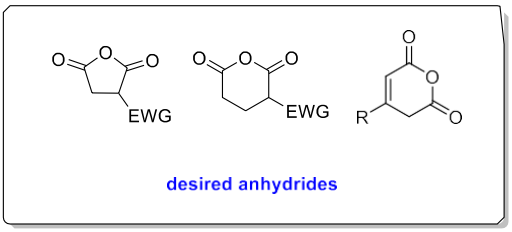
Would particularly suit a student who:

a) Can work out a plausible mechanism without reading the references below (**hint**: look carefully at the anhydride structures - the catalyst can act as a weak acid and a weak base simultaneously).

b) Would be interested in working on a real, current problem. A challenging but potentially rewarding project.







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A new approach to asymmetric nucleophilic catalysis

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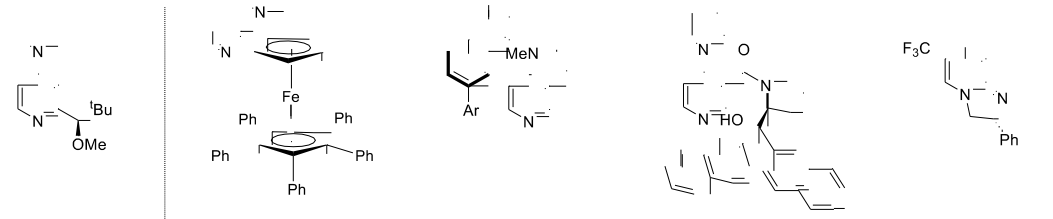
N,N-dimethylaminopyridine (DMAP) is the quintessential nucleophilic catalyst. In order to use the catalyst in asymmetric transformations one needs to install chirality. This poses a problem: in order to control the stereochemical outcome of a reaction it is best to install the stereochemical information as close to the nucleophilic nitrogen atom as possible; however, any steric bulk here significantly retards the nucleophilicity of the catalyst and destroys activity. Several designs have been reported (including from our group – see below) which attempt to extend the influence of remote chirality over the endocyclic nitrogen atom, without hampering nucleophilicity to a significant extent – with limited success. There thus exists an activity-selectivity conundrum associated with all such systems, which seriously hampers the field.



J. Am. Chem. Soc. **1996**, *118*, *1809*

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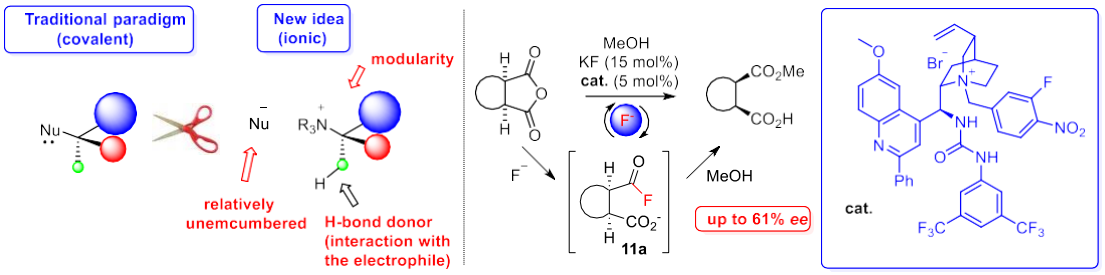
Recently, we have taken an entirely different approach: the divorce of the nucleophilic and chiral units completely through the design of chiral ionic catalysts. These are devised so that the nucleophilic anion can be as small as possible, and the chiral cation as large as possible, with the proviso that it must have functionality allowing it to interact with the electrophilic reaction component. This completely new approach allows the practitioner to 'have their cake and eat it': fast but also selective catalysis. We reported the first such example last year.



Chem. Commun. **2018**, *54*, 10108

In this project we intend to both refine the catalyst design and apply it in a range of transformations in which traditional catalyst systems are inadequate.

Exploitation and prebiotic significance of ancient biomolecules

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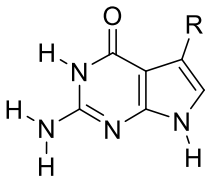
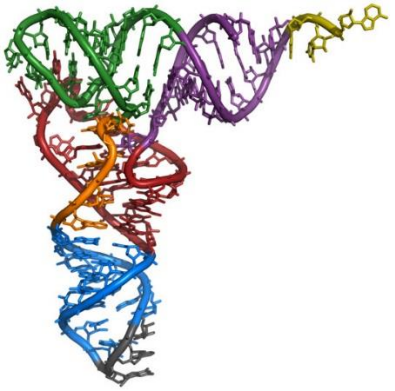
Research Project Description:
Deazapurines are an intriguing class of molecules, they are extremely rare in biological systems yet, in each of the 3 domains of life (archaea, eubacteria and eukaryotes), a slightly different, but related, deazapurine (DAP) is a substrate for an ancient enzyme. In each of the 3 domains a similar enzyme performs a similar task - it exchanges the appropriate DAP for a specific guanine in the transfer RNA (tRNA) of that organism. In bacteria and eukaryotes the appropriate DAP is exchanged with a guanine at position 34 (the wobble position of the anti-codon) but in archaea the DAP is exchanged with a guanine at position 15. Given that these 3 DAPs and enzymes alter the machinery of protein synthesis, are ancient and ubiquitous it is extremely surprising that their role within any of the 3 domains of life is poorly understood. In the case of eukaryotes, it is thought that the ancient enzyme was present in the last common eukaryotic ancestor and predates mitochondrial incorporation.
We have recently shown that analogues of these compounds can have a dramatic effect on eukaryotic systems and we are keen to build upon these results. There are **4 projects available** that will focus on the preparation of new analogues targeted at the different domains of life. Furthermore, a link to the prebiotic world is envisaged and a speculative investigation into this area could be undertaken.



General structure of deazapurines



Transfer RNA

Initial work in this area has led to the design of a novel nucleobase that exhibits unprecedented therapeutic efficacy in a mouse model of multiple sclerosis.

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S.J. Connon and J.M. Southern, Substituted Pyrimidine Derivatives useful in the Treatment of Autoimmune Diseases, WO2016050804 A1; S. Varghese, M. Cotter, F. Chevot, C. Fergus, C. Cunningham, K.H. Mills, S.J. Connon, J.M. Southern, and V.P. Kelly, *Nucleic Acids Res*., 2017, **45**, 2029 – DOI: https://doi.org/10.1093/nar/gkw847

