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55	Palina Bruyek	TUD	Reeta Joshi &. Mary Deasy	Development of Calixarene Based Surface Imprinted Polymer as a Novel Scavenging Device for Biological Contaminants in Water
56	Paul O'Dowd	RCSI	Darren Griffith	Exploiting Inverse Electron-demand Diels-Alder Click Chemistry for the Functionalisation of a Pt-based Anticancer Drug
57	Qinglu Chen & Heather McDonald	QUB	Steven Bell	SERS Analysis of Organic Extractants using 2D Hydrogel-based Nanoparticle Arrays
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59	Raphaël Abolivier	UCD	James Sullivan	Catalytic Approaches to the Valorisation of Lignin
60	Rebecca Lynch	UCD	Declan Gilheany	Development of the Catalytic Asymmetric Grignard Synthesis of Tertiary Alcohols
61	Riddhi Salotra	QUB	Pamela J Walsh.	Quantitative Estimation of Total Phenolic Content in Brown Seaweeds through 1H NMR Spectroscopy
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New Prospects of Carbohydrates as Chiral Auxiliaries for Tandem Cycloaddition Reactions: Batch vs Flow

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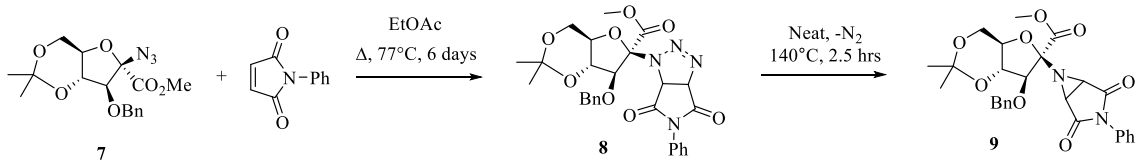
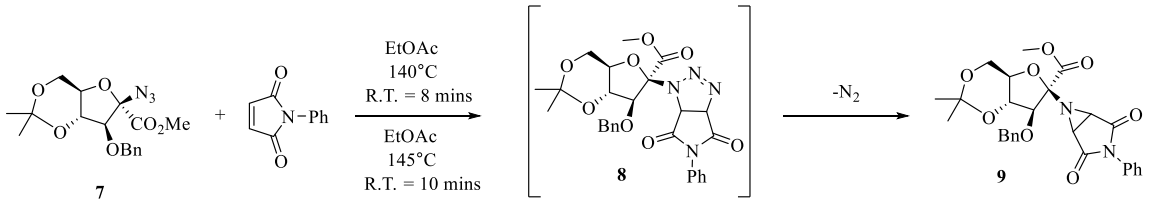
Carbohydrates are good candidates as chiral auxiliaries in a range asymmetric synthetic reactions as they are inexpensive, easily accessible and have multiple stereogenic centers[1]. Stereoselective Huisgen 1,3-diploar cycloadditions between a carbohydrate-linked 1,3-dipolar compound (e.g., an azide derivative) and a dipolarophile (e.g., an activated alkene) are examples of reactions where this stereoselective potential has been shown[2]. However, these types of cycloadditions can have long reaction times, often taking hours or days to reach completion[3-5]. Flow chemistry techniques have exhibited shortened reactions times and improved safety when applied to cycloaddition reactions[5, 6]. Here we show the potential of carbohydrates as chiral auxiliaries for a tandem intermolecular azide-alkene cycloaddition under batch and flow chemistry conditions.

Reaction in Batch



Tandem Reaction in Flow



The stereoselectivity of the intermolecular azide-alkene cycloaddition between a β-azido D-fructofuranose derivative (**7**) and an activated alkene to form the triazoline derivatives (**8**) is explored in this work, along with the subsequent decomposition to the aziridine derivative (**9**). The initial result of this work indicates the formation of major and minor triazoline diastereomeric products in a batch reaction, forming in a 5:3 ratio. The subsequent thermolysis of N_2 is achieved in a neat reaction to afford the aziridine derivative. Under flow chemistry conditions, a tandem reaction is observed with the triazoline derivative acting as an intermediate and the aziridine product forming. Flow chemistry also facilitates a much shorter reaction time.

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H-Phosphonate-Promoted Halogenation of Alcohols using Lithium Halides

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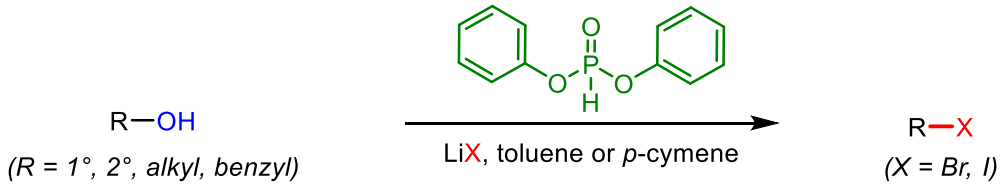
Nucleophilic substitution reactions of alkyl halides and related electrophiles are imperative transformations in academic labs worldwide, as well as the broader pharmaceutical industry.[1] Herein we report a novel redox-neutral protocol for the iodination and bromination of a variety of primary, secondary, aliphatic and benzylic alcohols, by exploiting the chemical behaviour of a H-phosphonate promoter. Alcohols are desirable precursors due to their ready availability and their environmentally benign nature.[2] Lithium halide salts are an attractive alternative for toxic molecular halogens and reactive halogenating agents. Their use enables an enhanced safety profile for this transformation, as well as significantly improving the halide incorporation and thus atom economy, relative to the current state-of-the-art.[3,4]



As H-phosphonates are accessible through hypophosphorous acid,[5] this protocol has the additional benefit of using a phosphorus source that is not derived from PCl_3. Reducing use of halogens at the source decreases energy consumption and minimizes the generation of halogenated waste.[6] This operationally simple protocol is also amenable for use in *p*-cymene as a biorenewable solvent, culminating in a lower net environmental impact for the process. Reactivity studies of the various proposed intermediates have been conducted which has revealed the likely mechanistic pathway of the reaction. The chemistry developed within this project enables a more sustainable synthesis of a versatile range of alkyl iodides and alkyl bromides from the corresponding parent alcohols in yields up to 97%, making this protocol a valuable addition to the synthetic chemist's toolbox.

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Chiroptically Active Copper Oxide Microstructures *via* Post-Synthetic Treatment of Copper-Aluminium Layered Double Hydroxides

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In recent years, much research has focused on the induction of chirality in inorganic nanomaterials, resulting in chiroptical activity being achieved in a wide variety of materials, such as nanosheets, nanowires, and tetrapods, among others.[1-3] Layered double hydroxides (LDHs) are a class of ionic 2D nanomaterials that are known for their anion-exchange properties. As such, they can host a wide variety of species in their interlayer – including chiral molecules.[4] However, despite this unique property, to the best of our knowledge no work has been reported in the literature on the treatment of LDHs with chiral ligands for induction of chiroptical activity.

In this work, carbonate-intercalated copper-aluminium ($CuAl\text{-}CO_3$) LDH nanosheets were synthesised by a simple, scalable co-precipitation procedure. The resultant 2D nanomaterials were treated with L- and D-Phenylalanine at room temperature in aqueous conditions, resulting in the induction of strong chiroptical activity in the visible region, far beyond the onset of the ligand circular dichroism signal. Time-dependent studies demonstrate a gradual transformation from achiral LDH nanosheets, to chiral copper (II) oxide (CuO) microstructural materials, exhibiting *g*-factors of up to 0.0035 (Figure 1). We expect that these materials could have potential future applications in enantiomeric separation and asymmetric catalysis.

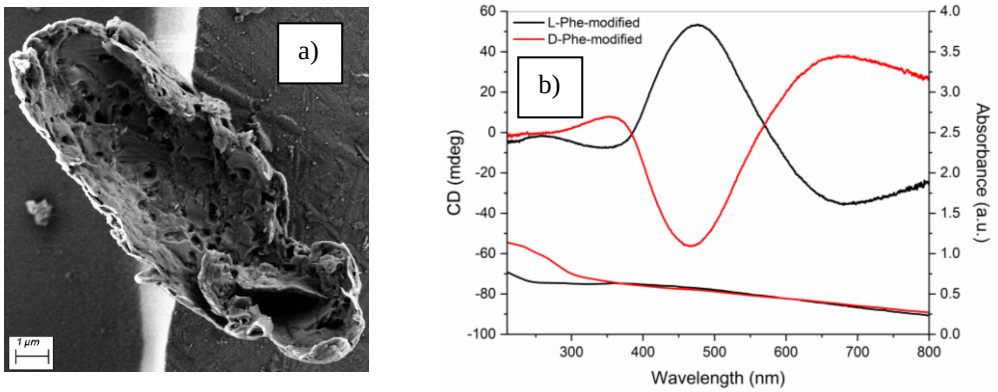

Figure 1(a): SEM image of LDH-derived CuO-D-Phe. (b) Combined UV-Vis and CD spectra of chiral CuO.

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Development of an Immunogold Mapping Strategy to Unravel the Biomolecular Architecture of Bionanocomposite Materials

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There is great optimism that nanomedicine holds the potential to revolutionize the diagnosis, monitoring and treatment of disease. However, many nanotherapeutics fail at the clinical stage due to a lack of understanding of the complex interactions that occur between nanomaterials and the biological environment.[1] It is a firm belief within our group that the biological recognition and behaviour of nanomaterials is, in part, controlled by the precise composition of their surface biomolecular architecture, which may be spontaneously or synthetically derived.[2,3] The biomolecular architecture, adsorbed or conjugated on the surface of the nanomaterial, is what the cell sees in a physiological environment, and thus constitutes a major element of the biological identity of the bionanocomposite structure, mediating interactions with cells and biological barriers.[4,5] Unveiling the composition of the surface biomolecular architecture is therefore of upmost importance in the fields of nanomedicine and nanotoxicology, as by identifying the biomolecules present, prediction of and rational investigation into the biological behaviour of the bionanocomposite material becomes possible.

Several methods to address this question have been established, predominantly based on the separation of proteins from the nanomaterial surface and identification of the recovered components through proteomic approaches such as mass spectrometry, gel electrophoresis or immunoblot analysis. However, the average compositional information obtained through such methodologies does not fully account for the complexity of bionanocomposite interactions *in vivo*, as a key role is played not only by what proteins are present, but how they are organised and oriented relative to one another on the nanomaterial surface. To this end, the present work has seen the development of an antibody-based labelling strategy to characterize the biomolecular architecture directly on the nanomaterial surface. The technique relies on the fabrication of immunogold constructs or labels, comprised of an antibody that binds a specific site of a protein of interest, conjugated to gold nanoparticles which permit identification of the target on the surface of individual bionanocomposites by transmission electron microscopy. Here, we present the fabrication of the immunogold constructs, and demonstrate their utility in elucidating the composition and structure of the biomolecular architecture of bionanocomposite materials.

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Synthesis of Negatively Charged 2D 2H-MoS_2 and Its Functionalization

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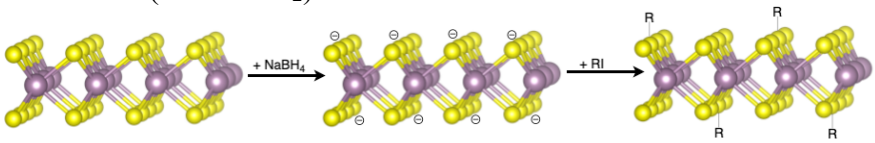
Molybdenum disulfide (MoS_2) has a range of desirable properties with a possible application in key sectors of catalysis, photochemistry and electronics.[1,2] Due to its graphene-like layered structure, it can be easily transformed to a Two-Dimensional (2D-MoS_2) counterpart. 2D-MoS_2 exists in two polymorphs: a 1T-phase with metallic properties and a 2H-phase which is semiconducting. 2H-MoS_2 is a naturally occurring form, but metastable 1T-MoS_2 can be acquired in the process of chemical or electrochemical reduction, resulting in formation of negative charge in the material. This negative charge stabilises the dispersion of 1T-MoS_2 in water and is used as a driving force in a covalent functionalisation by various electrophiles.[3,4] To date, functionalisation of 2H-MoS_2 has proven to be challenging on the account of the stability and inertness of the material.[5]

The aim of this project was to introduce negative charge to semiconducting 2H-MoS_2 and mimic the 1T-like reactivity with electrophiles. It has been achieved by reacting liquid phase exfoliated 2H-MoS_2 with sodium borohydride. The resulting negatively charged material (n-2H-MoS_2) has shown good stability in water and other polar solvents. Moreover, upon reaction with organohalides it has shown successful incorporation of various functionalities (f-2H-MoS_2).



2H-MoS_2 (SM)
Semiconducting LPE nanomaterial

n-2H-MoS_2
Dispersible in water and other polar solvents with negative charge

f-2H-MoS_2
Functionalised 2H-MoS_2 after reaction with electrophile

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Controlling the Polymorphism of Carbamazepine by Droplet-Confinement via Spray drying

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Controlling crystal polymorphism is one of the greatest challenges in the development of active pharmaceutical ingredients (APIs). Polymorphs of an API are different structural arrangements of the same molecule in a crystal lattice [1]. Each polymorph has different physicochemical properties such as: stability, solubility, and bioavailability [2]. Moreover, crystal polymorphism has historically brought about a lot of issues in drug development and patient safety; well-known cases include HIV-1 drug, Ritonavir, and antacid drug, Zantac [3-5]. As a result, control over polymorphism in the pharmaceutical industry has been highly sought after.

This study outlines a systematic one-step approach to controlling the polymorphism of carbamazepine (CBZ) via droplet confinement using spray drying as a continuous method of manufacture. In this process, CBZ molecules are confined within spray dried droplets of varying sizes during the nucleation process to investigate whether different levels of confinement result in obtaining different polymorphic forms. Spray drying is a continuous method for converting a liquid feed solution or suspension to powder in a single step [6]. Different atomising gas flow rates were used to vary the size of the droplet produced in the spray dryer. As a result, a trend emerged in the polymorphic form of the spray dried powders with respect to the sprayed droplet sizes. PXRD confirmed the largest droplet size (~38.55 µm) produced both the stable polymorph, form III, and metastable form IV, whereas only the metastable polymorph, pure form IV, was isolated from the smallest droplet size (~5.39 µm). Accelerated stability tests revealed that smaller level of confinement yields particles with higher stability. The amount of the most stable polymorph of CBZ, form III, present in the particles produced by the larger droplets increased during the stability test. However, the particles produced by the smaller droplets, remained as pure metastable CBZ form IV throughout the stability study. This method of controlling the polymorphism of CBZ and stabilising a metastable polymorph of CBZ by spray drying is a significant development which has the potential to be applied to control the polymorphism of other single crystals, cocrystals and multicomponent pharmaceuticals using a continuous method of manufacture.

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Development of a synthetic route to novel IMPDH inhibitors

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Despite being one of the most widespread diarrheal diseases, there are no effective treatments available for cryptosporidiosis, which is caused by an oocyst-forming protozoan, *Cryptosporidium*.[1] Severe illness resulting from *Cryptosporidium* infection can be life-threatening, especially in young children and people with weak immunity such as patients with HIV. Cryptosporidiosis outbreaks have been reported in countries all over the globe, including Ireland.[2] Inosine monophosphate dehydrogenase (IMPDH) has gained the attention of researchers in search of novel treatments of cryptosporidiosis. In the protozoan, IMPDH is involved in the *de novo* synthesis of guanine nucleotides.[3] This enzyme has a bacterial origin and is notably distinct from host cell enzymes. Cuny *et al.* have identified urea **1** as a potent inhibitor of *Cp*IMPDH (Figure 1).[4] However, **1** is prone to rapid *in vivo* metabolism.

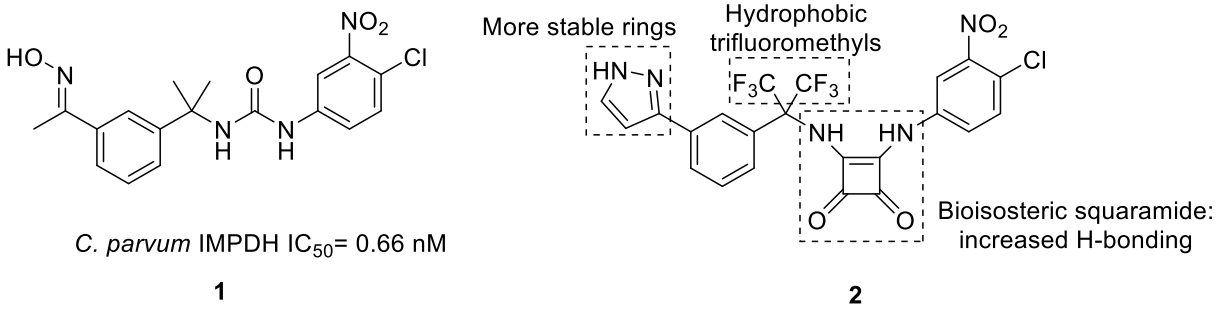

Figure 1. Comparison of lead structure with proposed changes.

We have identified several potential sites for modification to improve overall stability. For example, replacing the existing oxime in **1** with a more stable heteroaromatic ring as outlined in **2** should decrease the rate of metabolic degradation. Herein, we present our work to date on the development of a synthetic route to these novel IMPDH inhibitors. The key step in the synthetic sequence is a palladium-catalysed coupling to install the heteroaromatic ring. We compare the efficiency of two different preparative routes which incorporate the key Suzuki coupling steps at an early or late stage respectively.

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An Chomhairle um Thaighde in Éirinn

Characterisation of serum IgG glycosylation in Cystinosis

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Cystinosis is a rare autosomal recessive lysosomal storage disease. It is caused by a mutation in the CTNS gene that encodes for cystinosin, a cystine transporter and consequently cystine cannot be removed from the lysosome [1]. This results in the formation of cystine crystals in the lysosome, which affects the eyes, kidneys and liver. Left untreated, a decrease in glomerular filtration rate results in kidney failure. Increased immunoglobulin G (IgG) titres have been reported in urine samples of patients with Cystinosis [2]. The exacting role of IgG glycosylation have never been studied in Cystinosis, yet IgG glycosylation has played pivotal roles in other lysosomal storage disorders to warrant such a study. We will present results of a preliminary study that identifies, quantifies and characterises *N*-glycans (e.g. galactosylation, fucosylation and sialylation) from serum IgG of participants with/ without Nephropathic Cystinosis (age and gender matched, n=12) in a double blinded study in an effort to discriminate the patient cohort using statistical approaches (Figure 1).

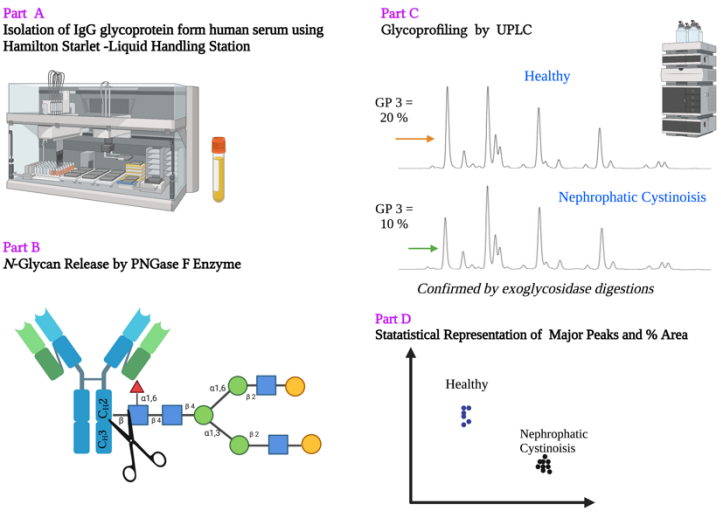

Figure 1. Illustration of N-glycan release from IgG, along with two glycoprofiles comparing GP3 peaks.

The experimental approach followed was adapted from previous technologies developed in our group utilising a Hamilton Starlet Liquid Handling robot [3]. In brief, the sample workflow involves capturing of IgG from human serum, release of *N*-glycans using PNGase F, fluorescently labelling of glycans using 6-aminoquinolyl-*N*-hydroxysuccinimidyl carbamate (AQC), identification, quantification, and characterisation of glycans using liquid chromatography (HPLC/UPLC) and exoglycosidase digestions using a series of recombinant enzymes and liquid chromatography mass spectrometry (LC-MS) following protocols designed in [4].

References

Design and synthesis of carbohydrate based galectin inhibitors

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Galectins are a family of protein which recognise mainly β-galactosides containing glycans. They are classified into three subfamilies, based on the structure and number of carbohydrate recognition domains (CRD). Galectins have a wide range of biological functions, including cell adhesion, migration, cell growth, apoptosis, autophagy, fibrosis, cancer and inflammation.

This poster will present the synthesis and biological evaluation galectin inhibitors derived from a ‘’clickable” intermediate **2**, which are compared with sulphated compound **6** prepared from methyl β-D-galactopyranoside. In addition, synthesis of a tetrazole derivative will be included from **4**. The affinity of these compounds are compared with high affinity glycan ligands for galectin-8 such as sialyl lactose.

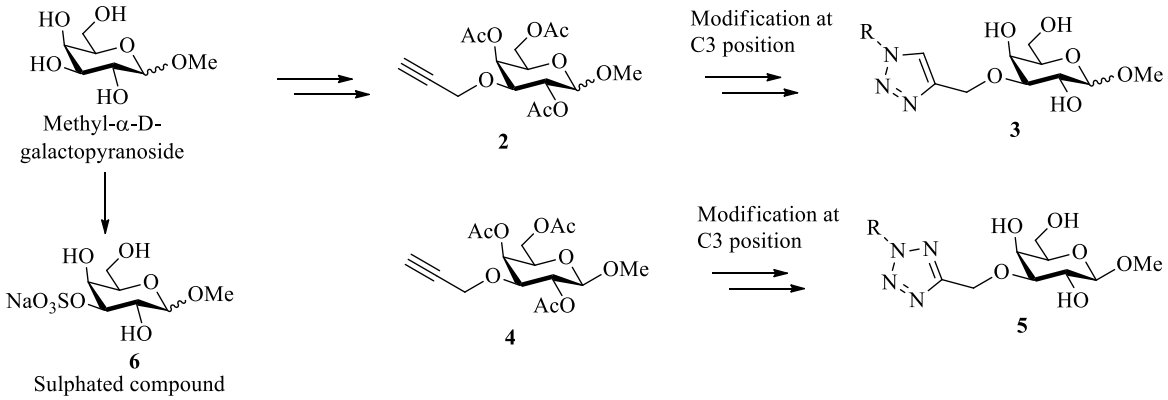

Fig: Summary of the synthesis of **3, 5** and **6**

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Scrambled Macrocycles for Greener Porous Liquids

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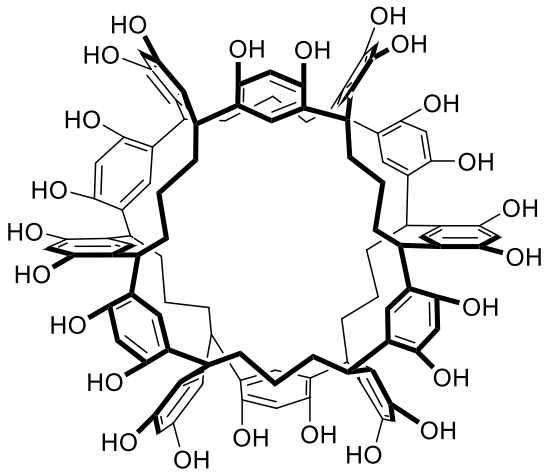
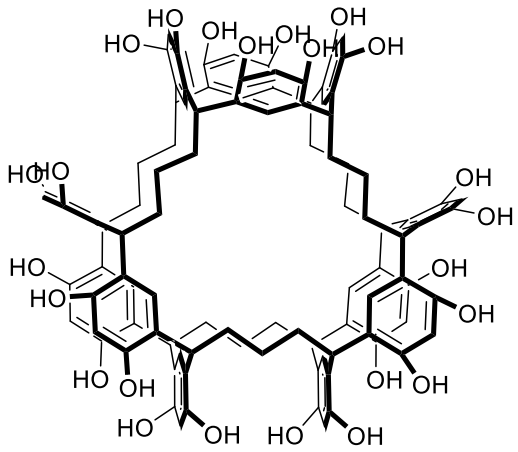
Porous liquids are a class of material combining the gas storage and separation capabilities of porous solids such as zeolites and MOFs with the fluid nature of liquids.[1] Porous liquids have shown applicability in gas sorption and membrane separation.[2] Type 2 porous liquids (T2PLs) are designed by the dissolution of discrete molecular hosts in bulky solvents. Noria, and the closely related cyclic oligomer R3, have been identified as suitable hosts in T2PLs due to their inherent rigidity, and the kinetic accessibility of their central cavities. Current T2PLs based on the Noria framework have shown a marginal increase in gas uptake in comparison to the neat bulky solvent.[3] Another issue is that the solvents employed in T2PL synthesis to date have been highly toxic, and so unsuitable for industrial application.



Noria



R3

This project focuses on the generation of more industrially applicable T2PLs based on the R3 framework. Solubility of the previously highly insoluble R3 is enhanced via alkylation of the hydroxyl moieties. The introduction of alkyl chains, coupled with a scrambling effect due to incomplete alkylation, leads to a much more soluble product.[4] This allows for the generation of a T2PL using a greener and more industrially relevant size excluding solvent, and at a much higher concentration in comparison to previous T2PLs based on similar molecular hosts.[5]

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Engineering and Physical Sciences Research Council

Effects of selenium application on growth and selenium uptake in lettuce.

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Selenium is an essential nutrient for human health that enhances thyroid function, promotes a healthy immune system, and acts as an antioxidant within the body (1) And while selenium is not an essential element for plants, some species can accumulate selenium without suffering adverse toxicity. Biofortification is the *"process of increasing the bioavailable concentration of elements in edible portions of plants through agronomic practices or genetic selection"* (2). This project focuses on agronomic an approach, specifically soil growth and hydroponics. Hydroponics is a method of growing plants that does not require soil. Instead, nutrients are dissolved in water and fed to plant root systems.

Varying concentrations of selenium in the form of sodium selenate have been applied to lettuce, a non-accumulator of selenium, after 30 days of growth. Selenium was added to the nutrient solution of hydroponic systems for two weeks or via foliar application once a week. After two weeks of treatment, plants are harvested, digested, and analysed for selenium uptake using graphite furnace atomic absorption spectrometry (GF-AAS). This poster presentation will present the physiological measurements of the plants as well as the analytical results to date.

When sodium selenate was applied continuously through the root application of lettuce, lettuce mass decreased with increasing selenium. Selenium content in plants increased with increasing selenium in hydroponics, to the determent of the plants. Selenium accumulated more in root systems than in shoots, which is contradictory to literature review of sodium selenate (3). When foliar selenium was applied once a week, plant biomass was not affected by selenium application, though selenium uptake was less than in foliar application than from root systems.

Future work intends to look at the secondary metabolites present in lettuce through liquid chromatography-mass spectroscopy (LCMS) and UV-visible spectroscopy methods.

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Studies in Intramolecular Buchner Reactions

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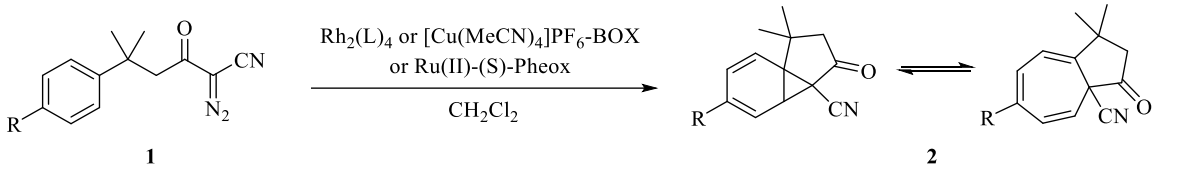
The Buchner reaction, addition of an α-diazocarbonyl compound to an aromatic ring, has been a subject of great interest since its discovery by Buchner and Curtius in 1885.[1-5] The multicyclic skeletal frameworks formed by an intramolecular Buchner reaction, such as bicyclo[5.3.0]decane, are commonly found in natural products.[6-8] These multicyclic structures are of particular interest due to their prevalence in natural products, their biological significance and synthetic utility. Central to this project was the design and synthesis of a series of α-diazo-β-ketonitriles (**1**) and investigation of their reactivity, focusing in particular on intramolecular aromatic additions furnishing bicyclic structures known as azulenones (**2**).



1

R = H, 4-Cl, 4-F, 4-Me, 3,5-di-Me, 3,4,5-tri-Me

2

BOX = bis(oxazoline)

Presented here is a summary of our work to date, namely the synthesis of a range of α-diazo-β-ketonitriles, as well as investigation of the use of rhodium, copper and ruthenium based catalysts in order to evaluate the efficiency and enantioselectivity of these transformations. The effect of both the nitrile functionality and the substituents of the aromatic ring on the efficiency of the transition metal catalysed intramolecular aromatic additions was also investigated.

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Grant code: GOIPG/2019/825

Stability and Biological Activity of Novel Silver-based Antifungals to Combat Antimicrobial Resistance

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While antibiotic-resistant bacterial infections are a widely recognised global health threat, much less media attention has been given to drug-resistant fungal infections. Globally, more than 300 million people suffer a serious fungal infection causing over 1,350,000 deaths.[1] *Candida* is a leading cause of healthcare-associated bloodstream infections in US hospitals.[2] Some types of *Candida* are becoming increasingly resistant to first- and second-line antifungals which is incredibly concerning. Clearly new therapeutic agents are required and work in our group focuses on designing antimicrobial metal complexes with different modes of action to existing therapeutics. Previous work in our group has reported a phenanthroline-oxazine ligand with atypical DNA binding abilities[3] and antimicrobial activity against *S. aureus* and *E. coli* which is greatly increased by improving lipophilicity by means of increasing the chain length **R** (**Figure 1**)[4]. These studies also showed enhanced antimicrobial activity against MRSA by complexation to copper(II). In this poster we report on the synthesis, solution characteristics and biological activity of a related family of silver complexes of the phenanthroline-oxazine ligands. I will present data on the solution stability of silver phenanthroline-oxazine complexes and their biological activity against *C. albicans* in nutrient rich and nutrient poor media. I will discuss the stability of the silver complexes in biological media as determined by UV-visible spectroscopy and the solution behaviour as determined by NMR spectroscopy.

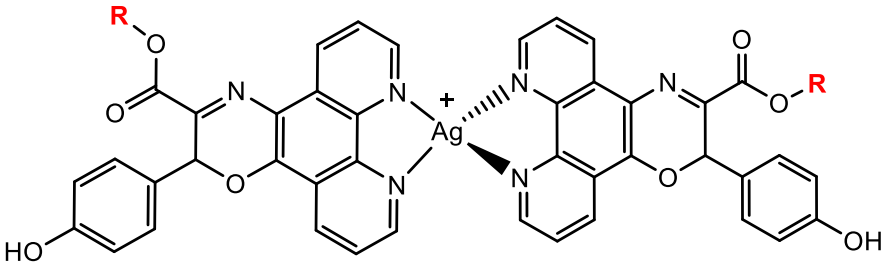

Figure 1: Silver complex of L-Tyrosine ester derived phenanthroline-oxazine, where R = methyl, propyl, hexyl.

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GOIPG/2020/1448

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The Design and Synthesis of Ruthenium (II) Polypyridyl Complexes as Luminescent Probes for Nitroreductase

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Poorly developed vasculature results in low intracellular O_2 regions within tumour tissues. Such areas of hypoxia are under intense reductive stress due to lack of O_2 and subsequent upregulation of reductive enzymes such as nitroreductases (NTRs).[1,2] NTRs are a particularly valuable marker for reductive stress being capable of reducing nitroaromatics to corresponding nitroso or amino derivatives, a feature that has previously been exploited in the design of hypoxia sensitive fluorescent imaging agents.[3] Several probes have been reported recently, however, there remains a lack of examples that display photophysical characteristics in the red or NIR regions. Ru(II) polypyridyl complexes display many of the desired characteristics including red emission, long luminescence lifetimes, large stoke shift and water solubility, but have not been exploited in this capacity to date. Thus, we have designed three novel Ru(II) poly(1,10-phenanthroline) complexes that act as substrates for NTR and give rise to a 'switch on' of the Ru(II) metal-to-ligand-charge-transfer (MLCT) based emission. One of the complexes, a 4-nitro-1,8-naphthalimide conjugate (Figure 1) displays a particularly sensitive and selective response to NTR and suggests that the Ru(II) polypyridyl scaffold is useful in the development of NTR probes. The presentation will outline our work on the design, synthesis and evaluation of the Ru(II) probes for NTR as well as some preliminary results on their use in biological models.

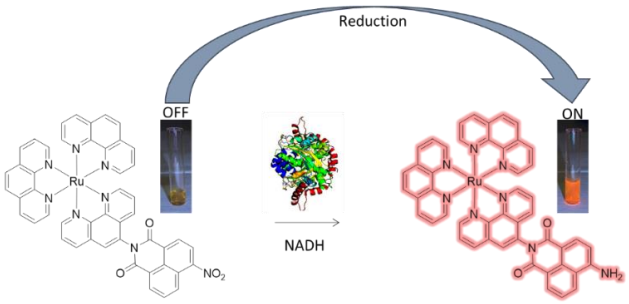

Figure 1: Schematic representation of Ru(II) polypridyl based luminescent probes for NTR.

References:

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The Development of PEG-based Antimicrobial Peptidomimetics

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Antimicrobial peptides (AMPs) are of interest in pharmaceutical applications due to their ability to kill microbes while also proving very difficult for microbes to develop resistance against. Due to the ever-increasing emergence of microbes that are resistant to common antibiotics, coupled with the lack of new antibiotics being developed, research in the use of AMPs as therapeutics has been investigated.[1] For a peptide to have an antimicrobial effect, it typically has to contain hydrophobic and cationic amino acid residues. This allows the peptide to coordinate to anionic lipopolysaccharide and insert into the microbial membrane and disrupt it by creating pores, resulting in cell death through leakage of cell contents. This targeting of the membrane is what makes antimicrobial peptides difficult to evolve resistance against.

However, problems with AMPs arise from their stability due to their degradation by proteases which decreases their bioavailability.[2] This research aims to develop AMP mimetics which possess a polyethylene glycol (PEG) backbone in place of the natural amide unit while also retaining hydrophobic and cationic side-chains similar to amino acids.

The amino acid side-chains that were selected for this research were tryptophan and arginine. First, two epoxides functionalized with their side-chains were synthesized (**Figure 1**) and they were then polymerized by anionic ring-opening polymerization to produce the corresponding PEGtide (**Figure 2**). The antimicrobial activities of this PEGtide against representative bacterial pathogens is now compared to those of its parent peptide.

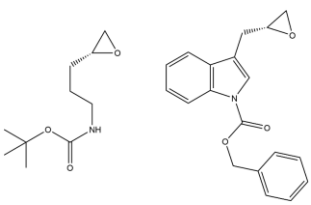

***Figure 1**: Structures of the epoxide monomers.*

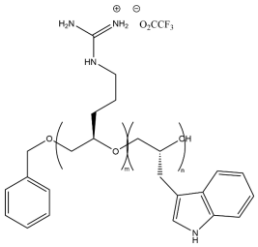

***Figure 2**: PEGtide of an AMP based on arginine and tryptophan.*

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Dá bhfuil romhainn
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19/FFP/6889

Phosphorus-based Reductive Etherification of Aldehydes

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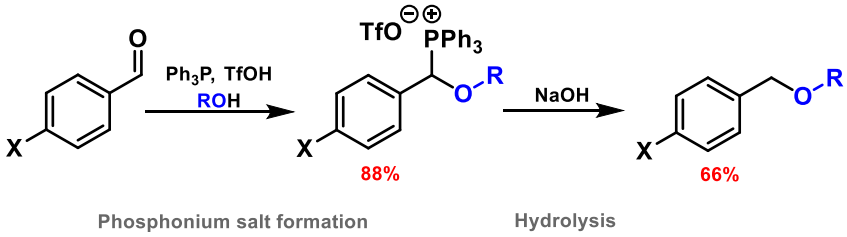
Ethers are common structural motifs found in a variety of bioactive compounds such as antivirals, antifungals and antimicrobial agents.[1] Tamiflu, an antiviral that contains an ether in its molecular structure, is used to treat Influenza A and B and had a market value of $1.1 billion in 2018.[2] Ethers are typically synthesised through the Williamson etherification, which involves the use of primary or secondary alkyl halides and an alkoxide to generate the desired ether. Other methods include alkoxymercuration which requires toxic mercury and thus is not desirable. Econazole, a common antifungal, is synthesised on industrial scale through the reaction of a tertiary alcohol and primary alkyl bromide to yield the active product. In all instances, toxic halide waste[3] must be carefully removed to avoid contamination.[4] The methodology proposed herein employs the use of an aldehyde as the stoichiometric alkyl source and negates the need for alcohol pre-treatment.



Scheme 1: Phosphorus-based reductive etherification of aldehydes

Aldehydes are generally non-toxic and more abundant than alkyl halides[5] and as such, are a significant improvement on alkyl halides at the stoichiometric alkyl source. It has been found that the key intermediate in the formation of benzyl ethers can be obtained in an 88% yield in a simple one step reaction. It is known in the literature that phosphonium salts can be hydrolysed by expulsion of a carbon leaving group.[6] Exploitation of this known reaction ultimately yields the intended benzyl ether in 66% yield. The methodology proposed herein, if generalisable, will provide an alternative means of access to this pharmaceutically relevant functional group in a halide-free manner which is also advantageous from a Green Chemistry point-of-view.

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Development of dual-action Pt(IV)-Tyrosine Kinase inhibitor pro-drug conjugates targeting colorectal cancer

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Side-effects due to the lack of selectivity toward cancer tissues is one of the major drawbacks to Platinum(II) anticancer agents (i.e. *cis*platin, oxaliplatin). Nevertheless, despite these severe side-effects, platinum-based compounds remain one of the first worldwide choice to treat a variety of tumours. Tyrosine Kinases (TK) are promising targets in oncology and play a major role in cell regulation pathways. For example, overexpression of Platelet Derived Growth Factor Receptor (PDGFR) is associated with angiogenesis and metastasis in colorectal cancer[1]. Colorectal cancer itself is the third most common cancer worldwide with the second highest mortality rate[2] and shows high resistance with respect to cisplatin treatment. Here-in we describe the successful synthesis of Pt(IV)-prodrugs tethering in axial position TK inhibitors (i.e. Imatinib/Nilotinib hybrid conjugates) with the aim to target colorectal cancers (Figure 1). While Imatinib and Nilotinib are successful BCR-ABL inhibitors, they also show potent PDGFR inhibition[3]. The synthetic challenges/successes encountered, different strategies used to successfully link Imatinib/Nilotinib in axial position of Pt(IV) and preliminary biological data will be discussed.

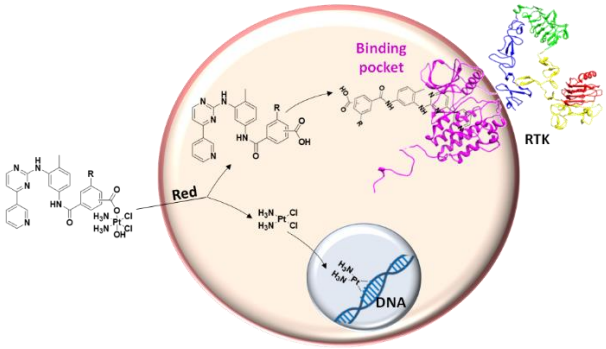

Figure 1. Mechanism of action of the Pt(IV)-Imatinib/Nilotinib Pro-drug.