Synthesis of luminescent supramolecular polymers and hydrogels

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Research Project Description:
The objective of this project is to develop and synthesize simple organic ligands that upon coordination to lanthanide ions such as Eu(III) and Tb(III) can give rise to the formation of novel luminescent supramolecular polymers and hydrogels. Recently, there has been great interest in the field of supramolecular- and material chemistry, as well as in nanotechnology in the development of functional transparent gels and supramolecular polymers, formed by using week non-covalent interactions such as hydrogen bonding, pi-pi stacking and electrostatic interactions.[1,2] In contrast, the use of metal-directed gelation in developing such supramolecular structures has only recently been explored,[3] but their use enable the formation of more ordered structures, in multiple directions (*i.e.* 2D and 3D) with added complexity and function. We have recently undertaken the development of several organic ligands that can be used in such metal directed synthesis of (hydro) gels and polymers, all of which are either colorimetric or luminescent. One of our samples is shown in Figure 1a. Here we used simple three arm ligands based on the use of C_3-symmetrical benzene-1,3,5-tricarboxamide (**BTA**), and through a covalent spacer, tethered three 2,2'6',2''-terpyridyl (*tpy*) moieties to this central core. Then by using lanthanide ions, the formation of highly ordered gels has been achieved, as is demonstrated in Figure 1b, using Scanning Electron Microscopy.[4] The aim of this project is to further develop this idea by changing the nature of **a)** the spacer used in connecting **BTA** to the *tpy* by using chiral building blocks and **b)** by changing the *tpy* ligands for other metal coordinating ligands to allow for the use of verities of other metal ions. We will then, **c)** investigate their spectroscopic properties in solution and in the solid state, and **d)** investigate the morphology of the gels formed from these ligands using various imaging techniques in collaboration with Prof. John Boland, as well as we will investigate the rheology of the material formed.

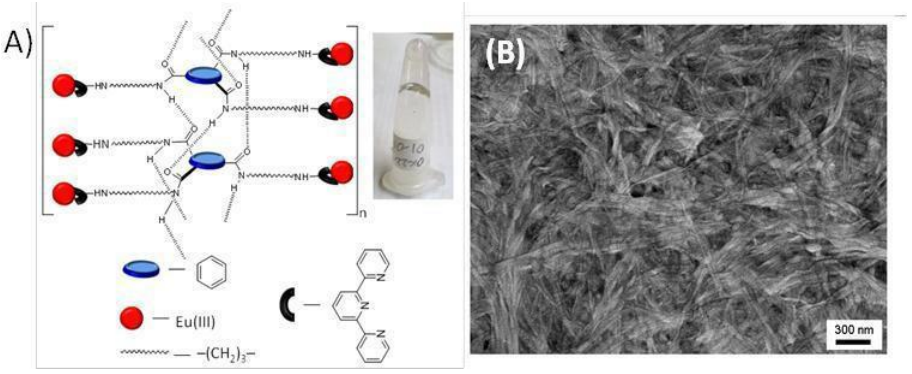

Figure 1. A) Terpyridine-based tripodal ligand (**L**) showing the europium binding sites that give rise to the formation of **$EuCl_3$-L**. B) SEM images of **$EuCl_3$-L**.

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Naphthalimide based Tröger's bases as DNA targeting molecules

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Research Project Description:
The aim of this project is to develop DNA targeting/binding luminescent probes and novel therapeutics for targeting cancer cells and will be carried out in collaboration with Professor John M. Kelly. The general structure of the target molecules are shown in Figure 1a and are based on the use of 1,8-naphthalimide chormophores, which can be synthetically modified at the imine side as well as on the aromatic unit itself. The Tröger's base is a well-known chiral cleft-shaped molecule, containing a diazocine ring, conjugated to two aromatic moieties. The chirality, with a C_2 axis of symmetry, is provided by the presence of the two bridgehead sterogenic nitrogen atoms of the diazocine ring.[1] We have recently employed this structure in the development of DNA targeting compunds[2], and for use as luminescent cellular imaging agents, as demonstrated in Figure 1b[3]. The main objectives of this SS project are to: **a)** Synthesize two new naphthalimide based Tröger's bases, based on the use of polyamines at the imide terminus. This is achieved in 3-4 steps synthesis depending on the nature and the length of the polyamines. If time allowed, the enantiomers will be separated using a column chromatography procedure developed in the laboratory of Professor Kelly. **b)** We will then investigate the binding of these to DNA by using absorption and fluorescence titrations and the binding strength and mode analyzed further by using thermal melding experiments, as well as CD and LD spectroscopies. **c)** Finally the biological properties of these compounds will be probed in collaboration with Prof. Clive Williams in the School of Biochemistry and Immunology.

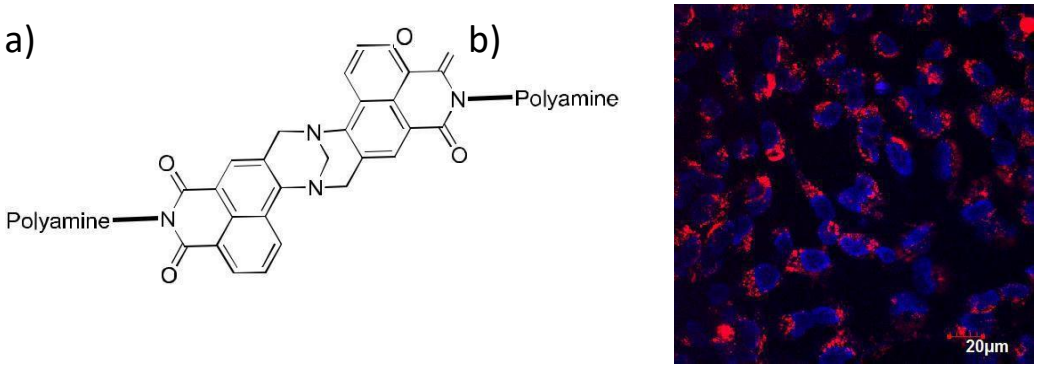

Figure 1. a) General structure of the Tröger's bases developed in this project. b) The confocal fluorescence image of a Tröger's base within HL-60 cells.

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Self-Assembly of Tröger's Base Based 2D Metallacycles

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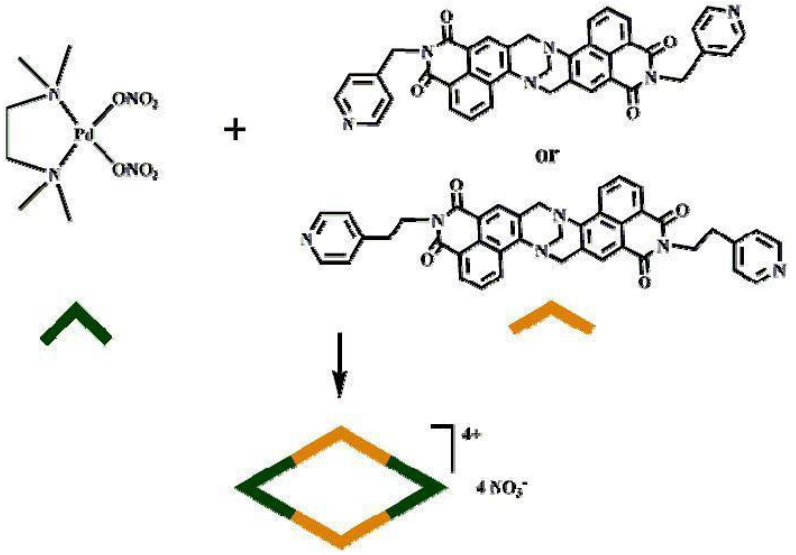
Research Project Description:
The underlying aim is to design and synthesis of novel shape- selective building blocks based on Trögers-base motif and they will react with *cis*-blocked Pd(II)/Pt(II) acceptors to make several [2+2] self-assembled chiral, fluorescence metallamacrocycles, that can be employed in gas-storage, chemosensing, DNA Binding and live cell-imaging. Examples of the kind of ligands that will be developed in this project are shown below. Incorporation of 1,8-naphthaliimide fluorophore causes the final macrocycles to exhibit strong emission characteristics. Having large internal concave aromatic surface, the final macrocycles (shown schematically belwo) are expected to act as macrocyclic receptor for large spherical convex guest such as C_{60}/C_{70}. The host-guest binding will be demonstrated using various spectroscopic methods (UV, Fluorescence, ^{13}C NMR and ESI- MS).