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A NEW RATIONALE TO DESCRIBE AMBIDENT REACTIVITY

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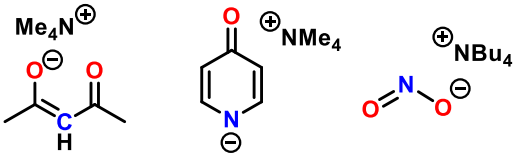
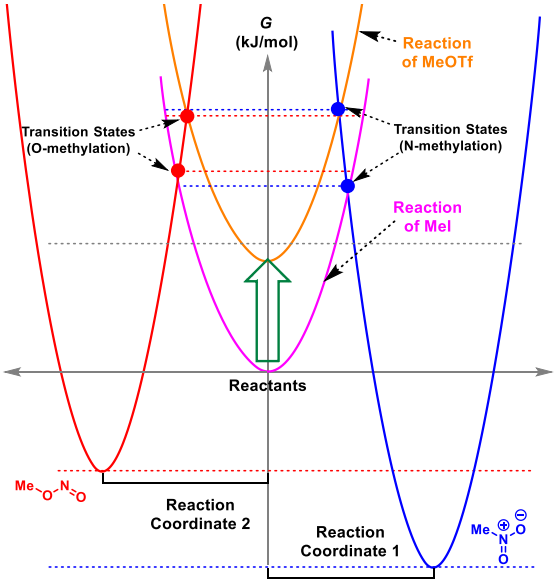
An ambident nucleophile is that which possesses two or more distinct nucleophilic sites that are linked through resonance and are effectively "in competition" for reaction with an electrophile. Examples include enolates, pyridone anions and nitrite anions (1). Reactions of ambident nucleophiles and electrophiles are extremely prevalent at all levels of organic synthesis.[1] The principle of hard and soft acids and bases (the "HSAB principle") is most commonly cited in the explanation of selectivities in such reactions. [2] Although this rationale is pervasive in any discussion on ambident reactivity, the HSAB principle predicts the wrong product in approximately 50% of all known reactions of ambident nucleophiles![3,4]

This project focuses on developing a new model for rationalizing ambident reactivity. Presented here is a new approach that incorporates computational calculations and experimental kinetic data to construct Gibbs energy profile diagrams. The preferred site of alkylation of nitrite anion with a range of 'hard' and 'soft' alkylating agents was established by ^{1}H NMR spectroscopy. Pseudo first order rate constants were measured directly by ^{1}H NMR reaction monitoring, and the corresponding second order constants and Gibbs energies of activation derived. These, in combination with DFT calculated standard Gibbs energies of reaction, were sufficient to construct Gibbs energy wells.

By representing the ambident system as a series of overlapping Gibbs energy wells (**2**) ('multiple parabolas') a more intuitive picture of ambident reactivity emerges. Here, previously unexplained switches in reactivity, in reactions involving closely related electrophiles, are elucidated.



(**1**)



(**2**)

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Application of a Supported Manganese Catalyst in C–H Activation and Reductive Transformations

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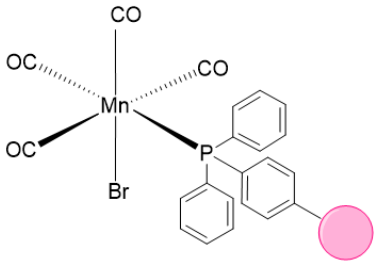
In recent years, the use of earth-abundant and environmentally benign non-noble metal catalysts has become increasingly popular.[1] Many important chemical and pharmaceutical processes require a metal-catalysed step along their route, and the over-reliance on expensive, toxic and unsustainable metals has driven a widespread search for suitable replacements.[2] Platinum Group Metals (PGM) have been classed as 'Critical Raw Materials' as a result of limited production capacities.[3] The construction of chemical compounds using Earth-Abundant metals instead of rare noble metals is a prevailing central topic in green chemistry.[4] However, a significant drawback associated with some of the chemistry catalysed by alternative metals, such as Mn, is the requirement of expensive and difficult to access ligands which are required for the transformations to be effective.[5]



- ✓ Facile preparation using cheap and commercially available ligand
- ✓ Bench stable
- ✓ Easy to remove from reaction
- ✓ Generally applicable

We have successfully managed to design and employ a bench-stable, polymer-bound manganese complex readily accessible from cheap and commercially available sources in a facile one-step process. To date, we have observed that this Mn-polymer complex enables a multitude of transformations which normally require pincer-type Mn complexes. Despite the simplicity of the catalyst, it displays promising results in protocols such as C – H activation and borrowing hydrogen methodologies as well as hydrofunctionalisation reactions, giving access to valuable products in moderate to good yields.

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Electroanalysis of dexamethasone using template free deposition of copper particles on glassy carbon electrodes with quantitation in pharmaceutical formulations

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Dexamethasone, a synthetic glucocorticosteroid and potent anti-inflammatory agent, has been shown to play a role in the treatment of patients hospitalised with severe COVID-19 infections. In this work, dexamethasone electroanalysis was examined with investigation of anodic and cathodic redox behavour at bare and modified glassy carbon electrodes in aqueous and non-aqueous supporting electrolytes. Quantitation in non-aqueous supporting electrolyte (0.1 M $LiClO_4$/methanol) resulted in an anodic peak at E_p = 1.3 V vs Ag | Ag^+ with sensitivity of $5.42x10^{-4}$ A mM^{-1} cm^{-2} over the range 0.83-3.0 mM, realising 101.77 +/- 2.54 % recovery (n=3) from a hydrocortisone cream formulation (0.25-0.5% dexamethasone). Electrosynthesis of copper particles using a triple and dual pulse potentiostatic method resulted in well dispersed copper nanoclusters and a microporous film respectively, the latter of which realised 4.6 fold enhancement in sensitivity to dexamethasone and 84.80 ± 3.5 % (n=3) recovery from solid dose pharmaceutical sample extraction. Surface analysis and electrochemical impedance spectrosopy served to characterise the copper surfaces. The optimal copper modified electrode allowed dexamethasone quantitation in alkaline conditions with sensitivity $3.20x10^{-4}$ A mM^{-1} cm^{-2} over the range 0.078-5 mM, with LOD of 58 μM and LOQ of 194 μM.

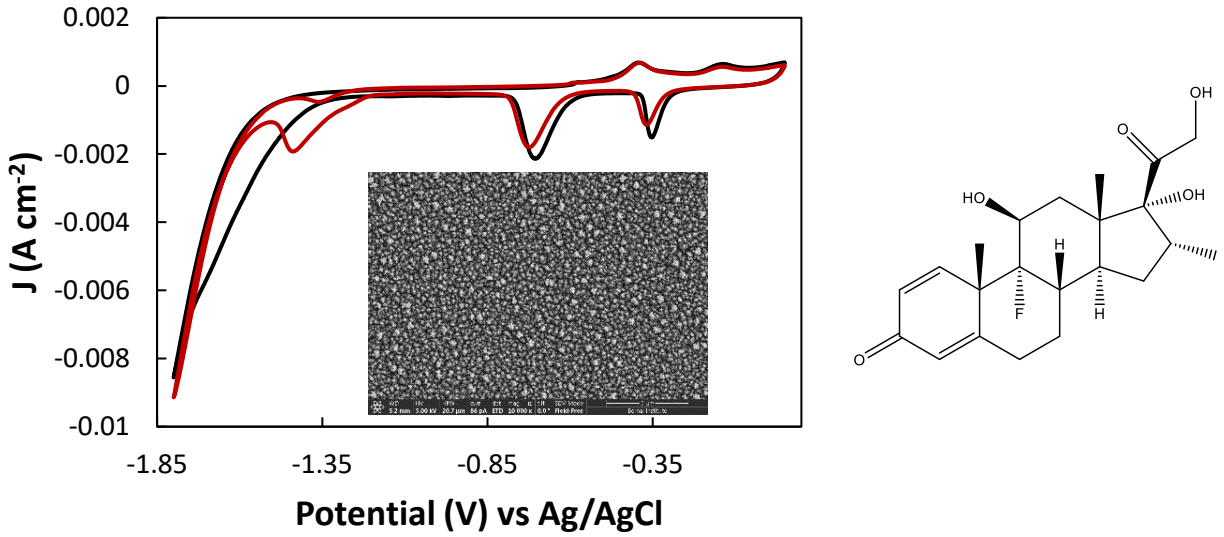

Figure 1. Voltammetry of 1 mM dexamethasone (red curve) in 0.1 M NaOH (black curve) at the copper microporous film modified GCE over the potential range -1.8 – 0.05 V at 100 mV s^{-1}. **Insert** SEM image of the copper microporous film electrodeposited at a glassy carbon electrode using a dual-pulse template-free electrodeposition approach.

Design, Synthesis and Biological Evaluation of Galactosidase Inhibitors

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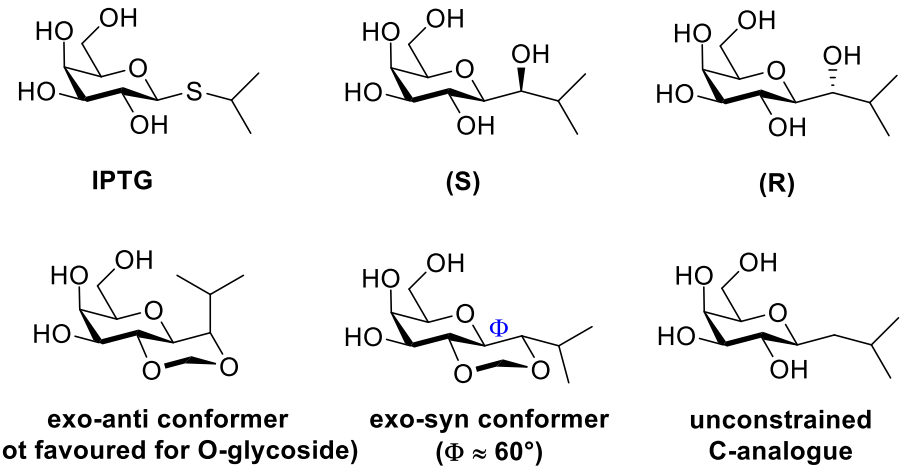
Isopropyl *β*-D-1-thiogalactopyranoside (IPTG) is a common molecular biology reagent used to induce protein expression in *E.coli* cell lines. It is itself a competitive inhibitor that operates by binding to the lac repressor, allowing the transcription of genes in the lac operon, such as the gene coding for *β*-galactosidase, which normally catalyzes the hydrolysis of *β*-galactosides into monosaccharides. The presence of the thioglycoside linkage in its structure means it cannot undergo hydrolysis in the cell. Therefore, the inducer cannot be degraded by the cell and its concentration remains constant during an experiment. Certain problems associated with IPTG include the need for storage under cold conditions as decomposition can happen over time. The compound can also degrade under culture conditions, meaning multiple additions of IPTG are often necessary for longer induction times. Therefore, a more stable version of IPTG would be desirable to circumvent these issues and provide greater control of protein expression, especially over long periods of induction. [1]



This project focuses on the total synthesis and biological evaluation of a series of C-glycoside analogues of IPTG comparing their performance as galactosidase inhibitors relative to the commercially available IPTG. The analogues were assessed in terms of their structure, comparing the flexible C-glycosides with the preorganized compounds. Presented here is a summary of our work to date, namely the development of a synthetic route and the results of the *β*-galactosidase inhibition assay.

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Click-Pt(IV)-carbohydrates pro-drugs for treatment of osteosarcoma

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The selectivity of cancer cells has always been a major drawback for chemotherapeutic agents and in particular for cisplatin, one of the most important anticancer drugs for the treatment of several kinds of tumours. One strategy to overcome this challenge is to modify the coordination sphere of the metallic centre with specific targeting vectors whose receptors are overexpressed on the tumour's cell membrane, such as monosaccharides. [1] Here we report the strategic synthesis of four novel glyco-modified Pt[IV] pro-drugs, based on a cisplatin scaffold (Figure 1), and their biological activity against osteosarcoma (OS), a malignant tumour which is common in adolescents and young adults. [2] The carbohydrate moiety (glucose and galactose) and the Pt scaffold are linked using the Copper-catalysed Azide Alkyne Cycloaddition (CuAAC) reaction, which has become the flagship of click chemistry due to its versatility and mild conditions.[3]
Cytotoxicity and drug uptake on three different OS cell lines, as well as on OS Cancer Stem Cells (CSCs) are discussed.[4]

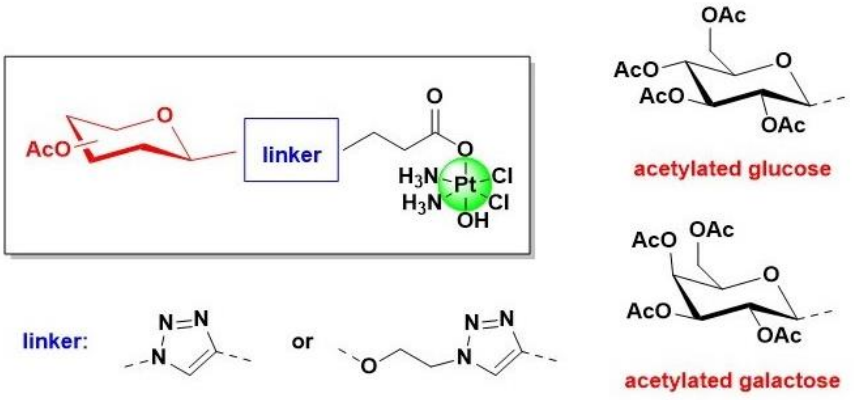

Figure 1. General structure of the novel Pt(IV) complexes based on cisplatin scaffold and functionalised with acetylated glucose and galactose.

Acknowledgements
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Development of Cu_2O/Ag_3PO_4 heterojunction photocatalysts for conversion of CO_2 into fuels.

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Since the industrial revolution fossil fuels have driven economic growth and now, approximately 85% of global energy generation comes from combustion of coal, oil, or natural gas. [1]. However, temperature increases due to rising CO_2 concentrations are projected to have many negative impacts and, therefore, scientists are looking for methods to tackle this. In nature, photosynthesis in plants occurs through a z-scheme mechanism that involves a two-step photoexcitation. First, electrons in photosystem (PS) II and PS I are excited to their respective LUMOs following visible light absorption. Next, the electrons in the LUMO of PS II are transferred to the HOMO of PS I through an electron mediator, neutralising the photogenerated holes therein. The remaining photogenerated electrons (used to reduce CO_2) and holes (used to oxidise H_2O) remain in the LUMO of PS I and the HOMO of PS II, respectively [2]. There is much potential to mimic this process artificially. Therefore, artificial photosynthesis (AP) using two distinct light absorbing species is an important area of research as a successful system would mean that waste CO_2 and free solar radiation can create fuels and valuable chemicals.

"Z-scheme" is the term used to explain the observed efficient electron/hole separation mechanism obtained using two co-located semiconductors [3]. These systems consist of a reduction semiconductor photocatalyst that is coupled with an oxidation semiconductor photocatalyst (SC II and SC I in figure 1, respectively). The relatively low energy electrons in the conduction band of SC I combine with the holes in the valence band of SC II. This leads to retention of strong redox abilities in the two semiconductors, spatial separation of charge carriers, and an extended light harvesting range (albeit with a decreased photon-to-exciton efficiency) [4].

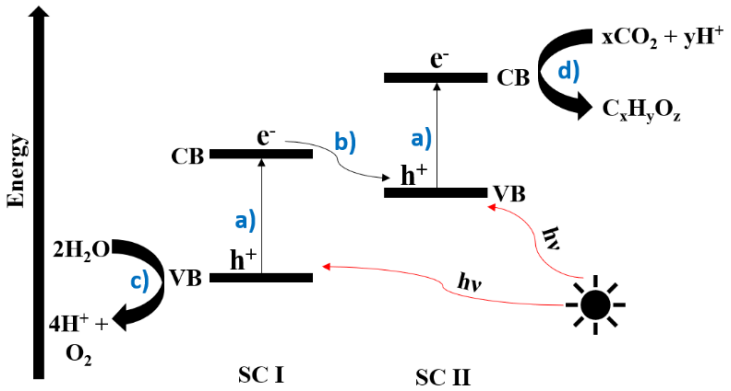

Fig. 1: schematic representation of the AP reaction mechanism using z-scheme photocatalysis where a) is photon absorption, b) is neutralisation and charge carrier separation, c) is H_2O oxidation, d) is CO_2 reduction.

Work to date has involved preparation and characterisation of families of Cu_2O/Ag_3PO_4 composite materials and characterising these using a wide range of techniques. UV-Visible spectroscopy and CO_2-TPD Experiments demonstrated that both the extent of visible light absorption and levels of CO_2 adsorption increase with the composite materials compared to pure components. These characteristics are potentially beneficial to the AP reaction and, hence, the composites should demonstrate enhanced reactivity compared to that of pure Ag_3PO_4 and Cu_2O.

Acknowledgements
This submission has been supported in part by funding from Science Foundation Ireland (SFI) under grant number 16/RC/3889 and is co-funded under the European Regional Development Fund and by BiOrbic industry partners.

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European Union European Regional Development Fund
Science Foundation Ireland For what's next
BiOrbic is an SFI Research Centre funded under the Science Foundation Ireland Research Centres Programme and co-funded under the European Regional Development Fund.
biorbic
Grant Code: 16/RC/3889

Towards the Design and Synthesis of a new biomimetic code: Squaratides

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Nature uses a large variety of molecular architectures to carry out a stunning array of complex tasks, from cell signaling to the catalysis of biochemical transformations [1]. However, the ability of chemists to reproduce these functions using synthetic systems remains an elusive challenge. The modular construction and structural diversity that nature displays in the biosynthesis of proteins provides ample inspiration for the design of new materials with controlled conformations and defined structures [2]. It is the 3-D arrangement of the protein that dictates its biological activity and control over structure is particularly important given the rise of peptide and protein based biologic drugs in recent years.

Taking inspiration from nature and through judicious molecular design we propose to design and synthesise a completely new peptidomimetic code based on squaratides – a hybrid mix of squaramides and peptides (Figure 1). We have set out to create a library of modified amino acid building blocks from which we will construct a new class of biopolymer; one that can be synthesised in an automated stepwise manner to create an unknowable diversity of peptidomimetic structures.

This poster will demonstrate our initial results where we have taken advantage of both solution phase and solid phase syntheses to assemble a series of squaratides of varying lengths. We will also outline our approach toward cyclic squaratides where we have already demonstrated the successful synthesis of several macrocyclic derivatives of varying ring size.

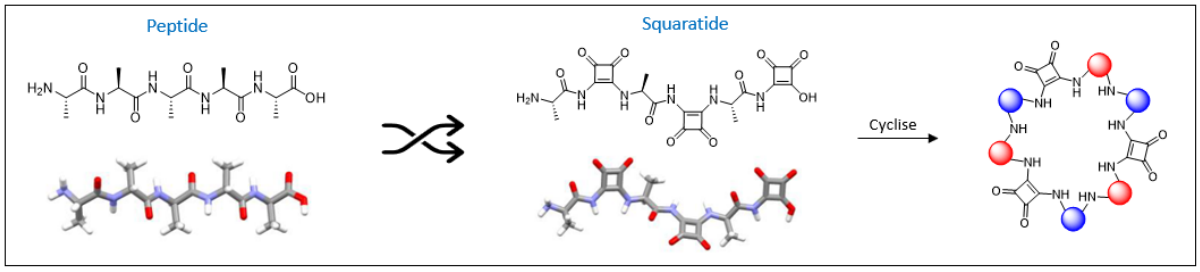

Figure 1: Schematic structural comparison of peptides vs. squaratides

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Novel Co_5 and Ni_4 Metal clusters by the combination of 2-Pyridyl Oximes with Polycarboxylic Ligands

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2-pyridyl oximes is a family of organic linkers with the general formula (py)C(R)NOH. The oximic group has the capability to link a large number of metal ions, leading to high nuclearity species. It also favours ferromagnetic exchange interactions between the metal centers, hence 2-pyridyl oximes have played a crucial role in the field of single chain magnetism and single molecule magnetism.