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Synthesis of novel ligands for lanthanide ions using 'click' chemistry

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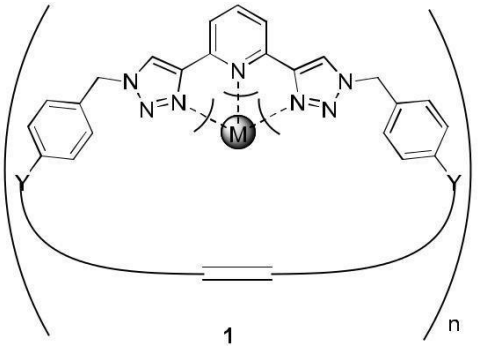
Research Project Description:

The objective of this project is to develop several new ligands based on the pyridyl unit shown below for use as novel coordination ligands for lanthanide and transition metal ions. These will be made by employing copper catalyst 1,3-dipolar cycloaddition (1,3-Huisgen) reaction reactions using variety of appropriate functionalised azides and alkyl derived pre-cursers. The use of 'click' chemistry to develop novel and functional organic structures form simple or complex molecules has become highly popular in recent times.[1] There use for developing novel ligands for metal coordination has, however, only recently been explored. We have developed various lanthanide luminescent systems, where two macrocyclic cyclen based complexes were conjugated together by the use 1,3-Huisgen reaction.[3] Recently we have extended this area of research further towards the development of structures such as **1** shown below, that are formed in a few steps synthesis from 2,6-bis((trimethylsilyl)ethynyl)pyridine. Compound **1** is currently being developed in our laboratory as a part of a PhD project. This system is formed by firstly using the 'click' chemistry to give an acyclic pyridyl di-triazole ligand which upon reaction with lanthanide ions such as Eu(III) can form a 1:3 (metal:ligand) complex, while using Ru(II) gives the 1:2 complex formation. These ions preorganise the ligand to allow for macrocyclisation reaction to take place; which can be achieved by using Grubbs' catalysed olefin ring-closing metastasis reaction. This gives interlocking supramolecular architectures such as [n]catenane and [n]rotaxane. The objective of this SS project is to build on this work and to develop two to three new ligands based on **2**, where both the pyridine as well as the phenyl ring will be synthetically modified in positions *X* and *Y* respectively. The aim is then to use the above ions (and possibly several others) to template the synthesis of novel supramolecular structures from these new ligands. The underlying aim is to form new luminescent material that can be employed for instant in cellular imaging and in luminescent sensing. Consequently, in-depth spectroscopic analysis uing both UV-Vis absorption and luminescence of **2** with these ions will be undertaken.



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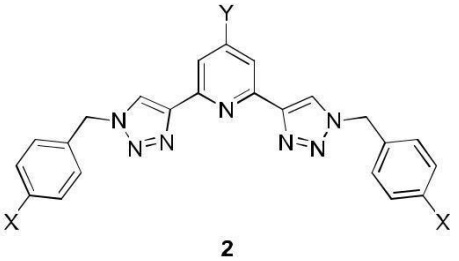

2

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School of Chemistry Senior Sophister Research Project 2021

β-Hairpin Cyclic Peptides as Inhibitors of Nucleotide Excision Repair

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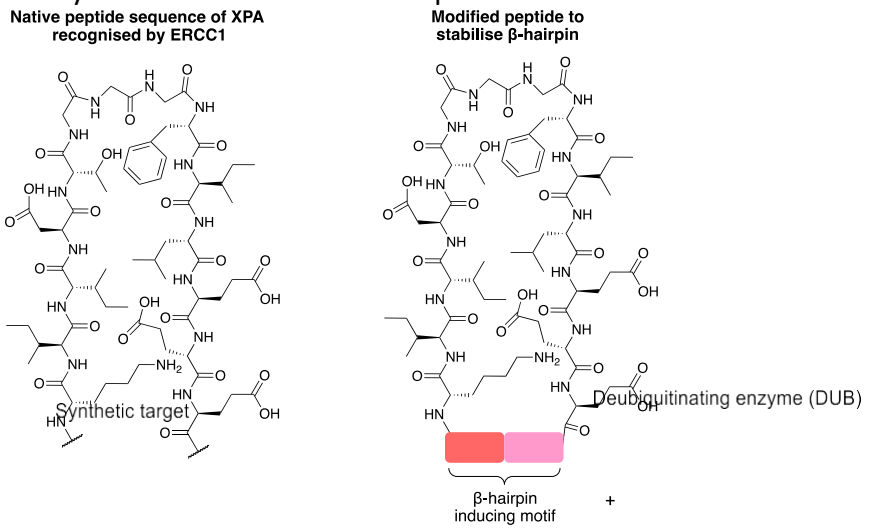
Targeting the DNA repair response is one of the most compelling and, as yet poorly exploited strategies for sensitising or re-sensitising tumours to DNA alkylating chemotherapy. Nucleotide excision repair (NER) is a key DNA damage repair pathway.[1] However many NER proteins are structurally disordered and, as such, hard to target for therapeutic intervention.[2] A key protein-protein interaction (PPI) in the NER pathway occurs between XPA protein and the endonuclease XPF-ERCC1.[3] Blocking the XPA-ERCC1 interaction thus prevents NER, and so can re-sensitize tumors to chemotherapy.[4]

Targeting protein-protein interactions (PPIs) expands what we can consider druggable targets beyond simple enzymes and receptors. However due to the large PPI surface small molecule inhibitors can lack efficacy. Cyclic peptides can confer increased specificity, particularly when targeting PPIs. β-hairpins are found at the active sites of variety of PPIs, making them ideal candidates for drug leads. Typically, these molecules are replicated synthetically and cyclised *via* the use of a β-turn template that can be derived from almost any β-turn-inducing motif.[5]

This aim of this project is to synthesize, characterize and test cyclic hairpin shaped peptides to mimic the binding motif of XPA. The student will gain experience in solid phase peptide synthesis, peptide purification (HPLC) and a variety of characterization techniques.



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Synthesis of photoactivatable inhibitor of a DNA damage repair enzyme

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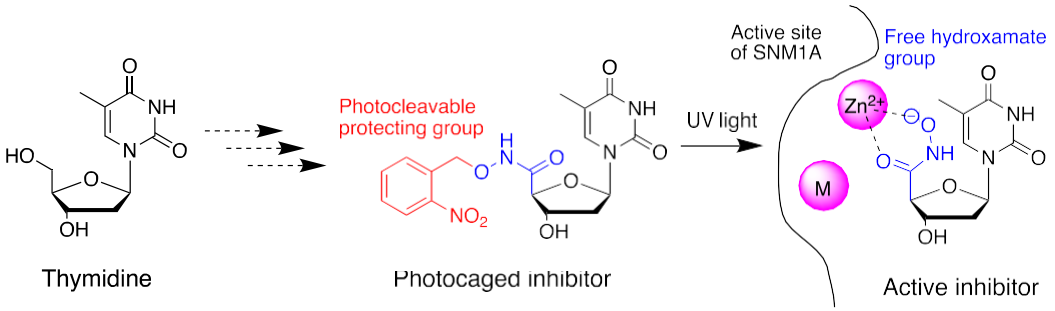
Research Project Description:
DNA damage repair enzymes play crucial roles in cell maintenance. SNM1A is a key DNA damage repair enzyme acting as a 5'-3' exonuclease, about which little is known. It plays vital roles in DNA repair, immune system development and telomere maintenance and has been linked to chemotherapy resistance.[1, 2] Despite its clear biological importance in cancer therapy, immunity and ageing, few inhibitors of this enzyme have been reported.

A nucleoside-based inhibitor of SNM1A has been reported by the McGouran group.[3] This inhibitor was synthesised *via* the incorporation of a hydroxamic acid group on the 5'-position of thymidine. The aim of this project is to generate a photoactivated derivative of this lead inhibitor for potential use in photochemotherapy. This will involve the installation of a photocleavable protecting group on the 5'-hydroxamic acid group.

The photocaged inhibitor will be generated by chemical synthesis of the 5'-modified nucleoside, using methodologies recently developed in the laboratory. Biological evaluation and photocleavage studies of the inhibitor will be carried out as time allows. The student will gain valuable skills in organic synthesis as well as biochemical and biological techniques.



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Molybdenum-Based Catalysts for Allylic Trifluoromethylation

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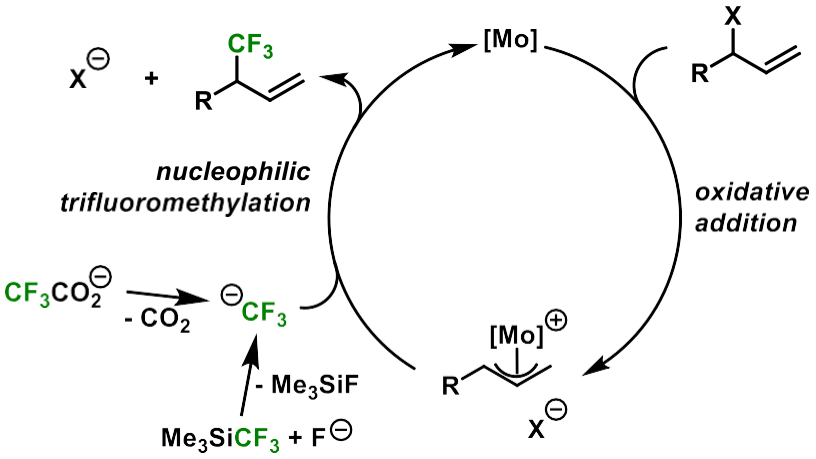
Research Project Description:

The incorporation of fluorine into organic compounds is of enormous significance in medicinal chemistry: as a small and highly electronegative atom, its presence can have profound effects on the chemical and biological properties of a molecule.[1] However, the extreme difference in reactivity between fluorine and the other halogens means that methods developed for the formation of C-Cl/Br/I bonds cannot be easily translated to C-F bond formation. The incorporation of CF_3 groups is particularly important, and is often reliant on expensive and highly reactive reagents – general methods are still lacking.

This project will explore the potential for Mo^0 complexes to catalyse the trifluoromethylation of allylic electrophiles (see proposed catalytic cycle below). Mo-based catalysts generally give branched products in allylic alkylation reactions, in contrast to Pd or Cu.[2] Previous work in the lab has demonstrated that nucleophilic attack by CF_3^- liberated by trifluoroacetate decarboxylation is possible, but that decarboxylation is very slow at 130 °C.[3] This project will continue to explore this pathway, as well as the use of more convenient (though costlier) sources of CF_3^- such as the Ruppert-Prakash reagent, Me_3SiCF_3, which should allow for lower reaction temperatures and higher-yielding reactions.



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Studies into the Mechanism of Allylic Trifluoroacetate Rearrangements

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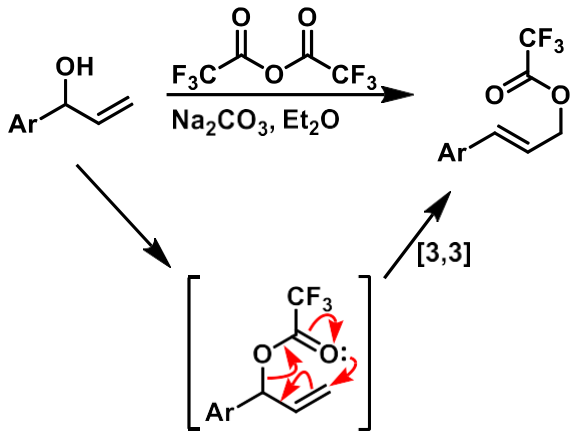
Research Project Description:

While preparing substrates for a different project (CP1 – see above), we observed an unexpected rearrangement reaction when acylating branched allylic alcohols – instead of obtaining the expected branched products, we occasionally found that the linear product formed preferentially.[1]



There are a number of potential mechanisms by which this could occur, the most likely would seem to be the pseudopericyclic [3,3]-sigmatropic rearrangement shown above.[2] Similar mechanisms have been implicated in related systems.[3]

The aim of this project is to develop a better understanding of the scope and mechanism of this process. This will involve some organic synthesis, and then physical organic chemistry studies. This is likely to focus on establishing linear free-energy relationships (e.g. Hammett plots) and measuring reaction kinetics, but could potentially include the measurement of kinetic isotope effects, or computational chemistry (DFT), if this aligned with the students' interests.[4]

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School of Chemistry Senior Sophister Research Project 2021

Guanidine piperazines to fight *Mycobacterium* infections

Prof. Isabel Rozas (IR1)
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Research Project Description: Regardless of the good progress in modern therapies to fight tuberculosis, the pathogen responsible of this disease, *Mycobacterium tuberculosis* (Mtb), is far from being eradicated. Resistance, persistence and co-infection with HIV make difficult the complete cure of this infection with current treatments. Hence, there is an urgent need to develop new drugs to treat mycobacterial infections.[1] Recently, the evaluation of a small library of amidine piperazine analogues (Fig. 1) in an *in vitro* assay against a Mtb strain has been reported,[2] and some of these compounds showed high antitubercular potency.