Although 2-pyridyl oximes have been investigated in combination with carboxylic or other types of ligands,[1-3] their use with isonicotinic acid (HINA) and 3,5-pyrazole dicarboxylic acid remains unexplored. This ligand combination is expected to be a source of compounds with interesting structural and physical properties. Herein, we describe the synthesis and characterisation of novel Ni_4 and Co_5 metal clusters (Fig.1) resulted by the thorough investigation of this ligand blend. Their crystal structures and physical properties are discussed in detail.

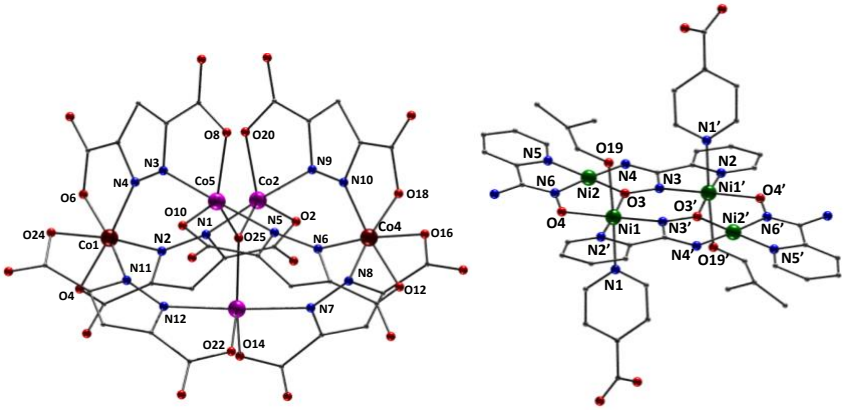

Figure 1. The crystal structures of two of the compounds discussed in this work

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Colloidal Synthesis of Copper Bismuth Selenide Nanocrystals as Ionic Semiconductors for Photovoltaic Absorbers

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In 2021 renewable energy accounted for 37% of electricity production in the European Union.(1) With this number increasing yearly, focus has been put on reducing the cost of solar cell production while using sustainable materials. Copper bismuth selenide (CBSe) has been mentioned as a potential compound for photovoltaics due to its earth abundance, non-toxicity, and cost efficiency.(2,3)

Electrodeposition and the solvothermal route have been reported to produce CBSe.(3,4) Unfortunately, these routes present limitations in terms of control of crystal size, shape, and phase. The colloidal hot injection method induces a single burst nucleation upon injection providing more control over the resulting nanocrystals. This method also allows for a cost-effective production of nanoparticles which can be optimized and used on a large-scale for low-cost photovoltaic device manufacturing.

The hot injection colloidal synthesis method was used in this investigation. The synthesis produces two phases of CBSe, the cubic phase of Cu_3BiSe_3 and the orthorhombic phase of $Cu_4Bi_4Se_9$. We are investigating the formation mechanism this reaction follows and aim to alter the synthesis to form a pure phase of Cu_3BiSe_3 nanocrystals. Controlling the phase of CBSe has proved challenging due to the limited Selenium precursor availability.

Once a pure phase is obtained, we aim to examine the CBSe nanocrystals properties for photovoltaic applications as Cu_3BiSe_3 is a strong contender due to its estimated band gap of $E_g \approx 1.3–1.5$ eV which is within the optimum range for photovoltaics.(5)

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A new 3-substituted BODIPY dye: Synthesis, crystal structure, and photophysical properties

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4,4-Difluoro-4-bora-3a,4a-diaza-s-indacene (BODIPY) derivatives are an important class of fluorophores. They have many excellent properties including high thermal and photochemical stability, good solubility, sharp absorption and emission bands in the visible region, high fluorescence quantum yields and negligible triplet-state formation.[1] As a result, they have found applications in a wide variety of research fields such as fluorescent sensors, biological labels and probes, tuneable laser dyes and sensitizers for solar cells. Another attractive feature of BODIPY derivatives is their tuneable spectroscopic and photophysical properties.[2] The incorporation of new substituents at the 3- and 5-positions of BODIPY core has a large impact on the spectroscopic and photophysical properties [3]. This approach has attracted great interest, especially in the design of new BODIPY-based fluorescent labels and sensors for biological applications.[4] This presentation will outline the design, synthesis, characterisation and photophysical evaluation of a novel pyrrole substituted BODIPY derivative (Figure 1) where the effect of the pyrrole attachment to 3-position of the BODIPY core was verified by computational HOMO-LUMO calculations. We envisage that this investigation will be helpful in the design of new BODIPY-based fluorescent labels and sensors for biological applications.

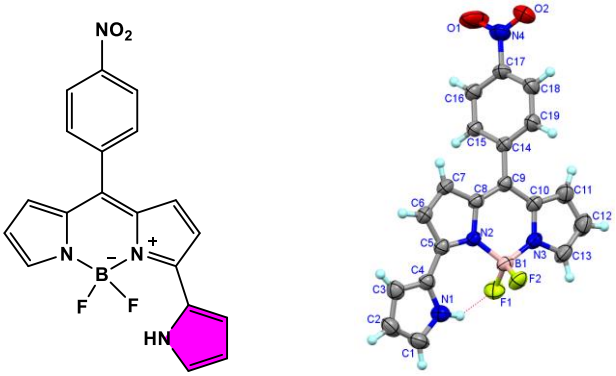

Figure 1: The chemical structure and X-ray crystal structure of a novel pyrrole substituted BODIPY derivative

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Supramolecular functionalisation of B/N co-doped carbon nano-onions for theragnostic applications

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Many modern chemotherapy drugs are known to have off-target activity, negatively affecting normal, healthy cells whilst trying to destroy cancer cells. This often results in terrible side effects for patients, such as nausea and hair loss. One method of circumnavigating this problem is by developing a theragnostic nanocarrier system that targets tumours. Boron/nitrogen co-doped carbon nano-onions (BN-CNOs) are a novel nanomaterial that could be used as a scaffold for these systems. Their biocompatibility, combined with their nanoscale size [1] gives them promising potential for use in drug delivery and biological imaging applications.

Our group has developed a low cost, one-step thermal annealing method to produce BN-CNOs [2]. In the pristine form, BN-CNOs suffer from poor aqueous solubility, like many other carbon nanomaterials [3].

In this work, our group has non-covalently functionalised BN-CNOs with a hyaluronic acid-1,2-dimyristoyl-sn-glycero-3-phosphoethanolamine (HA-DMPE) conjugate polymer to impart aqueous dispersibility and targetability for cancer cells overexpressing the CD44 receptor. By utilising the hydrophobic interactions between the BN-CNO surface and the phospholipid chains of the HA-DMPE, we have successfully coated the nano-onions with the conjugate polymer, increasing the water dispersivity of the BN-CNOS. This was confirmed by FTIR, UV-Vis absorption, and dynamic light scattering analyses. This work represents the first step in developing a novel BN-CNO based theragnostic platform to increase the efficacy and reduce the side effects of existing anticancer drugs.

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Applying Continuous Flow Techniques in the Synthesis of Sugar-based Therapeutics

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Glycomimetics are a class of therapeutics derived from sugars. These molecules function by inhibiting several classes of carbohydrate-binding proteins, such as glycoprocessing enzymes and lectins. Iminosugars are a subset of glycomimetic, in which the ring oxygen of a sugar is replaced by nitrogen. These mono-/bicyclic structures are potent inhibitors of many glycosidases and are currently marketed for treatment of Type 2 diabetes and for certain lysosomal storage diseases.[1] In addition to their current therapeutic uses, they have demonstrated potential as antiviral drugs.[2]

The anomerisation reaction in carbohydrate chemistry is the conversion of one anomer of a sugar (α or β) to its alternate configuration.[3] Anomers of the same sugar can show significant differences in biological activity, and as sugar-based drugs have a specific anomeric configuration, the optimisation of this reaction can be of significant benefit in the synthesis of glycomimetics.

Flow chemistry has received much attention in recent years in both research and industrial laboratories for its potential advantages over batch processes, such as greater mixing, higher heat transfer, easier scale-up and improved safety.[4]

My research is focused on improving the synthesis of valuable iminosugars scaffolds, such as 1-DNJ, as well as investigating the factors influencing anomerisation reactions, using continuous flow techniques. Currently, the anomerisation of thiogalactosides using a mixture of batch and flow techniques is being investigated.

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Exfoliation and Surface Functionalisation of Graphene in Water

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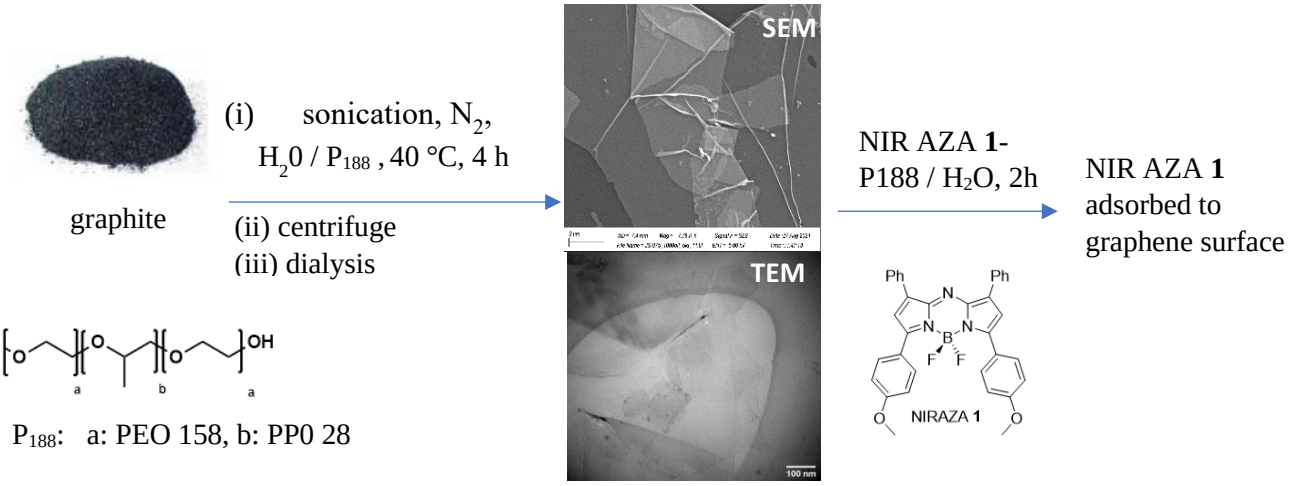
Graphene is a 2-D form of carbon existing as a single layer of atoms arranged in a honeycomb lattice. The exfoliation of graphite in water to produce graphene is particularly promising as it opens the door to a range of bio-applications such as drug delivery, imaging of biomolecules, printing electronics and coatings.[1,2.]

The production of graphene from graphite in water was achieved using the non-toxic clinically approved tri-block co-polymer P_{188}. Investigations into this liquid phase exfoliation determined that sonication of graphite in an aqueous solution of P_{188} for 4 h at 40°C was the optimal condition. Microscopic characterisation through TEM and SEM confirmed the presence of mono to few layer graphene sheets ranging in size from 100-500 nm. Graphene dispersions were shown to be stable beyond three weeks exhibiting complete re-dispersibility in aqueous media following freeze-drying.

Functionalisation of the aqueous graphene was demonstrated through adsorption studies utilising the fluorophore NIR-AZA **1** as a model hydrophobic compound. Additionally, the graphene suspensions were successfully applied as a 'graphene ink' to coat polypropylene fibres in FFP2 face masks. Developments of aqueous graphene hydrogels are undergoing optimisation. Additionally, uses of the graphene inks for 3D printing and spray coating of surfaces are under development.



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Surface Modification of Titanium Alloys for Biomedical Applications

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Individuals who are impacted by underlying bone diseases have a need for orthopaedic implant materials, which have gathered considerable demand over the years. One of the main obstacles to address is the frequency of revision surgeries due to implant failure. A promising approach is in the development of an implant with nano-rough surface topography that is comparable to bone.[1] This would enhance mechanical interlocking between the bone and implant, while stimulating bone cell growth and osseointegration. This can be achieved electrochemically by anodisation of titanium alloys, resulting in the formation of nanotubes under certain conditions. Metallic oxide coatings consisting of nanotubes are advantageous for implant materials due to their comparable tensile strength with bone,[1] corrosion resistance,[2] and biocompatibility.[3] TiO_2 nanotubes can be modified to include bone-growth promoters such as Mg^{2+} and Ca^{2+} ions. These ions stimulate growth of hydroxyapatite (HA), which aids in osseointegration.[4] As TiO_2 nanotubes possess self-sealing abilities (**Figure 1**), the inclusion and the controlled release of these ions provides an attractive approach for the functionalisation of the TiO_2 nanotubular layer for biomedical applications.

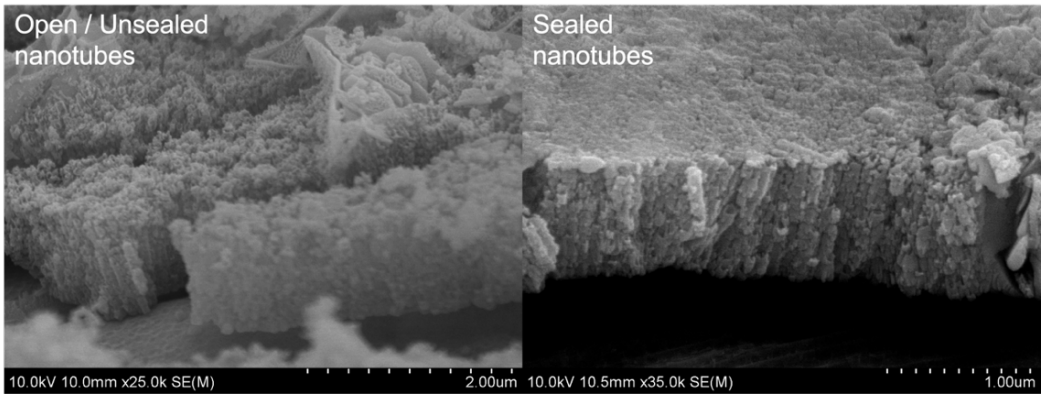

Figure 1: TiO_2 nanotubes formed from anodisation of Ti6Al4V.

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Stereoselective Synthesis of α-Galactosides

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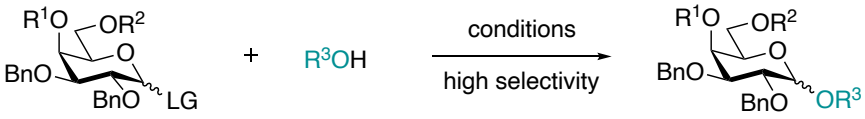
Nature employs carbohydrates as an integral source of structural biodiversity across all organisms. It is understood that the biological properties of these natural products can be fine-tuned *via* alteration of glycosidic patterns, particularly with respect to stereochemistry. Consequently, stereochemical control in glycosylation reactions is a significant objective within the field of carbohydrate chemistry.[1]

This work is concerned with stereoselective control in α-galactosylation reactions. α-Galactoside units are found in many biologically important compounds, for example in the 'capping' motif of the mammalian glycome.[2] However, existing methods for the α-selective synthesis of galactosides that are broadly applicable to a range of galactosyl substrates are limited.[3,4] Thus, further understanding around the stereochemistry of α-galactosylations is required.

As part of our ongoing research into glycosylation methodologies,[5,6] we investigated the effect of different protecting groups at positions 4 and 6 of galactosyl donors on the stereochemical outcome of glycosylation reactions. A range of galactosyl donors were accessed *via* regioselective ring-opening of 4,6-*O*-benzylidene-protected galactosides and, for example, subsequent esterification using Mukaiyama's salt. It was found that some galactosyl donors gave excellent α-selectivity (**Scheme 1**).[7] In this poster, we will report on our findings of the scope of these galactosylations.



Scheme 1. Galactosylation reactions using donors bearing a range of protecting groups at the 4- and 6-positions.

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Two-Dimensional Porphyrin-Based Covalent Organic Frameworks as Photosensitizers for Light-Driven CO_2 Reduction

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With the dramatic rise in CO_2 levels in the atmosphere, it has never been more crucial to decarbonise the energy and chemical sectors to reach the climate change targets[1]. Thus, researchers are exploring the use of CO_2 as a carbon source in light-driven reactions to produce fuels and other value-added chemicals[2]. Organic dyes have been widely used as photosensitizers to facilitate the electron transfer for the CO_2 reduction process, and, when functionalized, can enhance the light-harvesting properties of the materials[3]. Nevertheless, efficiency, stability and scale-up challenges still need to be solved in order to have an economically feasible process[4].

Photosensitizers can be used as building blocks to form photoactive 2-D covalent organic frameworks (COFs). Research into COFs has grown in the last years due to their high stability, tunability, potential for post-synthetic modification and excellent electron transport efficiency [5]. This work proposes the construction of porphyrin-based COFs as potential materials for CO_2 reduction by combining two different photosensitizers in a 2-D arrangement. These novel materials aim to surpass current state-of-the-art photosensitizer technology and move towards the development of a highly promising CO_2 reduction technology.

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ICI Chemistry Colloquium at UCD 2022

The Development and Characterisation of a Biosensor for the Real-Time Neurochemical Monitoring of Lactate

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Lactate in recent years has gained recognition as more than a waste metabolite of anaerobic respiration. Lactate is involved in shuffling between producer and driver cells, gluconeogenesis and plays a role as a signalling molecule and an energy source (1). It has also been shown to be a biomarker for sleep (2) and to play a role in synaptic plasticity (e.g., memory formation) (3). It's role in metabolism is complex and controversial as highlighted by the astrocyte-neuron lactate shuttle theory (ANLS) first proposed by Magistretti *et al.* (4) in the late 90s.

This project is focusing on the characterisation and validation of an electrochemical biosensor suitable for the real-time neurochemical monitoring of lactate *in-vivo*. The biosensor utilises a 2 mm Pt(90%)/Ir(10%) cylinder active surface (60-μm radius) which is modified with various components to produce a sensitive and selective biosensor. The first step in the manufacturing process is the electropolymerisation of *o*-phenylenediamine (*o*-PD) onto the electrode surface which acts as a self-sealing interference rejection layer. The electrodes are then dipped into solutions of Styrene, Lactate oxidase (LOx), polyethylenimine (PEI), a mixture of bovine serum albumin (BSA) and glutaraldehyde (GA), and finally cellulose acetate (CA).
Lactate calibrations were performed in a standard three electrode electrochemical cell containing 15 mL phosphate buffer saline (pH 7.4), the reference (Saturated Calomel Electrode (SCE)) and auxiliary (Pt wire) electrodes and four lactate biosensors. Lactate calibrations (0-5 mM) were performed using constant potential amperometry at +700 mV *vs*. SCE.

The development and *in vivo* validation of this sensor will aid our understanding of neurological energetics which may give us insight into psychiatric illnesses that are associated with non-typical neurological metabolism such as schizophrenia and mood disorders (5). In schizophrenia, lactate levels are increased due to atypical energy metabolism (6). A greater understanding of these processes will allow for more accurate and efficient treatment of such disorders, a potential which has already been highlighted in the literature (7)

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Quantum Chemical Study of Low-Valent Aluminium Compounds

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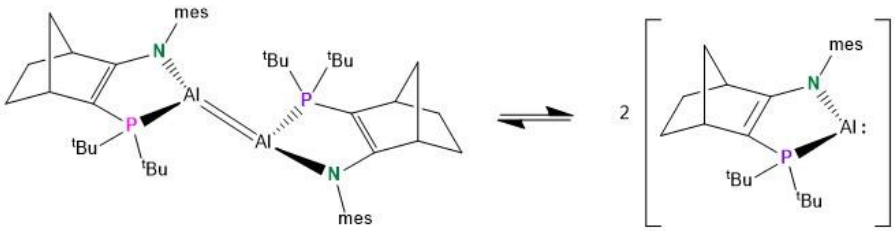
Most catalysts employed in industrial and small-scale synthesis are based on precious transition metals such as rhodium, palladium, or platinum. Developing non-precious metal alternatives to current transition-metal based industrial chemical processes is an enduring challenge, stimulated by the impetus to transition to sustainable feedstocks and minimise our dependence on scarce and expensive resources. Considering this, aliminium is a promising candidate, given its relative abundance and non-toxicity. Specifically, aluminium(I) compounds have shown a great deal of promise in recent years, in the areas of catalysis and small molecule activation, despite the synthetic challenges in accessing them. Sitting alongside prototypical Al(I) compounds such as Schnöckel's $(Cp^*Al)_4$ and Roesky's Al(I) β-diketoiminate (NacNacAl) compounds[1,2], there exists a class of compounds named dialumenes. Dialumenes can be split into two categories, transient and base-coordinated. For this poster, I will be focusing on base-coordinated dialumenes. Prior to 2021, there had only been two reported base-coordinated dialumenes, both from the Inoue group. The first, in 2017, is a silyl substituted dialumene, coordinated by an N heterocyclic carbene (NHC), and the second in 2020, with a Tip aryl substituent.[3,4] In collaboration with the Cowley group (University of Edinburgh) we reported the synthesis and electronic structure analysis of a third exemplar of a base-coordinated dialumene, supported by an amidophosphine ligand framework[5]. As well as being the third example of a base-coordinated dialumene, it is the first example of one that reversibly dissociates in solution to its monomeric form. I will outline the electronic structure analysis of this dialumene that was undertaken. Using Natural Bond Orbital analysis, the Electron Localization Function (ELF) and Quantum Theory of Atoms in Molecules analysis (QTAIM), key insight was gained into the non-classical double bonded character of this highly interesting main group multiple bonded species. Further reactivity is currently being explored.



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Design and Synthesis of Sialyl Triazoles as Siglec-8 Ligands

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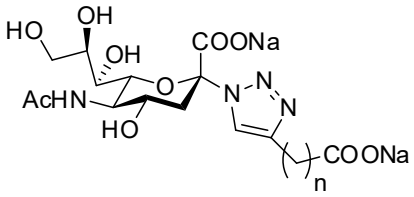
Siglecs are sialic acid-binding immunoglobulin [Ig]-like lectins, a family of single-pass transmembrane cell surface proteins in humans [1]. Siglec-8 is a human immune-inhibitory receptor is expressed by human eosinophils, basophils and mast cells [2]. Siglec-8 upon binding with antibodies or glycan ligands results in apoptosis in human eosinophils and inhibits the release of mediators from human mast cells without affecting their stability. Thus, potential glycan ligands may be ideally used as inhibitors for treatment of eosinophil and mast cell-related diseases, such as asthma, chronic rhinosinusitis, chronic urticaria, hypereosinophilic syndromes, mast cell and eosinophil malignancies and eosinophilic gastrointestinal disorders by targeting Siglec-8.[3].

In a previous study, mimetics of 6'-sulfo-sLe^x, a specific ligand for siglec-8, were identified. Keeping the neuraminic acid (sialic acid) and replacement of galactose with a cyclohexyl derivative led to a more high affinity ligand [4]. Here, we will present the design and synthesis of ligands with a triazole ring having carboxylate group with different aliphatic chains as a replacement for the sulphated galactose residue. The triazole moiety has predicted additional interaction with siglec-8 based on glide-docking.



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Development of norbornene-based compounds with proposed synergistic anti-biofilm and anti-adhesion activities

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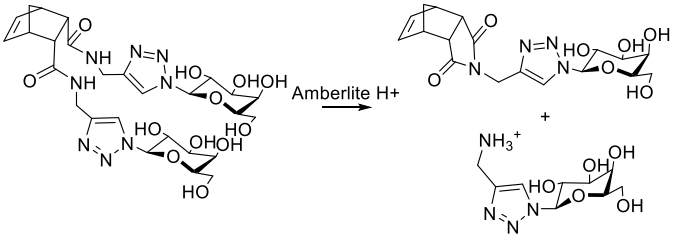
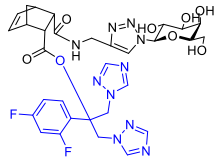
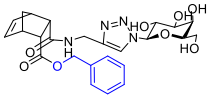
pH-responsive compounds exhibiting synergistic anti-biofilm and anti-adhesive effects against fungal pathogens have great potential as a new class of antifungal agents due to the acidic microenvironments in which fungal pathogens such as *C. albicans* are commonly found in.[1] Through previous work in the lab of Dr Velasco-Torrijos at MU, the elimination reaction shown below was observed:



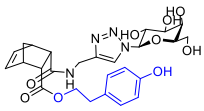
This led to the design of glycoconjugates built on *cis*-norbornene scaffolds with the potential to release bioactive compounds. Building on this work, a series of asymmetric compounds containing both carbohydrates and non-carbohydrate moieties have been prepared to study the structural requirements for these elimination reactions to occur in acidic pH using HPLC and NMR. Secondly, the synthesis and characterization of a number of hybrid *cis*-norbornene compounds **1**-**4** (shown below) which combine anti-adhesive carbohydrates with known antifungal agents was proposed. Fluconazole is a fungistatic agent and is widely used clinically [2]Tyrosol and Farnesol have both been shown to produce anti-biofilm activities against different Candida species. [3] While Benzyl alcohol was used as a model nucleophile for assessing the feasibility of the proposed synthesis. It is envisaged that the local release of the active compound combined with the inhibition of adhesion should lead to an enhanced antifungal activity.



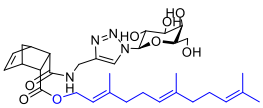
1
Fluconazole hybrid



2
Benzyl alcohol hybrid



3
Tyrosol hybrid



4
Farnesol hybrid

References:

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BU 1300244

Developing a roadmap to effective Spray Drying of Biomolecules

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To date most of the biological therapeutics are delivered in either one of the two ways, via intravenous infusions or subcutaneous injections. However, these are no longer the preferred method of administration as they are inconvenient and uncomfortable for some patients while limiting compliance of drug uptake. With the current increase in demand for biologics on the market, there is a significant interest for finding innovative formulation and delivery approaches. However, formulating biologics brings many challenges as they are more complex and larger in size than the smaller molecule drugs. One of the major challenges of formulating the biological therapeutics is their increased risk of instability upon exposure to elevated temperatures or mechanical forces. One of the most common methods of increasing the stability of biologics is dehydrating the liquid formulations leading to improved long-term stability at increased temperatures and humidity due to lower molecular mobility and less intermolecular interactions. Freeze drying has been the most frequently used technique for solidification of biologics to date however, high energy consumption, large capital investment for infrastructure and long drying times have made it difficult to cope with the increased market demands.

Therefore, this project looks at the one-step continuous process, spray drying. A dry powder is produced from either a liquid or slurry through rapid drying using an inert gas at elevated temperatures. The spray drying process can potentially lead to particles most suitable for pulmonary delivery application (1-5 µm) [1]. The development of a spray drying process of biomolecules has been proven, to be challenging due to their sensitive nature. This project focuses on spray drying biomolecules, specifically the model enzyme, lysozyme [2] to investigate the effect of different atomisation gas flow rates on the enzymatic activity and physiochemical properties. All samples were spray dried at 50˚C outlet temperature, 1.5 ml/min feed rate and 473 L/hr, 601 L/hr and 742 L/hr atomisation gas flow rates. The applied shear stress during the atomisation process is a significant factor in determining the final stability of biomolecules that has been overlooked in previous research activities carried out on lysozyme. It has been shown that lysozyme in the solid form is increasingly deactivated as the atomisation gas flow rate increases with the lowest residual bioactivity of lysozyme sprayed at the highest atomisation gas flow rate (742 L/hr). On the other hand, samples atomised at the lowest atomisation gas flow rate (473 L/hr) showed the highest residual bioactivity (88%). These experiments show the direct implication of atomisation gas flow rate *i.e.* shear force on the denaturation of lysozyme. These results have implications in changing the current biologics delivery methods *i.e.*, intravenous, and subcutaneous injections with inhalable drug delivery methods. This could promote better patient compliance along with faster delivery outcomes.

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A Photocatalytic and electrocatalytic investigation into Rhenium Tricarbonyl N-Heterocyclic Carbene complexes for CO_2 reduction

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Converting CO_2 into usable products has the potential to reduce the level of CO_2 in the atmosphere. Carbon dioxide concentrations are rising mostly because of fossil fuels and our current concentration of CO_2 in the atmosphere has reached unprecedented levels, at 416 ppm. The importance of reducing CO_2 emissions is recognised as a matter of urgency. Ireland's efforts at cutting greenhouse gas emissions are way off target, with an annual increase in emissions of 6% predicted. In this presentation, we will demonstrate how novel rhenium tricarbonyl N-heterocyclic carbene (NHC) compounds (see Figure 1) can be used for both photo- and electrocatalytic CO_2 reduction. To understand the mechanism involved, we have studied the photophysical properties of these compounds using time-resolved techniques, and assessed their ability to generate carbon monoxide photocatalytically. In addition, we have also probed the ability of these compounds to generate CO electrocatalytically.

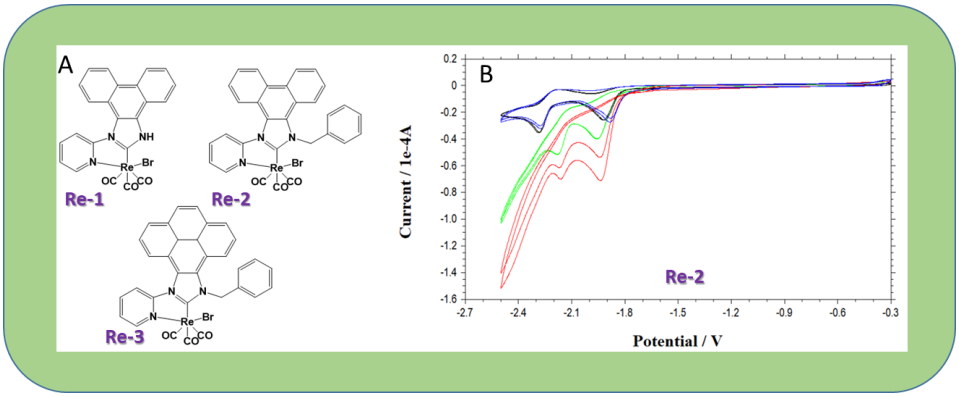

Figure: a) Structures for the complexes studied Re-1, Re-2, and Re-3. B) Electrocatalysis performed in a 0.1M solution of $TBAPF_6$ in acetonitrile solution following 1) purging of the solution with N_2 (Black), the subsequent addition of water (Blue), purged with CO_2 (Green) and subsequent addition of H_2O (red).

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Biphenyl Bridging Ligands as Building Blocks for Photoluminescent One-Dimensional Gold Coordination Polymers

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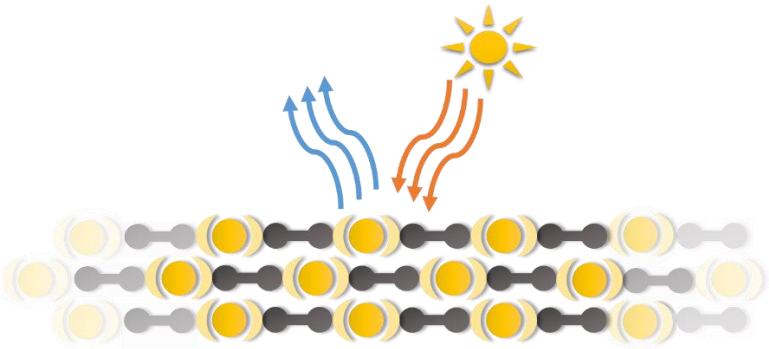

Gold complexes possess unique photo-responsive properties with possible applications in sensing and security materials[1]. Gold luminescent coordination polymers (LCPs) offer a useful platform to expand on these characteristics since they form practical solid-state materials with features that can be tuned *via* rational ligand design[2,3]. For example, increased inter-metallic distance and highly conjugated ligands can suppress charge recombination following the photogeneration of electron-hole pairs. Meanwhile, restricted rotation around bridging ligands can promote the formation of rigid structures with beneficial morphological features such as channels and layered architectures.

To this end, we report the synthesis of one-dimensional gold coordination polymers using symmetric biphenyl dithiol bridging ligands. The highly conjugated nature of the ligands increases conductivity, while thiol functional groups ensure stable binding to the gold sites. A rigid acetylene spacer was also incorporated to increase inter-metallic distance, restrict ligand rotation, and enhance photoluminescent properties[4]. In this work, the synthesis and characterization of three biphenyl bridging ligands will be presented, along with preliminary studies of gold LCPs.

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Next-Generation Gallium Complexes to Combat Antimicrobial Resistance

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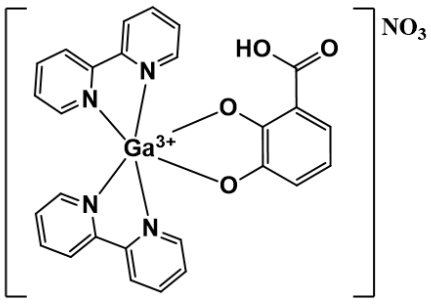
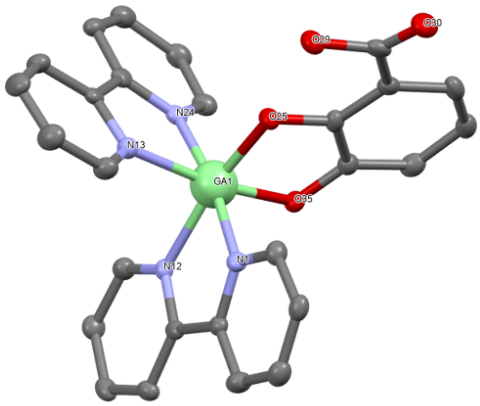
There is an urgent need to develop novel antibiotics as antimicrobial resistance (AMR) is reported to be one of the leading causes of death worldwide. Multi-drug resistant pathogenic infections were associated with approximately 4.96 million deaths annually in 2019, with 4.95 million of these being directly associated to bacterial AMR[1]. The antimicrobial properties of metals have been well known for centuries, with many metal-based compounds playing important clinical roles as therapeutics and diagnostic agents. [2]Bacteria have a high demand for Iron (Fe) as it plays a vital role in DNA synthesis and oxygen metabolism. To satisfy this high requirement pathogenic bacteria produce Fe-scavenging molecules known as siderophores, which sequester Fe from their extracellular environment and the hosts innate Fe transporting proteins. [3] Consequently, Siderophore Fe uptake systems can therefore be targeted. Cefiderocol for example is a new class of antibiotics known as siderophore drug conjugate's (SDC's) that hijack the bacteria's own iron (Fe) acquisition system to internalize a cephalosporin antibiotic. [4] This new strategy is of particular interest due the drugs activity against all three critical gram-negative bacteria.[5] We are particularly interested in the development of novel-Gallium (Ga) based complexes as antimicrobial agents. The antimicrobial properties of Ga can be attributed to its interference with the bacteria's metabolism of Fe. Ga^{3+} shares many chemical and physical properties to that of Fe^{3+} and is well know to exhibit antimicrobial properties.-[7]



$[Ga(bipy)_2(2,3Dhba)][NO_3]$



X-ray crystal structure of $[Ga(bipy)_2(2,3Dhba)]$

A Novel series of Ga(bipy) catecholate complexes has been successfully designed, synthesised and fully characterised by EA, NMR, IR and Mass spectroscopy including X-ray crystallography. Preliminary toxicity studies have demonstrated

Outcome of docking of some simple sialic acid derivatives to influenza hemagglutinin and synthesis of glycoclusters based on tetraphenylethylene scaffold

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Influenza is a disease responsible for over half a million deaths each year. It was responsible for both the 1912 Spanish Flu pandemic where an estimated 50 million died and also the 2009 pandemic resulting in close to half a million deaths. The virus consists of two main envelope proteins Hemagglutinin (HA) and neuraminidase (NA).[1],[2],[3] Current approved treatments rely on vaccines which have to be updated seasonally and small molecules targeting NA which influenza has been developing resistance to in recent years. HA is a trimeric protein responsible for binding to host cells via complex glycoproteins terminating with a sialic acid residue and thus can be seen as a valid target in treating the disease.[4]

Influenza viruses are capable of infecting both birds and mammals, in human infective viruses HA is specific towards biantennary glycans terminating with a Siaα2- 6Gal sequence. However the binding of monomeric sialosides to HA have been shown to be quite weak (mM range).[3] With this information in hand we set out to develop more potent inhibitors or HA with the help of screening various modified sialic acids *in silico.* Our study initially consisted of an initial library of 500 sialic acid compounds containing various functional group modifications. These compounds were then docked with the target protein using Schrödinger's Glide and ranked according to their GlideScore, which is an empirical scoring function that approximates the ligand binding free energy. To validate the docking protocol used we also studied sialylated glycans and compared their poses with known crystal structure data. We will report the outcome of this docking investigation.

We will also report synthesis and evaluation of new glycoclusters with sialic acid headgroups grafted on a tetraphenylethene scaffold, given that multivalency is one approach to increasing affinity of inhibitors of HA and this scaffold and has been used to great success in the group before.

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Activation of a $Mn^{II}Mn^{III}$-Peroxide with relevance to the Catalytic Cycle of Ib RNRs

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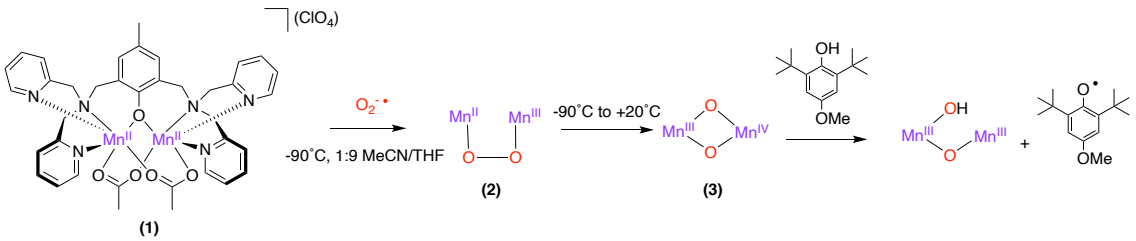
Ribonucleotide reductase (RNR) enzymes are implicated in converting ribonucleotides to the corresponding deoxyribonucleotides, providing precursors for DNA synthesis and repair in all organisms.[1] Class Ib RNRs initiate ribonucleotide reduction via oxidation of a tyrosine radical via a dimanganese cofactor. Stubbe et al. demonstrated that Ib RNRs require superoxide as an oxidant for catalytic activity and postulated a $Mn^{III}Mn^{IV}$ species as the active oxidant.[2] Limited experimental evidence was available for this postulate.

To probe this postulate, the reaction of a biomimetic complex $[Mn^{II}_2(BPMP)(OAc)_2](ClO_4)$[3] (**1**) with superoxide was monitored via UV-vis spectroscopy. A $Mn^{II}Mn^{III}$-peroxide species (**2**), was identified as the product of this reaction, supported by EPR and XAS analyses.[4] Thermal decay of **2** resulted in the formation of a new species (**3**), which was revealed using low-temperature EPR studies to be a $Mn^{III}Mn^{IV}$, moiety, with mass spectrometry indicating **3** was a bis(μ-oxo)$Mn^{III}Mn^{IV}$ complex. Upon addition of phenol to **3** (in analogy to tyrosine in RNRs) an immediate reaction was observed. UV-vis and EPR of the post-reaction mixture displayed the formation of the corresponding phenoxyl radical species. This work contributes experimental support for the postulated mechanism of class Ib RNRs and also provides possible identities of the unknown species in the reaction.