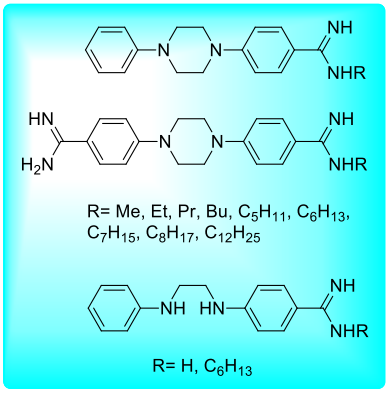

Figure 1

Even though a clear target was not established, the good antibacterial results reported as well as the known amidine-guanidine similarity, encouraged us to screen a number of guanidine derivatives from our in-house compounds' library[3] in collaboration with Prof. Stephen Gordon (Conway Institute-UCD). Because of the safety problems associated to the causative agent of tuberculosis (Mtb) due to its slow growth and high virulence, these compounds have been tested against *BCG* which is prepared from an attenuated strain of bovine tuberculosis bacillus, *Mycobacterium bovis*, that has lost its ability to cause disease in humans. So far, results have shown that some of these guanidine analogues (Fig, 2 green) are quite active against BCG.

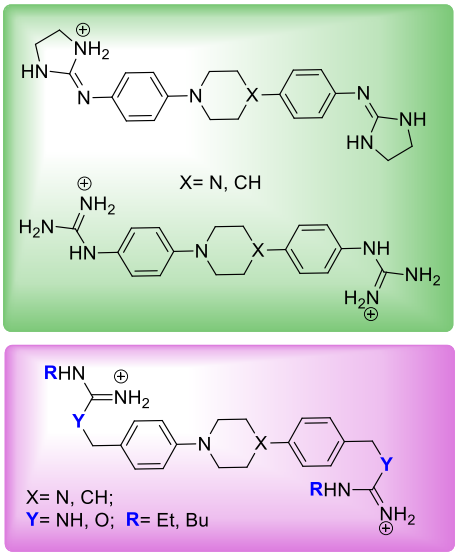

Figure 2

Thus, in a ligand-based design approach, in this project we will prepare new piperidine/ piperazine guanidines (Fig. 2, purple) and, we will test their anti-mycobacterial activity, in collaboration with Gordon's lab, using a resazurin microtitre plate method.[4] Minimum inhibitory concentrations (MIC) for the tested compounds will be calculated, with the antibiotic kanamycin used as a positive control. Moreover, a study of the physicochemical properties of the compounds (logP, logD, pK_a) will be carried out to find correlation to their potential activity.

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School of Chemistry Senior Sophister Research Project 2021

Targeting Guanine-Quadruplexes in a dual attack

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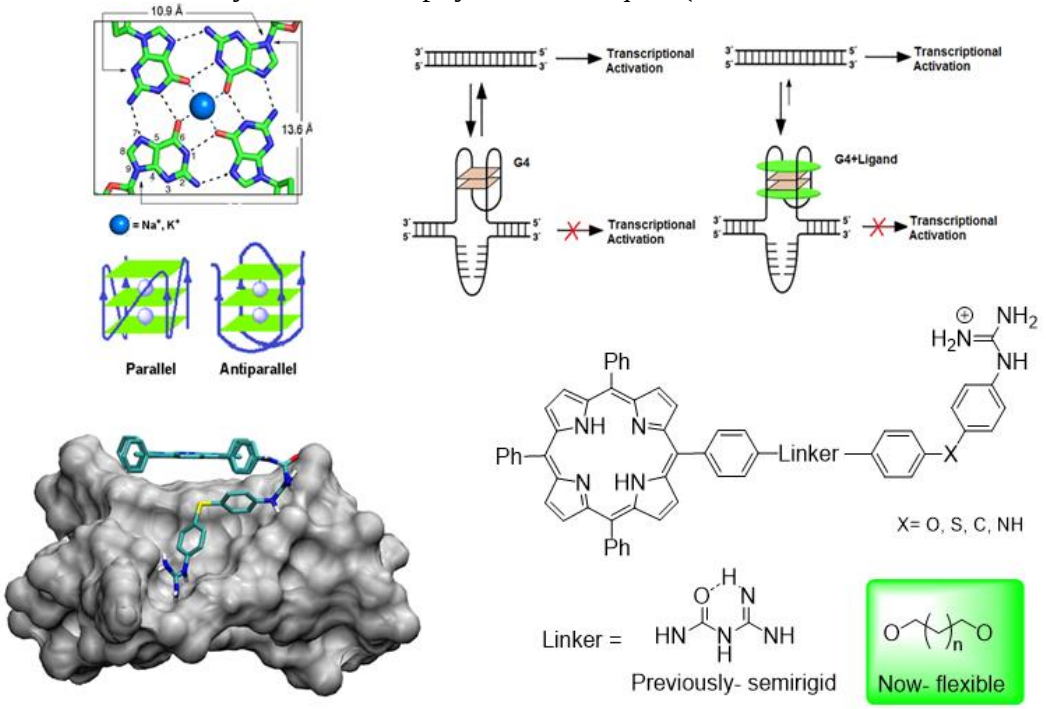
Research Project Description: Nucleic acids within the cell are not only present as the classic Watson-Crick duplex, but also can form different non-canonical, multi-stranded structures such as guanine quadruplexes (G4s). These G4s are 3D structural arrangements formed by G-rich DNA regions resulting from the stacking of several *G-quartets* stabilized by cations such as Na^+ and K^+ (Fig. upper left).[1] G4s are stable under physiological conditions and have been visualized *in vivo* in human cells.[2] Also, they are involved in numerous diseases such as HIV, malaria, Alzheimer's, ALS or cancer. G4s are present in biologically important regions, such as the telomeres end (h-Tel) as well as in the regulatory regions of oncogenes (*e.g.* c-MYC, c-KIT, B-Raf, K-Ras).[3] Formation of G4s in gene promoters results in the suppression of transcription; therefore, ligands that stabilized G4s in those promoters will inhibit transcriptional activation (Fig. upper right).

We have recently developed a series of porphyrin-diaromatic guanidine conjugates connected by a semirigid linker that selectively bind to G4s over dsDNA (Fig. down).[4] Thus, based on our previous results and modelling the objectives of this project are i) to synthesize fluorescent and selective G4 probes by conjugating diaromatic guanidines with appropriate porphyrins by means of flexible linkers (Fig. down right), and ii) the biophysical study of the binding and selectivity of the prepared ligands to different G4s and dsDNA by means of biophysical techniques (i.e. UV-thermal denaturation, CD).



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Development of a Peptide Macrocyclization Strategy Towards Synthesis of Ovarian Cancer Therapeutics

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In the last decade over 30 peptide based drugs were approved for clinical use in the EU. This represents approximately 3% of all drugs approved in the EU in the last decade and it is believed that the focus will continue to shift onto peptide based therapeutics in the coming years as new diseases emerge and still incurable ones persist. With this comes a need for more practical and efficient strategies to access peptide structures synthetically. Cyclic peptides in particular have increased resistance to peptidases compared to their linear counterparts due to the absence of either terminus giving them potentially greater bioavailability and making them very attractive drug candidates.[1, 2] This research project will specifically focus on the development of a cyclization methodology for synthesizing cyclic peptide structures.

Groundbreaking techniques in peptide synthesis such as solid-phase peptide synthesis (SPPS)[3] and native chemical ligation (NCL)[4] have allowed the number, size and variety of synthetically accessible peptide structures to explode. However these techniques are not without their limitations. Cyclization of a linear peptide using NCL is limited to those containing a cysteine or alanine residue. This project aims to use the thiol-ene 'click' reaction to insert a thiol group into alternative amino acids thus expanding the scope of residues that can be used at an NCL site for cyclization. The cyclic DWLPK peptide, which has been shown to be effective in treating mice with patient-derived xenografts of metastatic ovarian cancer,[5] is a model target for demonstrating this methodology due to the lack of either a cysteine or alanine in its structure.