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Fondúireacht Eolaíochta Éireann Dá bhfuil romhainn

A Supramolecular Approach to Anti-Microbial Resistance: Anionophores that Induce Disruption of Bacterial Chloride Homeostasis

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Anion transport has in recent years become an increasingly important aspect of supramolecular chemistry.[1] Indeed, the cross-applicability of anion transport in the field of medicinal chemistry has stimulated a wealth of research.[2] For example, a number of synthetic anion transporters have already been proposed as possible treatments for Cystic Fibrosis (CF) or as potential anti-cancer therapeutics.[3] However there is a lack of anion transporters being exploited as antimicrobial agents. This work describes the design, synthesis and biological evaluation of four novel semi-squaramide indolium conjugates which possess strong chloride binding affinity and potent chloride transport capabilities (Figure 1). Moreover, using cell based assays and label-free quantitative (LFQ) proteomics we investigate, for the first time, the underlying mechanism of the observed antimicrobial effect induced by these anionophores. We expect the results from this study may inform the design of a new class of antimicrobials that act through disruption of bacterial chloride homeostasis.

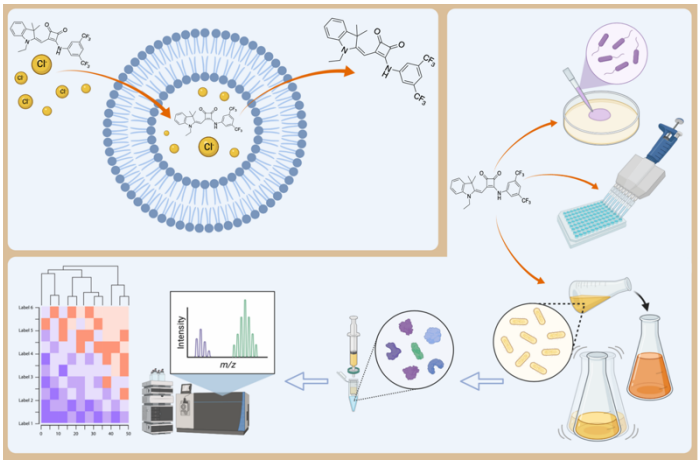

Figure 1: Synthetic anion transporters investigated as novel therapeutics to tackle antibiotic-resistant Gram-positive bacteria.

References:

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Antibiotic Metabolites: Synthesis and Characterisation of the Human Metabolites of Ciprofloxacin

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Antimicrobial resistance (AMR) has been a key focus of global healthcare surveillance in the years preceding Covid-19. The Interagency Coordination Group (IACG) on AMR stated in April 2019 that deaths due to drug-resistant diseases were estimated at 700,000 per year with a forecasted rise to 10 million deaths per year by 2050 if no action was taken on this issue. [1] A study on bacterial AMR published by the Lancet in January 2022 has estimated that in 2019, bacterial AMR was responsible for 1.27 million deaths with a total of 4.95 million associated deaths. [2]

There are numerous pathways by which resistance to antibiotics can occur, however a current gap in knowledge is whether the metabolites of antibiotics present in the environment play any part in this process. This gap in knowledge was identified in a recent report by the Environmental Protection Agency in November 2021 examining the environmental dimension of AMR in preparation for Ireland's second One Health Action Plan on Antimicrobial Resistance 2021-2025 (iNAP2). [3]

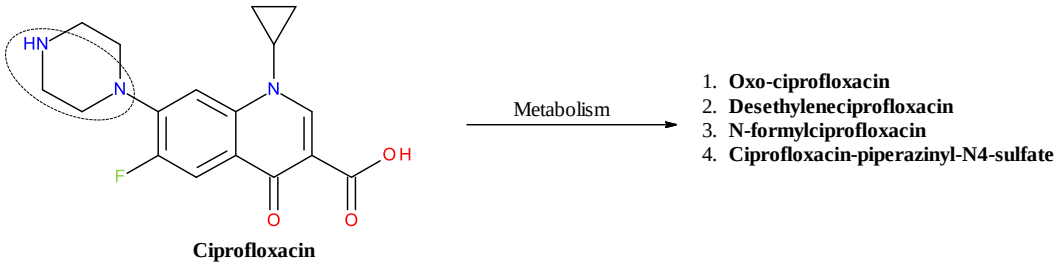

Figure 1: Structure of Ciprofloxacin and Areas of Metabolism, in Humans

Ciprofloxacin is a 2nd generation fluoroquinolone antibiotic first introduced in the late 80's. It is on the WHO's list of essential medicines, however, bacterial resistance was first reported to Ciprofloxacin in the 90's. [4][5] The four main human metabolites of Ciprofloxacin are shown above in Figure 1. [6] To date, two of these have been synthesised and characterised with biological studies currently ongoing.

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Mechanistic Insights into the Ferration of Aromatic Substrates via Intramolecular Sodium Mediation

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Heterobimetallic systems utilising the cooperativity of a highly polar alkali-metal amide and a lower polar metal amide (e.g. Al or Fe) have emerged as a powerful class of reagents for the selective deprotonation of arenes.(**1**) Mechanistic studies on the direct zincation of benzene have also been reported, although the chemical models chosen for the constitution of the bimetallic base in the computational studies were rather simple compared to the experimental system.(**2**) This can lead to deceptive conclusions as we have recently shown for NaFe bimetallic systems, where very bulky bases favour deprotonation of pentafluorobenzene forming a sodiation intermediate, followed by the sequential transmetallation between Na and Fe instead of the direct ferration.(**3**)

In this poster communication, I will present our theoretical insights on the cooperation of [Na(HMDS)] and [Fe(HMDS)$_2$] (HMDS = hexamethyldisilazide) to demonstrate the importance of this bimetallic partnership as observed in experiments, which show that neither Na nor Fe amides are able to achieve deprotonative ferration of pentafluorobenzene alone.(**3**) An unexpected reaction pathway uncovering the cooperativity of Na and Fe in a synchronised manner will be conveyed during the presentation together with the key roles that both Na and Fe play in this reactivity. In addition, I will show how this newly found knowledge has led to the rational design of novel NaFe complexes with [Na(TMP)] (TMP = 2,2,6,6-tetramethylpiperidine), allowing the ferration of less activated substrates such as anisole and toluene (see Figure), which were confirmed by experimental studies. Overall, this novel NaFe system provides direct regioselective C–H activation metalation reactions at room temperature, creating a valuable tool in organic synthesis, which quantitatively and cleanly produces the desire ferrated product.

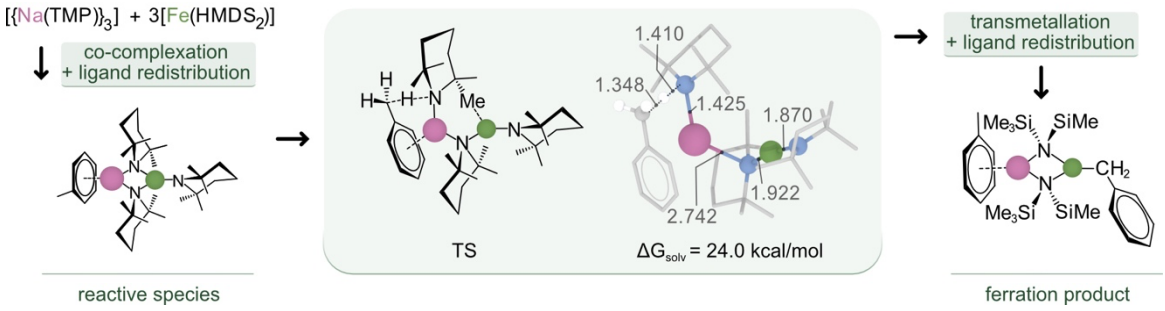

Figure 1. Ferration of toluene with equimolar [Na(TMP)] and [Fe(HMDS)$_2$].

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Compositionally Tunable Cu-Sb-M-S (M= Zn, Co and Ni) Nanocrystals Synthesis and their Transport Properties.

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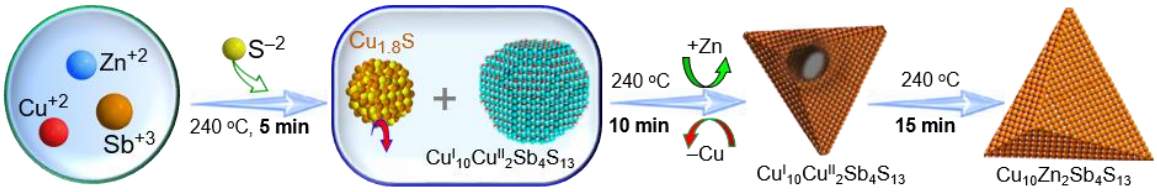
Multinary composition with the combination of nanocrystal size and solution based colloidal synthesis has allowed for the design of new inorganic materials that have a large variety of applications.[1, 2] Group I-II-V-VI semiconductors containing $Cu_{12-x}M_xSb_4S_{13}$ (M= Zn, Co and Ni) substituted tetrahedrite nanostructures remain a new class of multinary material that have not been widely explored yet. These are widely explored for tuning the thermal and electrical conductivity as a function of size, composition and crystal phase.[3, 4] In this work a facile hot injection approach for the synthesis of three different tetrahedrite substituted NCs ($Cu_{10}Zn_2Sb_4S_{13}$, $Cu_{10}Co_2Sb_4S_{13}$,and $Cu_{10}Ni_{1.5}Sb_4S_{13}$) and their growth mechanisms are investigated. We reveal that thiophilicity of Zn, Ni and Co precursors is a key to obtaining pure phase NCs with a controlled size and shape. While all the synthesized crystal phases display outstanding low thermal conductivity, $Cu_{10.5}Sb_4Ni_{1.5}S_{13}$ system shows the most enhanced electrical conductivity compared to $Cu_{10}Zn_2Sb_4S_{13}$ and $Cu_{10}Co_2Sb_4S_{13}$. The maximum ZT value of 0.17 was found for $Cu_{10.5}Sb_4Ni_{1.5}S_{13}$ at 700K. This study highlights an effective synthesis strategy for complex quaternary nanocrystals growth with high potential for application in thermoelectric.



Scheme: Mechanistic illustration for the synthesis of Cu-Sb-M-S (M= Zn) Nanocrystals.

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One Pot Tandem Wittig Hydrogenation Reactions to form C(sp^3)-C(sp^3) in Water

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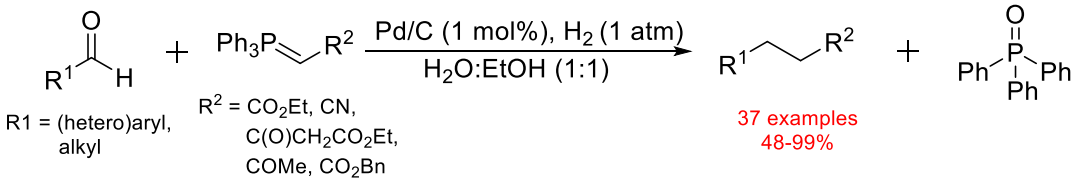
The Nobel Prize winning Wittig reaction comprises of phosphonium ylides reacting with carbonyl containing compounds to produce alkenes.[1] Shortly after its discovery, the reaction was applied in industry with the synthesis of Vitamin A being one of the noteworthy examples.[2]

In recent years, the Wittig reaction has been shown to work in/on water, a green solvent, with short reaction times and excellent yields.[3] Within the McGlacken group, a one-pot tandem Wittig Hydrogenation reaction has been reported. This involved the reaction of stabilised ylides with a range of aldehydes forming C(sp^3)-C(sp^3) bonds. An excellent substrate scope has been achieved with high yields in a green H_2O:EtOH solvent.[4]

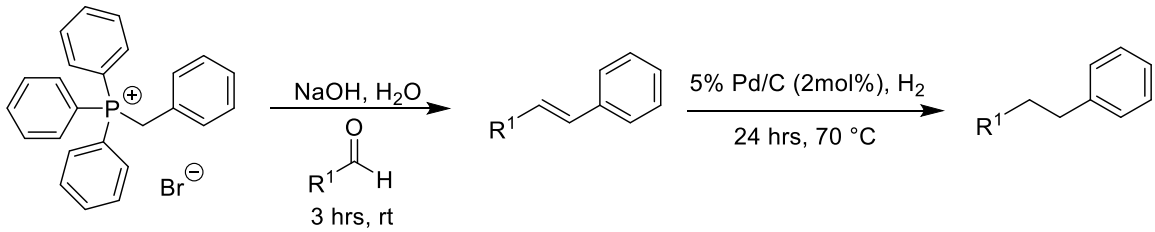
Published by the McGlacken group

"Dump and Stir"



This work focuses on utilizing semi-stabilised ylides for tandem Wittig hydrogenation reactions carried out in water, a green, environmentally benign solvent, to access a range of substituted diphenylethane substrates. Reaction conditions have been optimised thus far, with the Wittig step reacting for 3 hours at room temperature followed by hydrogenation occurring at atmospheric pressure at 70 °C for 24 hours in the one pot. Yields of 77-88% have been achieved thus far.

This project



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IRISH RESEARCH COUNCIL An Chomhairle um Thaighde in Éirinn GOIPG/2020/408

Ollscoil na hÉireann National University of Ireland

Computational Studies in Human Tau Protein screening for understanding the impact in Alzheimer's disease

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Alzheimer's disease (AD) is classified as a neurodegenerative disease and the main symptom is dementia or memory deficit. The causes are still unknown but AD is correlated with alteration of brain cells and proteins such as Tau. The function of Tau is the assembly and stabilization of microtubules, which help normal neuron functions. In AD, this protein loses that capacity and does not bind microtubules. It happens due to posttranslational modifications such as phosphorylation at Ser residue which results in misfolding.[1] Moreover, if the phospho-serine is close to a Lysine, it might give a highly reactive dehydroalanine (Dha) residue, capable of crosslinking with glutathione or Lys, His and Cys residues.

Here, a Tau protein library has been prepared from the Protein Databank (PDB) and was analysed by a developed Python script for selecting nearby Ser and Lys residues. Then, using Pymol Posttranslational modifications tool (PYTMs), a phosphate group was added to all Ser residues (Fig. 1.B). A ranking of 10 structures was obtained based on the PDB: 6HRE result (Fig. 1.A). Finally, the analysis of these structures with NAMD, a molecular dynamics programme, will allow for the design and subsequent synthesis of novel phosphoserine peptides which will help our understanding of the aggregation in Tau proteins.

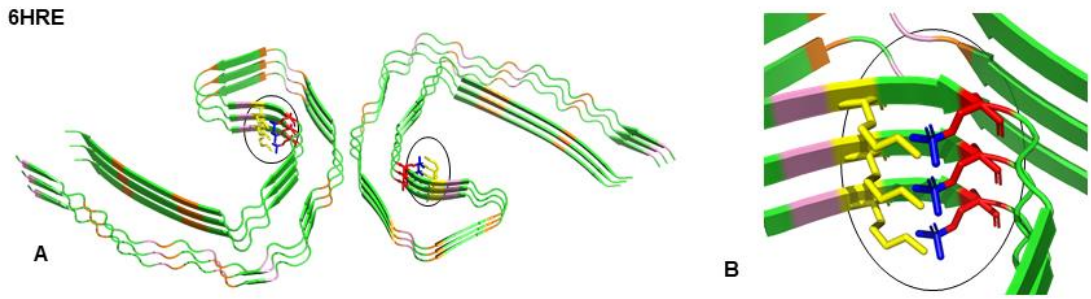

FIGURE 1. A) 6HRE (PDB code) tau protein, coloured in pink: serine, orange: lysine, red: Ser^{356}, yellow: Lys^{353}, blue: phosphate group. B)P-Ser^{356} and Lys^{353}

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A Time-Resolved Spectroscopic Analysis of Novel Porphyrins and Utilisation of their Aggregation in Dye-sensitized Solar Cells.

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[b]*Department of Chemical Sciences, School of Natural Sciences, University of Limerick*

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Aggregation can play a key role in enhancing the performance of non-linear optical materials and in designing materials for dye-sensitized solar cells.[1] Aggregation can have a significant effect on harvesting solar light and on photocurrent production.[1] Our interest lies in utilizing this property in designing new porphyrin-based materials. Both H- and J-aggregation are possible, and J-aggregation is particularly relevant to absorbing light in the near-infrared spectrum. We have synthesized novel conjugated porphyrins containing; carbazole, phenoxazine, and phenothiazine units attached to the meso-position in porphyrins, all of which displayed aggregation. Photophysical studies were used to study the singlet and triplet energies, and to investigate the impact of the aggregation on fluorescence, phosphorescence, and singlet fission.[2] The optoelectronic properties of the photoelectrodes in dye-sensitized solar cells can be controlled/modified by using dye aggregation, such as displayed by the mentioned porphyrins above. These materials have the potential, to play a key role in photovoltaic performance.

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Keywords: Dye-Sensitized Solar Cells, Self-Aggregation of Porphyrins

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Preparation of 1,2-Dioxolanes *via* the Enantioselective Peroxidation of γ,δ-Unsaturated-β-Keto Esters

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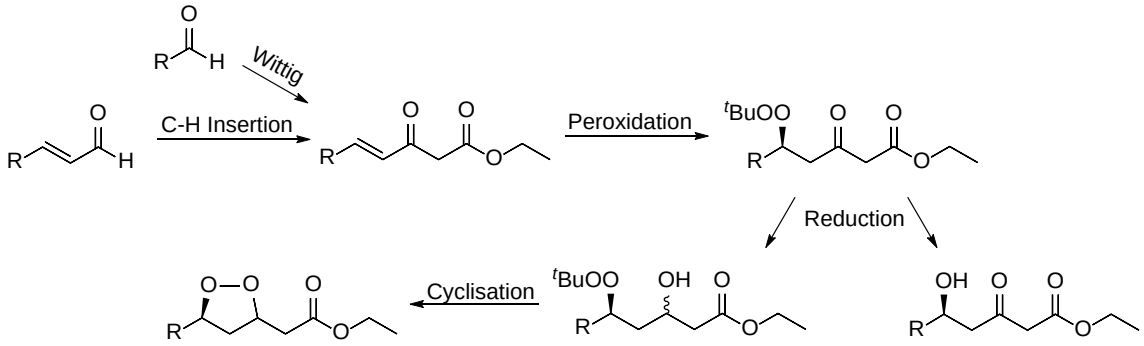
More than 600 cycloperoxides have been isolated from diverse natural sources.[1] Many of these natural peroxides have shown remarkable activity against a variety of diseases that impact both human and animal health.[2] Accordingly, peroxide-containing compounds are an attractive synthetic target, and there have been countless developments in the preparation of peroxides, including direct oxidation reactions, metal-catalysed reactions and enzymatic routes.[3] More recently, the importance of organocatalysis as a powerful tool in asymmetric synthesis has been underlined by the awarding of the 2021 Nobel prize for chemistry to this field.[4]

Our group have previously established an organocatalysed asymmetric peroxidation of unsaturated aldehydes.[5] This work builds upon these findings and exploits this approach for the synthesis of chiral 1,2-dioxolanes.[6] Herein, we describe a highly enantioselective, organocatalysed peroxidation of γ,δ–unsaturated-β-keto esters. Following extensive optimisation, this novel peroxidation methodology proceeded in good yields with e.r.s as high as 95:5 across a wide range of substrates. This degree of enantioselectivity has not been previously reported for similar carbonyl substrates. The resulting δ-peroxy-β-keto esters serve as useful precursors to chiral 5-membered cycloperoxides. As the resulting peroxides may be readily reduced to the corresponding chiral alcohols, this chemistry opens up new routes to important molecular building blocks.



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Smart carbon nano-onion systems for drug delivery

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There are many issues associated with free drug delivery—the most prominent of which include: adverse side-effects, multi-drug resistance, premature drug degradation, lack of tissue penetration, and non-specific toxicity. Targeted delivery, which utilises nanocarriers as payload delivery vesicles, has the potential to address and alleviate these prominent issues. Specifically, it involves nanomaterials functionalised with targeting agents, allowing for the selective uptake of these nanocarriers by cells overexpressing specific receptors. This approach explicitly increases the drug concentration in the target cell of interest whilst minimising the exposure of healthy cells to the therapeutic agent.

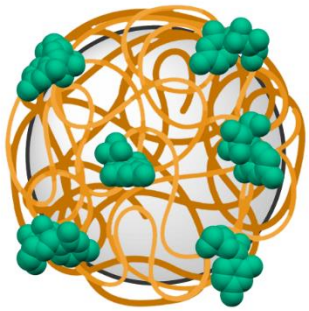

Fig 1. A carbon nano-onion (grey) based nanocarrier for the delivery of gemcitabine (green) to tumours through hyaluronic acid (orange) mediated targeting of CD44 receptor overexpressing cancer cells.

In this poster presentation, carbon nano-onions (CNOs) will be presented as a potential vesicle for nanocarrier-type drug delivery systems [1]. CNOs, or multi-layer fullerenes, consist of multiple concentric layers of sp^2 hybridised carbon. In our lab, we synthesise and functionalise CNOs and explore their drug-delivery potential. A novel CNO-based nanocarrier containing hyaluronic acid, a well-optimised targeting agent, for the specific delivery of gemcitabine (GEM) to CD44 receptor overexpressing cells [2] will be presented (Fig 1). After screening $CD44^+$ & $CD44^-$ human pancreatic adenocarcinoma (PDAC) cells, we found that fluorescently-labelled CNOs were selectively taken up by $CD44^+$ cells without showing significant toxicity in the range of 0.5-20 µg/mL. These data suggest that CNOs are devoid of toxicity and could be utilised to deliver GEM directly to $CD44^+$-PDAC cells.

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Grant ID: GOIPG/2019/1820

Novel Mixed-Ligand Coordination Polymers and Metal-Organic Frameworks

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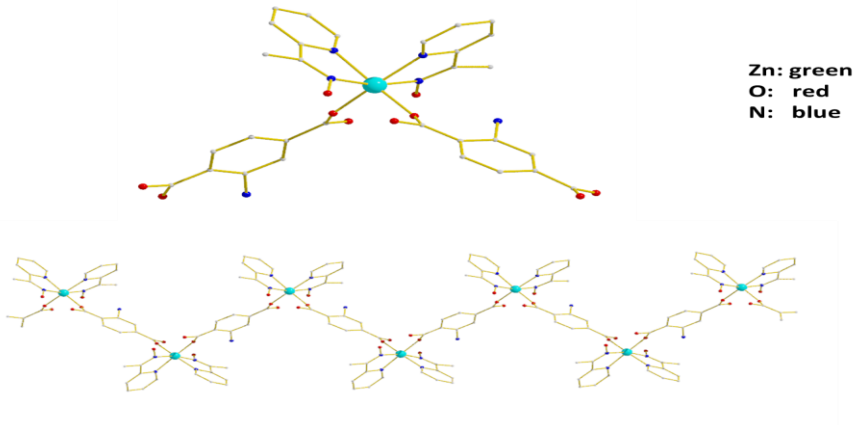
Metal–organic frameworks (MOFs) are a special category of coordination polymers, which have gained a special attention during the last years because of their highly porous structures and their prospective industrial, biomedical, and environmental applications.[1] Our group has investigated the employment of mixed ligands' strategy for the synthesis of new MOFs.[2] This approach can enrich the library of the known MOFs leading to new structural topologies, while combining the porosity of these materials with other interesting properties, such as magnetism, photoluminescence etc.

Herein we report some recent results from the use of 2-pyridyl oxime and polytopic carboxylate ligands. Exploring the synthetic parameters that affected these mixed ligands we have synthesized a new 1D zinc coordination polymer. The study of the topological arrangement and the packing of the polymeric chains gave us insights how to increase the dimensionality of the polymerization giving access to a novel 2D zinc metal-organic framework. The crystal structures and the geometrical and topological features of the two compounds will be presented in detail.



Acknowledgment: Mona extends her appreciation to the Ministry of Education in Saudi Arabia for a Saudi Arabia government scholarship.

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Tuning polytypism in transition metal disulphides by precursor reactivity manipulation and their application in electrocatalysis

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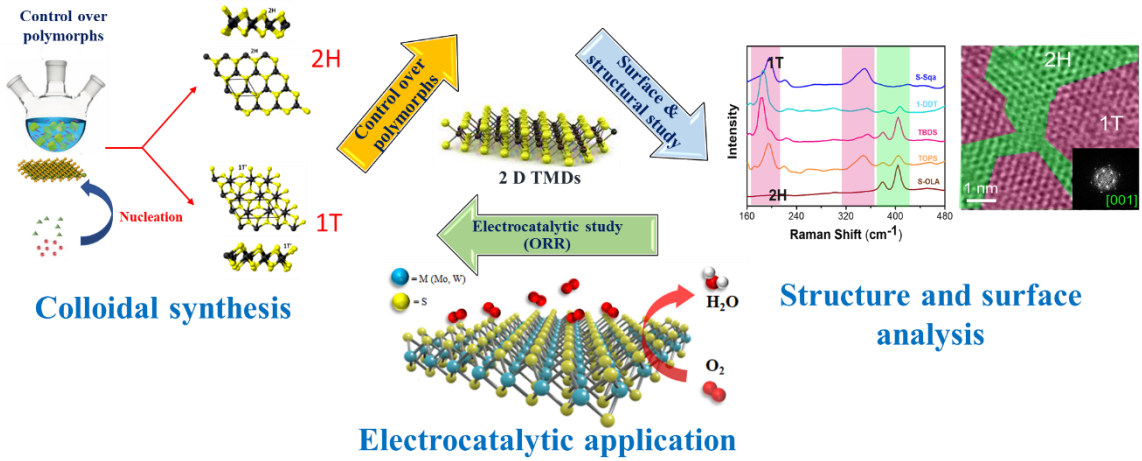
Two-dimensional (2D) transition metal dichalcogenides (TMDs) such as MoS_2, WS_2, ZrS_2, and TiS_2 have emerged as an intriguing class of functional materials due to their distinct chemical and physical properties.[1] Their peculiar structure and exceptional electronic, optical and mechanical properties have stimulated various applications in the fields of catalysis, energy storage, electronics, and optoelectronics. [2] TMDs can exist in several structural polymorphs, including 2H, 1T and 3R. [3] In this regard, several methods have been employed to induce controlled phase formation. However, the synthetic control over a specific phase is challenging due stability of a particular phase. In these instances, the colloidal chemistry approach can access metastable phases and compositions with precise control over the polytypism between polymorphic interfaces. This work has developed a practical phase control strategy for layered transition metal disulphide NC synthesis by manipulating precursor reactivity.



In this project, by varying precursor-ligand chemistry, 2H, 1T' and polytypic MoS_2 and WS_2 were synthesised. The flexibility to fine-tune varied reactivity in commercially available S and metal sources allowed control over polytypism. Different polymorphs, namely 2H and 1T', were obtained by varying reactivity of the precursors. The formation of 1T' was facilitated by the highly reactive metal and S source, whereas less reactive sources led to the formation of thermodynamically stable 2H. In addition, the formed TMDs exploited as electrocatalysts for the oxygen reduction reaction. Polytypic MoS_2 displayed the highest onset potential of 0.82 V (vs RHE) among all synthesised materials. The insights provided by this work will be instrumental toward the design of scalable solution-based pathways to control polytypes in layer transition metal dichalcogenides. Furthermore, this synthesis approach has the potential to be extended to multiple TMDs, enabling exquisite control over polymorphism in TMDs. Presented here is a summary of our work, namely, tuning polytypism in transition metal disulphides by precursor reactivity manipulation and their application in electrocatalysis.

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Development of Calixarene Based Surface Imprinted Polymer as a Novel Scavenging Device for Biological Contaminants in Water

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In recent years, there has been a significant rise in reported outbreaks of waterborne bacterial and viral diseases. Traditional water analysis for microbial contamination requires lengthy and laborious laboratory testing creating a need for on-the-spot analysis techniques and scavenging devices. Recently, the surface imprinting technique has gained popularity to design biomimetic sensors.[1] Imprinted polymers have been used to generate cavities complementary in shape, size, and target cell functionality on polymer surface to bind chemical and biological templates such as bacterial cells, human cells, and viruses. The aim of this project is to design and synthesise calixarene macrocycles and use them to create surface imprinted polymers (SIPs) (**Figure 1**) for selective detection and removal of *E.coli*, Cryptosporidium, and norovirus from water. Novel acryloyl calixarene was used as a functional monomer to synthesise SIP for *E.coli*. The rebinding studies conducted so far showed the ability of newly synthesised SIPs to selectively bind *E.coli*, showing great potential for application in scavenging and detecting device fabrication.

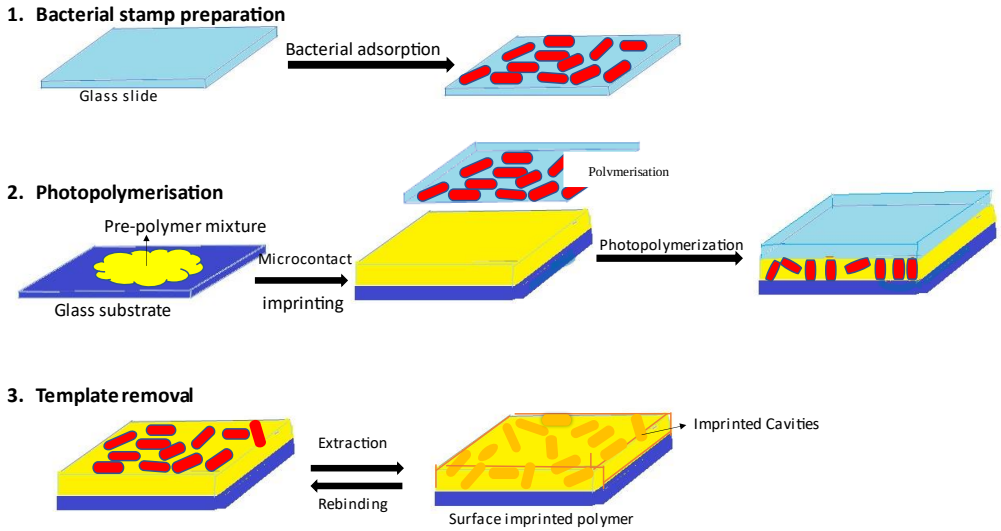

Figure 1: Schematic representation of the SIP generation[2]

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Exploiting inverse electron-demand Diels-Alder click chemistry for the functionalisation of a Pt-based anticancer drug

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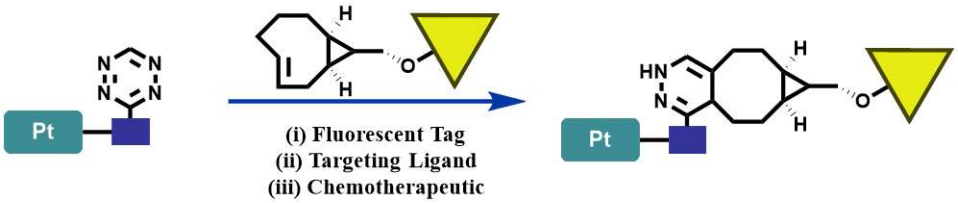

Platinum (Pt)-based drugs such as cisplatin, carboplatin and oxaliplatin, play a very important and well documented role in treating cancer and are employed in nearly 50% of anti-cancer treatments. The primary mechanism of Pt-based drugs is associated with their ability to cross-link nuclear DNA; the Pt-DNA adducts interrupt transcription, generate DNA perturbation damage responses and ultimately induce apoptosis. Pt(II) anticancer drugs also react with a range of other nucleophiles, including RNA, mitochondrial DNA and proteins. The clinical effectiveness of Pt anti-cancer agents is hampered by toxic side-effects and both intrinsic and acquired resistance.[1] There has therefore been a continued drive to develop novel classes of more effective and better-tolerated Pt(II) and Pt(IV) drug candidates, as well as to better understand the precise cellular activity of Pt complexes.[2]

The development of innovative inverse electron-demand Diels-Alder (iEDDA) based techniques to functionalise Pt(II) and Pt(IV)-based complexes is anticipated to greatly aid this enterprise. Click chemistry is widely used throughout synthetic chemistry and biology, showing tremendous versatility, whilst being atom-efficient and in some cases, bioorthogonal.[3] The chemical synthesis, characterisation and biological evaluation of a click functionalisable Pt-based drug will be presented.

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SERS Analysis of Organic Extractants using 2D Hydrogel-based Nanoparticle Arrays

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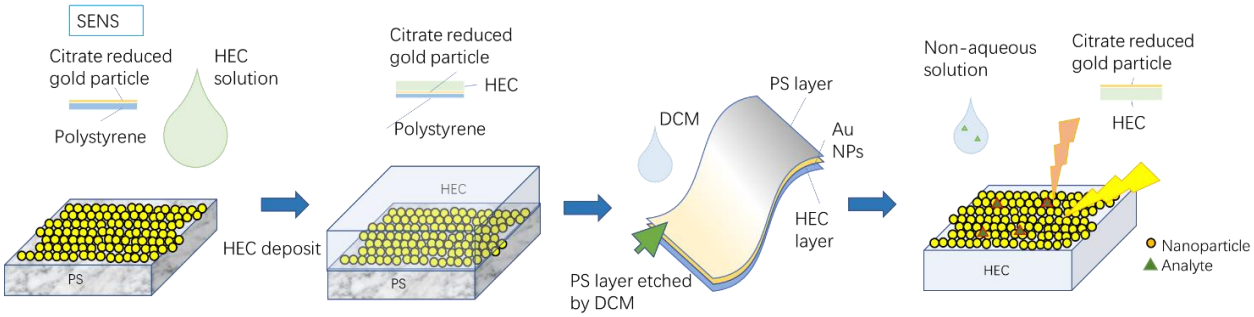
Surface enhanced Raman spectroscopy (SERS) is a sensitive technique for identification of molecules adsorbed onto rough silver or gold surfaces or nanoparticles[1]. When combined with liquid-liquid extraction, SERS had numerous applications in the detection of food additives[2], illicit drugs[3] and environmental PAH pollutants [4]. In the QUB's group's previous work, surface-exposed nanoparticle sheet (SENS) was developed using nanoparticle self-assembly at liquid-liquid interfaces to create uniform and easily-prepared solid SERS active substrates[5] composed of a 2D array of particles fixed to a polystyrene base. However, the polystyrene base of SENS limits its use in organic solvent analysis. In this work, we used SENS as a template to prepare hydrogel-based supported nanoparticle arrays which are SERS active and can be used in SERS analysis of compounds dissolved in organic solvents extractants, particularly DCM.



The preparation process is summarized in the Figure above. This method allows arrays ca. 16 mm^2 films to prepared. In these substrates the HEC support is flexible, since it is ca. 600 µm thick, and can stored for extended periods. Importantly, the particles in the film remain accessible to molecular analytes and are not submerged in the polymer support which means that they remain SERS active and can be used to detect analytes dissolved in DCM even though the polymer is not soluble in this solvent. These substrates have the potential to be used in simple field tests where targets are extracted from water into DCM and then detected by SERS using handheld detector systems.

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Carbon Dioxide Utilisation for Construction of High Value Carboxyl-Containing Organic Products and Biologically Active Compounds

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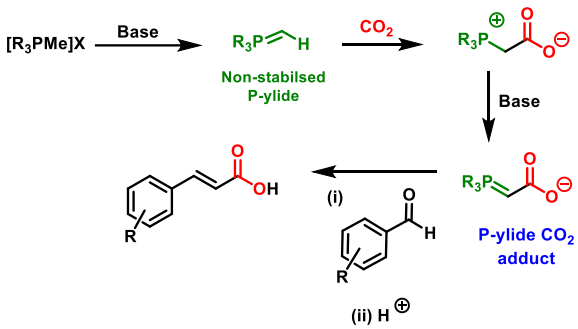
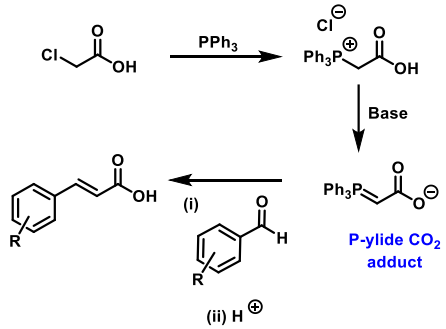
Employing waste products as starting materials for chemical transformations is a key step in addressing the global challenges of sustainable production and consumption. Greenhouse gas CO_2 is perhaps the most significant waste product of the industrialised world.[1] Developing a method for the conversion of a harmful environmental waste product into high-valuable organic products can allow CO_2 to be used as a one-carbon (C1) chemical building block. Phosphonium ylides (P-ylides) have the ability to activate CO_2 into reactive P-ylide CO_2 adducts.[2,3] This activated form of the C1 feedstock can be incorporated into carboxyl-containing products and biologically active compounds.

Cinnamic acids, α,β-unsaturated carboxylic acids, are structural motifs present in biologically active natural products and medicines.[4] It has been found that cinnamic acids can be synthesised using two comparable synthetic routes. The CO_2 utilisation methodology involves the *in-situ* generated P-ylide activating gaseous CO_2, forming the P-ylide CO_2 adduct. A novel Wittig reaction occurs between the P-ylide CO_2 adduct and various benzaldehydes forming cinnamic acids in good yields. A range of sources of gaseous CO_2 have been explored.

A route for CO_2 independent generation of the activated P-ylide CO_2 adduct starting with carboxymethyltriphenylphosphonium chloride has also been developed. This novel route can be used to test substrate suitability and reaction conditions independent of the CO_2 utilisation methodology, limiting our use of gaseous CO_2. This route is advantageous due to efficient access to the P-ylide CO_2 adduct following deprotonation of the carboxymethylphosphonium salt.



CO_2 utilisation methodology



CO_2 independent methodology

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Catalytic approaches to the valorisation of lignin

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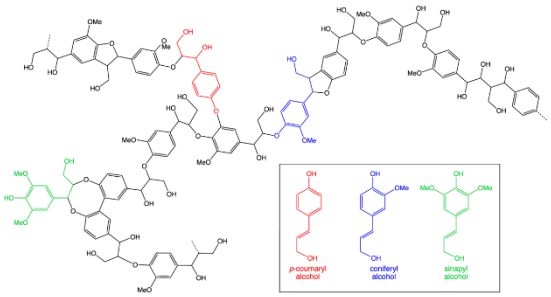
Lignin is a robust heterogeneous biopolymer present within lignocellulosic materials, the backbone of all plants. Lignin's structure is based on three phenol-like building blocks (coumaryl alcohol, coniferyl alcohol and sinapyl alcohol, see below) randomly linked through either ether or carbon-carbon bonds (so-called "linkages") [1]. As fossil fuel feedstocks are replaced over the coming decades (due to the problems associated with their use), the cost-effective generation of platform chemicals within biorefineries will be a crucial step for the future of the chemical industry. These compounds are expected to partially replace certain feedstocks currently obtained in a non-sustainable manner from petroleum-refining processes [2].

This project focuses on the heterogeneously catalyzed hydrogenolysis pathway specifically targeting the cleavage of a class of linkages (ether bonds). A commonly used method to simplify processes that are of interest here is the use of model compounds (rather than lignin itself) as substrates [3]. These are small molecules that contain lignin's most common linkages. The use of these eases the analysis of the products but will still allow insights on potential lignin-related depolymerisation chemistry. Presented here is a summary of our work to date, namely, the characterization of the synthetized catalysts and the tuning of the different reaction conditions to optimize the conversion and selectivity of the selected substrates under both thermal and photocatalytic reactions.