Over the course of this project the student will become familiar with valuable synthesis and analytical techniques such as SPPS, NCL, non-natural amino acid synthesis, NMR, mass spectrometry and HPLC. This project is aimed at students that are interested in using synthetic organic chemistry for wider biological applications.

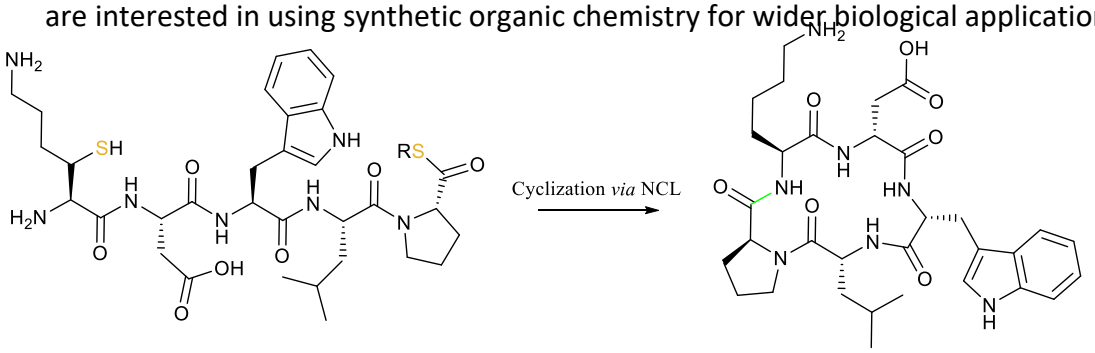

Figure 1. Cyclization of linear peptide precursor to synthesize the cyclic DWLPK peptide

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Synthesis of a potential SARS-CoV-2 peptide therapeutic using a novel aspartic acid mediated peptide ligation

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Research Project Description:
Peptide drugs have revolutionised modern medicine and continue to be a major focus of pharmaceutical R&D. The chemical synthesis of large peptides as a single chain is impractical due to incomplete reactions, difficulties with purification and low overall yields. Recombinant methods for peptide synthesis also suffer from the formation of heterogenous mixtures. Modern strategies for peptide synthesis involve the ligation of two smaller peptide fragments which can be reliably synthesised using Solid Phase Peptide Synthesis (SPPS). The Native Chemical Ligation (NCL) methodology developed by Kent *et al*. in 1994 has revolutionised chemical peptide synthesis.[1] However, its use is restricted by the requirement for the relatively rare amino acid cysteine at the ligation site.

The aim of this project is to develop a ligation methodology that overcomes the need for cysteine. The approach will involve the incorporation of an unnatural thioaspartic acid residue at the ligation site to mediate the ligation reaction. After ligation, the thioaspartic acid may be converted into the relatively common amino acids, aspartic acid or alanine, under mild, metal-free and green conditions.

This novel ligation methodology will be demonstrated through the synthesis of the promising SARS-CoV-2 peptide therapeutic, LCB1, designed by Cao *et al*.[2] LCB1 is a 56-amino acid peptide that binds to the spike protein of SARS-CoV-2 and inhibits viral attachment with IC_{50} values in the picomolar range (**Fig. 1**). The student undertaking this project will gain experience in the organic synthesis of unnatural amino acids, Solid Phase Peptide Synthesis (SPPS) and peptide purification (HPLC). The project would appeal to students interested in medicinal chemistry, organic synthesis and drug discovery.

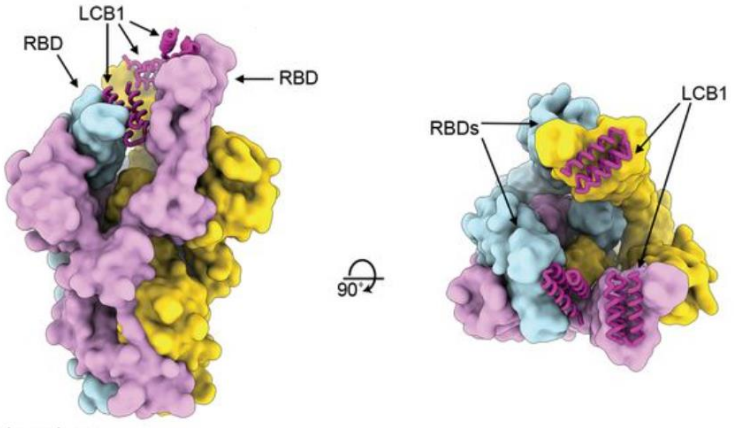

Figure 1. LCB1 bound to the receptor binding domains (RBDs) of the spike protein of SARS-CoV-2.[2]

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The Pigments of Life – Chemistry of Tetrapyrroles

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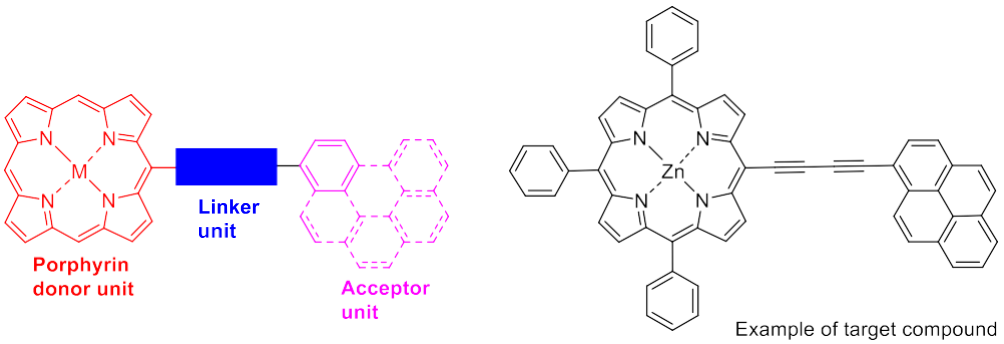
Research Project Description:

Tetrapyrroles are a unique class of ubiquitous natural compounds and are targets of strategic importance in biology, industry (pigments, catalysts, sensors, nanomaterials) and medicine (cancer therapy and neuropsychiatry). Recent breakthroughs in their synthesis, biochemistry, industrial use, and medicinal relevance are opening tremendous application opportunities in bio- and information technology. We use tetrapyrroles as biologically relevant 'molecular systems' for an interdisciplinary approach towards health and materials science research.

Currently our chemical studies focus on the unique optical, photophysical, biological, and structural properties of porphyrins. In order to fully utilize the application potential of tetrapyrroles we aim:

- to overcome existing limitations in the synthetic accessibility of porphyrins,
- to advance the understanding of the interrelationship between their chemical properties and biological function, esp. with regard to energy and electron transfer processes.
- to construct porphyrin-based nanomaterials on surfaces as intelligent electrooptical materials.

Donor-acceptor chromophore arrays play a crucial role as light harvesting systems in nature. To study the role of spatial orientation and distance for the electronic and energetic communication between such donor-acceptor moieties, our group investigates in the synthesis of chromophore dyads that are connected by different spacer as well as rigid linker groups.



Objectives:

- Synthesis and characterization of porphyrins-perylene/pyrene dyads.

Tasks:

- Synthesis of porphyrin precursors via condensation reactions.
- Introduction of functional groups suitable for organometallic coupling reactions.
- Optimization of Suzuki, Sonogashira and click reactions for coupling with aromatic acceptor units.
- Photophysical characterization of donor-acceptor dyads.

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Core-accessible Free Base Porphyrin Receptors

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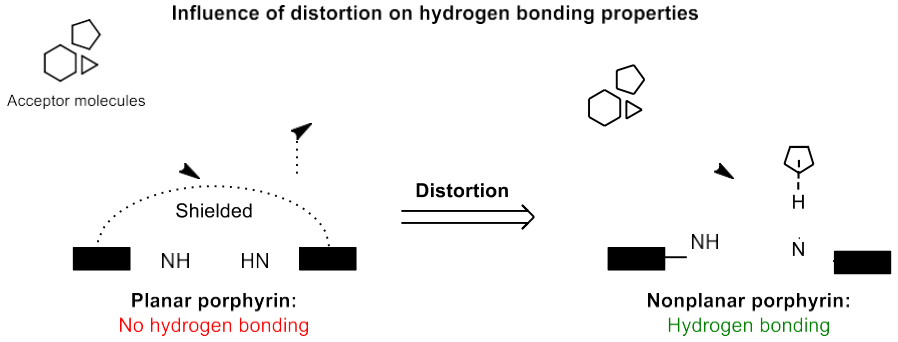
Research Project Description:
Porphyrins are involved in all aspects of life, materials science and medicine a n d play an important role as cofactors, regulators, drug targets, clinical agents and (photo)active reagents. Much of their chemical reactivity relates to specific macrocycle conformations, i.e. the inherent flexibility of the tetrapyrrole macrocycle which can be modulated by metal, steric and environmental effects. Thus, porphyrins can exhibit different distortions of the aromatic system ranging from planar to highly nonplanar. Typically, porphyrin-metal complexes are used in nature for countless biocatalytic processes. Their catalytic activity is dependent on a metal ion complexed by the tetrapyrrole scaffold and they offer an economic and efficient method to accomplish a wide range of fundamental organic transformations.
A new concept, porphyrin-based organocatalysis and sensing utilizes nonplanar free base tetrapyrroles for the activation and binding of small molecules *via* hydrogen bonding. While typically porphyrin N-H units are not involved in intermolecular bonds as they are "shielded" by the macrocyclic system, distortion may increase the accessibility to the porphyrin core. Notably, substituents on the periphery of the macrocycle can distort the molecule due to *peri* interactions. This forces the central N-H units into an outwards orientation, exposing them to acceptor molecules.



Objectives:

- Preparation and characterization of double-sided nonplanar picket-fence porphyrins.

Tasks:

- Synthesis of functionalized precursor aldehydes for porphyrin condensation reactions.
- Synthesis of highly substituted nonplanar porphyrins with functional groups for secondary stabilization of substrates.
- Spectroscopic and structural characterization of sad-distorted porphyrins.
- Spectrophotometric characterization of porphyrin-analyte binding.

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Chemistry, nAChRs and the brain

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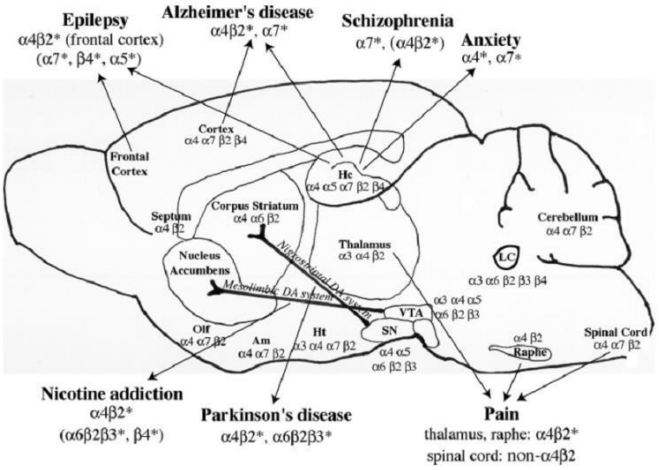
Research Project Description:
This project is concerned with developing new compounds that have the potential to mediate a number of cognitive disorders such as addiction, depression, ADHD and Tourette syndrome. Our lead structure is a compound that has been shown to reduce cravings in human subjects addicted to nicotine, cocaine and/or alcohol but it can be improved. The lead has also been shown to reduce self-administration of a wide variety of abused and addictive drugs in animal models. The overall aim of the project is to modify the structure to prepare more effective compounds that will be employed to probe the molecular mechanisms of addiction with the long-term aim of understanding the underlying neurochemistry and providing an effective treatment. The lead compound is a neuronal nicotinic acetylcholine receptor (nAChR) antagonist and these receptors have been strongly implicated in the process of addiction, a debilitating condition that causes huge suffering and financial drain on individuals and the state. The neuronal nAChRs are family of ion channels made up of 5 subunits, each of which is a 4-transmembrane protein. To date 12 neuronal sub units have been identified, α2 - α4 and β2 - β10 and some of their postulated roles are shown below. However, the precise roles of different subtypes in addiction, and the many other cognitive processes that they are thought to mediate, is poorly understood.
Note that this project will involve multi-step synthetic chemistry.



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Epilepsy, AMPA receptors and decanoic acid

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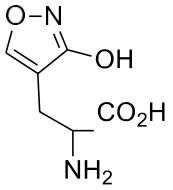
Research Project Description:

Epilepsy is a serious condition that results from a distortion of the usual balance of inhibitory and excitatory pathways within the brain. During a seizure excitatory activity dominates and this is mediated by glutamatergic pathways i.e. those employing glutamate as the key neurotransmitter. Of particular significance are the AMPA family of glutamate receptors. The AMPA receptors are a subset of glutamatergic ion channels that are selectively activated by α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA). Upon activation the ion channels allow the influx of sodium, potassium and occasionally calcium cations (depending on specific sub-type) causing a depolarisation of the neuronal membrane.

Current epilepsy drugs can provide relief of symptoms in many cases but a subset of patients suffer from mitochondrial or refractory epilepsy for which current treatments provide little, if any, relief. However, the ketogenic diet (high fat, adequate protein, low carbohydrate) so named on account of the production of high quantities of ketone bodies (acetone, hydroxyl butyric acid and acetoacetate) during fat metabolism has can reduce seizures dramatically in the case of refractory epilepsy. The MCT (medium chain glyceride) variant of the ketogenic diet (MCT-ketogenic) is particularly effective. The diet is rather restrictive in nature and far from balanced with a number of detrimental short and long-term consequences. Metabolic analysis of the patient on the MCT-ketogenic diet shows that high concentrations of decanoic acid are produced. Decanoic acid is an AMPA antagonist that reduces the number of seizures in mitochondrial epilepsy by preventing the (excitatory) depolarisation of neuronal membranes by preventing activation of the AMPA receptor.

To date, the development of drugs for mitochondrial epilepsy has been seriously hampered by the lack of suitable model for the disease. Fortunately, Prof. Mark Cunningham (School of Physiology, TCD) has recently developed a successful model.[1] The aim of the project is to work with Prof. Cunningham to develop novel derivatives of the simple decanoic acid structure to determine the factors associated with activity, with the long term aim of developing compounds to treat mitochondrial epilepsy effectively and without having to resort to the restrictive and problematic MCT-ketogenic diet.



α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA)

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Theoretical Study of Phase-Transfer Catalysts for Asymmetric Conjugate Additions of Cyanide

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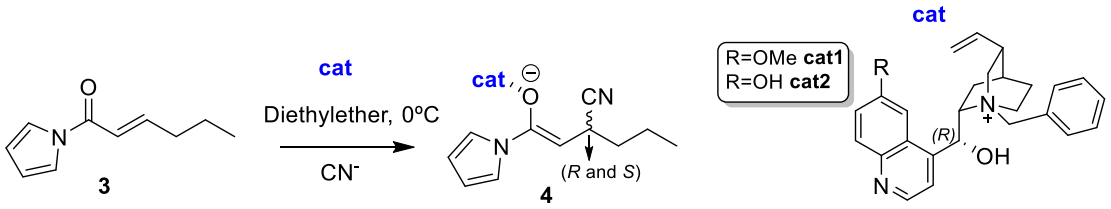
Research Project Description:

A wide variety of asymmetric transformations catalysed by chiral catalysts were developed for the synthesis of valuable organic compounds in the past several decades. Within asymmetric catalysis field, phase-transfer catalysis was recognized as a powerful method for establishing useful procedures for organic synthesis.

While the field of asymmetric organocatalysis is currently growing exponentially, an understanding of the mechanistic details involved in most of these reactions has often lagged far behind the pace of catalyst development, which in return retards rational catalyst design. Therefore, continuous efforts should be made toward the design and development of new catalysts classes, as well as understanding existing relationships between the structure of the catalyst and its ability to transfer stereochemical information.

Catalytic asymmetric cyanation of prochiral unsaturated compounds were extensively studied in recent years as their reaction products are considered highly desirable building blocks for pharmaceutical compounds. Here in, the mechanistic picture of the enantioselective conjugate cyanation of unsaturated ketone catalysed by a *Cinchona* alkaloid quaternary salt will be studied. An improved PTC derivative to the existing system is proposed in order to increase the enantioselectivity of a model reaction and therefore a theoretical study of the free-energy profile will be performed.



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School of Chemistry Senior Sophister Research Project 2021

Study of Tuneable Bioactive Anion Transporters

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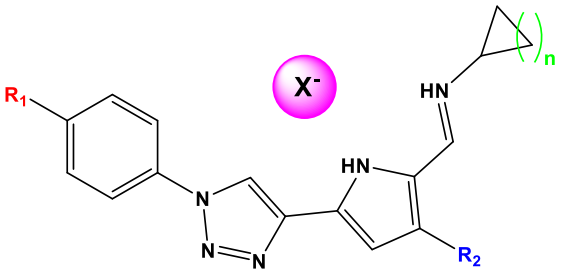
Research Project Description:

The development of supramolecular anionophores for transmembrane ion transport is driven by their potential utility as tools for studying ion transport processes and as therapeutics for diseases arising from mis-regulation of protein ion channels.

Significant effort has been devoted to designing mobile carrier systems with high anion transport activity in vesicles (particularly for chloride), and more recently, in cells. Transmembrane ion transport by synthetic anionophores is typically achieved using polar hydrogen bonding anion receptors. As with naturally occurring ion transporters, anion selectivity is crucial, and depends on the delicate balance between transporter anion binding selectivity and anion desolvation.

A theoretical study of the different non-covalent interactions established between anions and bioactive anion transporter molecules is proposed. An analysis of the anion-anionophore encounter and characterisation of the different interactions established are crucial to induce variations within the anion-transporter molecule to increase the affinity and therefore improve the anion transporter process.



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Physical, Computational and Materials Chemistry

Stimuli-responsive Hydrogel Structures

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Research Project Description:
Hydrogels are three-dimensional, hydrophilic polymer networks, capable of water uptake. By incorporating molecular switches in their structure, stimuli-responsive hydrogel actuators can be developed, that respond to a variety of stimuli, such as light (Fig. 1), electric or magnetic fields, or a change in the local environment.[1-5] The aim of this research will be to investigate the feasibility of using responsive hydrogels as micro-machines, capable of doing mechanical work in response to chosen stimuli. Moreover, new functionalities such as sensing, and switchable uptake and release of molecular guests, will also be incorporated in the same hydrogel material, in order to create synthetic units with biomimetic features.

During this project the student will explore several bioinspired microstructures based on stimuli-responsive hydrogels. The development of new synthetic protocols for functional monomers based on molecular switches and polymer optimisation will prove integral to this investigation. A variety of polymerization approaches will be investigated to control the nature of the hydrogel and to best translate the molecular change to a macro response. The project will involve synthesis and characterisation of the molecular switches using a variety of spectroscopic techniques (NMR, FT-IR, UV-Vis and fluorescence spectroscopy), the optimization of the fabrication process and complete characterization of the hydrogel structures (optical microscopy, SEM).

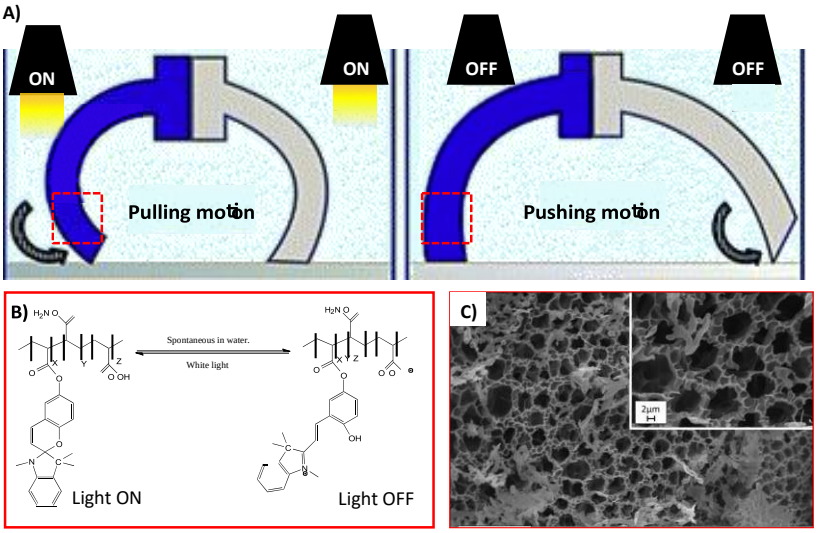

Figure 1. A) Schematic illustration of a photo-actuated hydrogel micro-walker; B) Chemical structure of the polymer used for the fabrication of the photo-actuated hydrogel micro-walker; C) SEM image showing the high porosity of the hydrogel material.

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