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Development of the Catalytic Asymmetric Grignard Synthesis of Tertiary Alcohols

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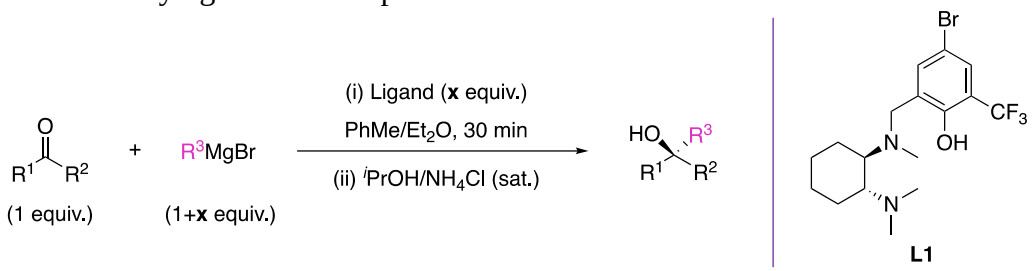
Chiral tertiary alcohols are an important structural motif, in many natural products as well as in pharmaceuticals.[1] Direct 1,2-addition of an organomagnesium reagent to the carbonyl group of a ketone, known as a Grignard reaction, is one of the simplest methods to access tertiary alcohols. However, rendering this reaction asymmetric is difficult. The complex Schlenk equilibrium, potential for enolization and reduction side reactions as well as competition between a radical and concerted mechanism complicate the task.[2,3] Most effective protocols require an additional metal additive to achieve high enantioselectivity. The use of a simple chiral tridentate ligand in the direct asymmetric organomagnesim addition to a carbonyl at -82 ˚C in toluene/ether has been reported by our group.[4] These half-salan type ligands are comprised of a "privileged" diaminocyclohexane backbone and a phenol with varying substitution pattens.



The methodology benefits from broad substrate scope and fast reactions times. However, a notable drawback is the requirement for a stoichiometric quantity of ligand. While ligand recovery is possible, a catalytic system is nevertheless desirable. Presented here are details of our efforts towards the development of a catalytic variant of our asymmetric Grignard system. Ligand **L1** and derivatives, with *o*-CF_3 substitution have exhibited catalytic activity at room temperature. In some cases, ligand loading can be decreased to 10 mol% without significant erosion of enantioselectivity.

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Quantitative estimation of total phenolic content in brown seaweeds through ^{1}H NMR spectroscopy

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Marine algae or seaweeds are recognized as an important component of marine ecosystem. Seaweeds have been reported as a rich source of nutrients and bioactive compounds including proteins, polyphenols, carbohydrates,lipids, alkaloids, and peptides[1]. Amongst them, polyphenols have become materials of high interest from the past few years owing to their multifunctional potential as natural antioxidants, antimicrobials, and other health benefits. However, the applications of seaweed polyphenols have been limited, in part due to factors related to their quantitative and qualitative analysis. This is because of the diversity of the phenolics in terms of their structures that vary from simple to highly complex. Hence, it provides a challenge for the scientists to produce some standardized procedure for their quantitative analysis. Colorimetric assays such as Folin-Ciocalteu have been used extensively so far to quantify the total phenolic content, but still, it is not a selective procedure as it provides approximate measurements for the overall phenolics in extracts and can suffer from interference from other non-phenolic components. To overcome these limitations of the FC assay, a more reliable method has been presented in this study for the determination of total phenolic content in brown seaweeds using ^{1}H NMR spectroscopy[2]. The DMSO-d_6 aprotic and strongly hydrogen bonded solvent was used to determine the sharp resonances of phenolic hydroxyl protons in the range of 8-14 ppm. The NMR experiment was performed first for the model compound phloroglucinol in DMSO-d_6 using trimesic acid as internal standard. This involved the irradiation of the residual water signal which causes the suppression or elimination of the phenolic -OH groups due to proton exchange. The resultant NMR spectrum was recorded with the integration of the specific phenolic signal (that was previously suppressed), that allowed the quantification of phenolics in a more accurate manner. This method has been applied to the complex extracts of four brown seaweed species (*Ascophyllum nodosum, Fucus serratus, Fucus vesiculosus, and Fucus spiralis*) and the results of the total phenolic content were compared with Folin-ciocalteau reagent method to ensure the correlation between the two quantitative methods. Furthermore, this HNMR method can be used for producing rapid and effective determination of phenolics in complex matrixes.

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Stability of Co-crystals a Density Functional Theory study

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Co-crystals are crystals of more than one molecule held together through dispersion interactions such as Hydrogen bonding, dipole-dipole interactions, and Van der Waals interactions. Co-crystals have also been more stable than their single-crystal counterparts, as indicated by their higher lattice enthalpy.[1] In literature, hydrogen bonding has been the main focus to account for the stability of co-crystals;[2] however, other dispersion interactions like Van der Waals could be necessary for stabilising co-crystals.

In this poster presentation, various Density functional theory (DFT) methods have been used to calculate the lattice enthalpy of experimentally made thermodynamically stable co-crystals. These methods include using both the Tkatchenko and Scheffler (TS) and the Many-Bodied dispersion (MBD) dispersion corrections. This co-crystal set includes simpler molecules, 4,4'-bipyridine and oxalic acid, and more complex active pharmaceutical ingredients, aspirin and paracetamol. These are all experimentally made structures. Previous work has shown that most co-crystals are thermodynamically stable, so this means calculations are expected to have a negative enthalpy.[1]

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Pharmaceutical Salts of Piroxicam and Meloxicam with Organic Counterions

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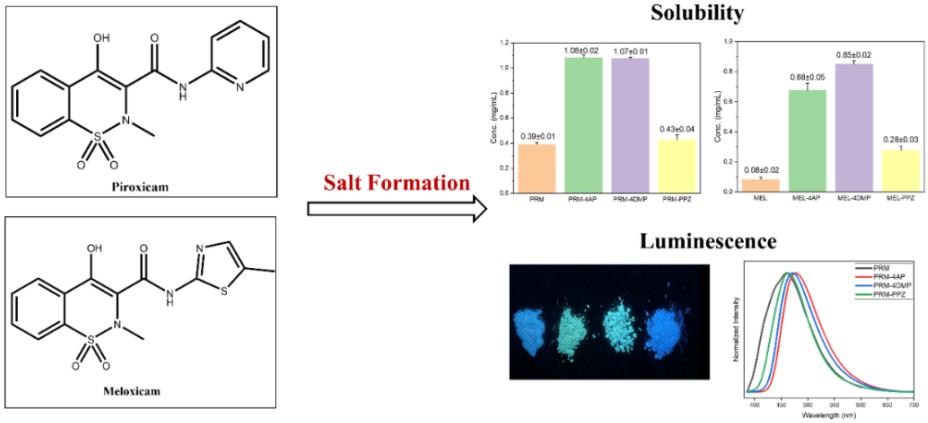
Organic multi-component crystalline materials have attracted attention in a wide range of high-technology applications. In this study, the interest is in examining cocrystallization as a means to alter the properties of solid-state fluorescent materials. Piroxicam (PRM) and meloxicam (MEL) are two nonsteroidal anti-inflammatory drugs, belonging to the Biopharmaceutics Classification System (BCS) Class II drugs.[1-2] In this study, six novel pharmaceutical salts of PRM and MEL with three basic organic counterions, i.e., 4-aminopyridine (4AP), 4-dimethylaminopyridine (4DMP) and piperazine (PPZ) were prepared by both slow evaporation and slurrying. These salts were fully characterized by single crystal and powder X-ray diffraction, thermal analysis, and Fourier transform infrared spectroscopy.



From the solubility experiments, all six salts, especially MEL-4DMP and MEL-4AP, showed a significantly improved apparent solubility and dissolution rate in sodium phosphate solution compared with the pure APIs. Furthermore, the salts also exhibit similar solid-state luminescent properties. Hirshfeld surface analysis and HOMO-LUMO analysis supported the luminescent studies and the mechanism for the observed luminescence is discussed. [3]

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Elemental Screening of Cell Culture Media using Microwave Plasma Atomic Emission Spectroscopy

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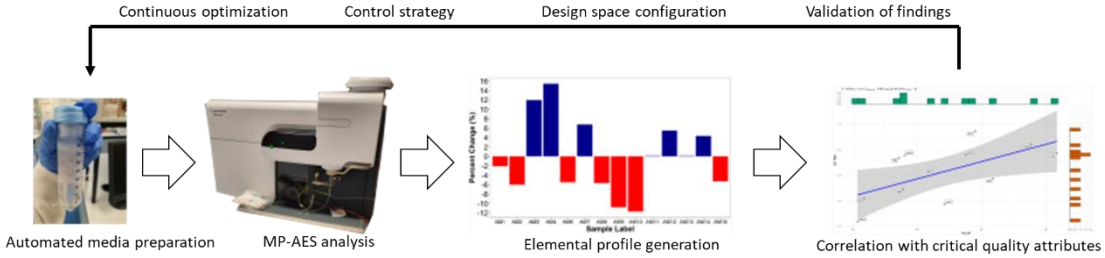
Biopharmaceutical manufacturing is rapidly growing with diverse applications [1]. Compositional variation in raw materials required for manufacturing can impact process performance. Despite industry-wide shifts to usage of chemically defined media (CDM), variability remains a concern [2]. Media variability occurs due to changes in molecular and/or elemental composition from improper manufacturing, storage, or contamination [2]. Transition element variability can impact quality and yield of the biologic [2]. Alkali/earth elements are important for numerous biological functions but lack investigation likely due to their high concentrations [3]. These can also be a source of trace impurities introduced through inadequate supplier process controls [2]. Thus, it is important to screen for lot-to-lot variability. Microwave plasma atomic emission spectroscopy (MP-AES) is an inexpensive elemental analysis technique which has not yet received wide-scale adoption as it is not as established as inductively coupled plasma (ICP) based techniques [4].



This work focuses on application of MP-AES for elemental screening of CDM. Our research to date is briefly presented with emphasis on development of MP-AES methods featuring various signal correction approaches to improve precision and accuracy. The above figure shows how MP-AES may be implemented as a Process Analytical Technology (PAT) in biopharmaceutical manufacturing for the purpose of continuous bioprocess monitoring and optimization.

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Project ID: GOIPG/2019/1947

Development of Holliday junction-stabilising complexes via click chemistry: a new gene targeting strategy for metal-based drugs

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Common cancer therapeutics such as cisplatin are effective at crosslinking guanine residues on B-DNA duplexes, inducing apoptosis. Resistance mechanisms and toxicity associated with existing therapeutics generates motivation for the research of alternative cancer treatments. The Holliday junction (HJ) is a non-canonical, sequence dependant 4-way junction and was first described in 1964 by Robin Holliday [1] (Fig. 1A). HJs mediate the mechanisms of recombination and repair in DNA, through a process known as homologous recombination (HR). Brogden *et al*. developed one of the best studied small molecules that interact and stabilise the HJ using a bis-acridine ligand which displace two adenine nucleotides that 'flip out' at the ACC core upon non-covalent binding of the agent [2].

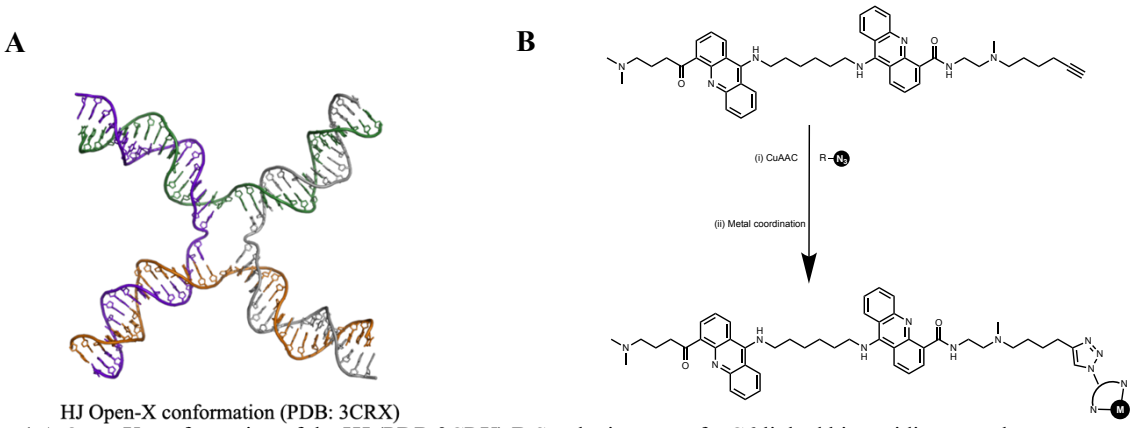

Fig. 1 A Open-X conformation of the HJ (PDB 3CRX) **B** Synthetic route of a C6 linked bis-acridine complex.

This research aims to develop new HJ stabilising compounds using click chemistry, including copper(II) complexes which can selectively recognise and cleave higher-order nucleic acid structures, and ruthenium(II) complexes which serve as probes for non-canonical DNA structures (Fig. 1B). The HJ is an attractive biological target as HJ stabilisation and inhibition of HJ resolution may prevent the elongation of telomeres in the alternative lengthening of telomeres (ALT) pathway in immortalised human tumour cells [3]. This research presents a potentially new approach for targeted cancer therapy.

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Synthesis of Cholesterol-Modified Antimicrobial Peptides

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The World Health Organisation (WHO) describes antimicrobial resistance (AMR) as the adaptation of bacteria, fungi, parasites and viruses to no longer respond to medicines resulting in more difficult to treat infections, an increased risk of the spread of disease, severe illness and death [1]. With the extent of AMR posing a serious global threat, there is a current focus on the development of novel therapeutics necessary to avoid antimicrobial treatment failures. Antimicrobial peptides (AMPs) have been described as a viable alternative to current therapeutics given they are natural, effective, and are associated with high fitness costs of resistance.[2]. Natural AMPs are generally non-stable with a short half-life in circulation but through modification of the peptide, including numerous forms of conjugation, improved stability can be seen. Lipidation is one such method which enhances hydrophobicity, secondary structures, and self-assembling formation while retaining the ability to bind to target receptors resulting in better metabolic stability, membrane permeability, and bioavailability [3]. Lipidation, frequently involving fatty, or related, acids, can been extended to cholesterol, with the utilisation of a cholesterol moiety initially validated with fusion inhibitor sequences used as antiviral agents [4],[5] but has also been shown to improve the antimicrobial activity and selectivity of an AMP [6]. This work outlines the development of a novel synthetic strategy to facilitate the modification of antiviral and antibacterial peptides with cholesterol, at either the peptide N or C-terminus, or even internally in its sequence, with the ability to overcome short-comings of current cholesterylation methods.

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Development of a Bismuth Modified Molybdenum Disulfide Sensor for the Detection of Antibiotic Drugs in Water Environments

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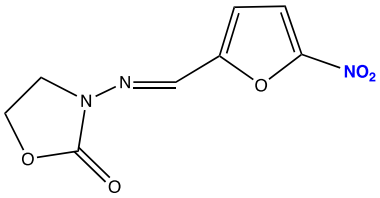
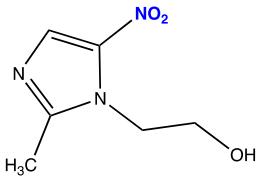
2D layered transition metal dichalcogenides (TMDs) form a unique and varied class of 2D materials with a formula of MX_2 where M is a transition metal such as Mo or W, and X represents the chalcogen atoms, S, Se or Te [1]. Two-dimensional materials exhibit very good electrocatalytic properties, high conductivity and robust mechanical features. They are attractive for use as sensors because they are affordable and easy to develop and fabricate [1]. Furthermore, the development of conductive layered transition metal dichalcogenides (TMDs) with high sensitivity properties for use as environmental sensors is an effective way of detecting pharmaceutical or antibiotic drugs in contaminated water resources, and thus reducing the increase in antimicrobial resistance due to the presence of excess antibiotics in water [2].

Furazolidone (**I**) and Metronidazole (**II**) are both antibiotic drugs available in the market and are used for treating bacterial and protozoal infections [2]. Metronidazole is a nitroimidazole derivative that is used commonly to treat protozoal diseases including trichomoniasis and giardiasis [3]. Similarly, Furazolidone, is used to treat diarrhoea caused by protozoan or bacterial infections [3]. Both molecules have a nitro group, $–NO_2$, that can be electrochemically reduced and this was used in the electroanalysis of the drugs.



Furazolidone (**I**)



Metronidazole (**II**)

In this poster, we present our recent results on the electrochemical detection of Metronidazole and Furazolidone in water using a combination of the dichalcogenides (MoS_2) and bismuth nanostructures. An electrodeposition approach was employed to form a composite of MoS_2 and Bi at a carbon electrode. The performance of the MoS_2/Bi modified carbon sensor was studied using cyclic voltammetry and differential pulse voltammetry. Highly sensitive and selective detection of the two drugs was observed.

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For what's next

Synthesis and characterization of PEG_{400}-DOPA for multifunctional coatings

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Mussel foot proteins (MFPs) play an important role in the ability of mussels to attach tightly onto various surfaces in underwater conditions. L-DOPA (L-3,4-dihydroxyphenylalanine) is found at high amounts in MFPs, contributing to the strong underwater adhesion via a range of different chemical interactions of the 3,4-dihydroxyphenyl (catechol) moiety with different surfaces. In an effort to mimic the structure of MFPs, synthetic oligomers and polymers modified with L-DOPA and their coatings have been widely employed in the field of antifouling and biomedical science. The aim of this research was to evaluate the hydrophilicity of coatings made from L-DOPA-modified PEG oligomers using various process parameters. A facile chain-end modification of a linear bifunctional PEG oligomer with M_n = 400 Da was conducted by a direct esterification reaction[1, 2] with L-DOPA. The PEG_{400}-DOPA product was studied by Fourier transform infrared (FTIR) spectroscopy, proton nuclear magnetic resonance (^{1}H-NMR) spectroscopy, mass spectrometry, differential scanning calorimetry (DSC) and thermogravimetric analysis (TGA). FTIR and ^{1}H-NMR spectroscopies confirmed the successful esterification and incorporation of L-DOPA in the product structure. In terms of coating fabrication, glass substrates were immersed in different PEG_{400}-DOPA aqueous solutions for 18 h. Some of the key process parameters that were investigated included concentration, solution ageing effect, aqueous solvent and post-coating thermal annealing. The interaction between the PEG_{400}-DOPA coating and glass substrate was investigated by water contact angle (WCA) measurements. Results showed that PEG_{400}-DOPA was successfully immobilized on the substrate and that hydrophilicity improved when compared to the bare substrate. Coatings cast from Tris HCl buffer (pH 8.5) appeared to be very promising in terms of enhanced hydrophilicity (WCA values lower than 20°). Post-coating thermal annealing at 120 °C for 3 h resulted in significantly increased WCA values (showing up to a 5-fold increase when compared to the as-coated specimens), possibly due to coating dehydration and conversion of catechol moieties to quinone. These results indicate that L-DOPA modified PEG oligomer coatings could be used for antifouling and hydrophilic coating applications.

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Bis-heteroaryl synthesis *via* pyridylsulfonium salts.

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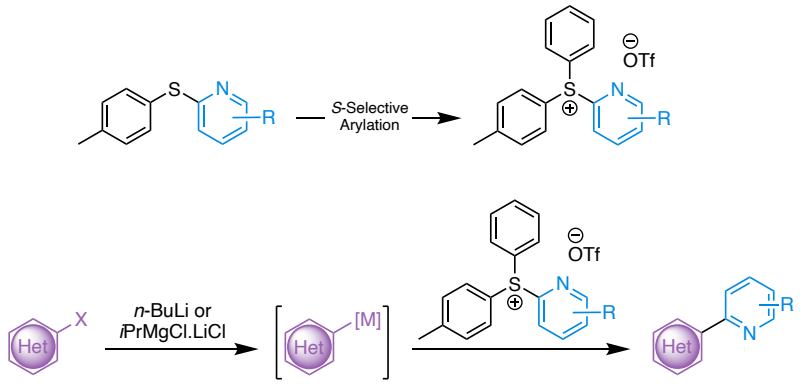
Sulfonium salts are a class of compound finding increased use in organic synthesis, notably in C-C bond formation.[1] Triarylsulfonium salts containing a pyridyl moiety are notably limited in the literature and thus represent an underexplored example of these salts.[2-5] Recently, bis-heteroaryls have been synthesised via phosphorus- and sulfur-mediated ligand coupling methodologies.[6,7]

Presented herein is a general S-selective arylation of 2-pyridylsulfides to the corresponding pyridylsulfonium salts. The resulting salts were then applied in the synthesis of bipyridines *via* a transition metal-free coupling methodology (**Scheme 1**). The method shows extensive functional group tolerance and allows access to both symmetrical and unsymmetrical 2,2'-, 2,3-' and 2,4'-bipyridines.[8,9] As well as bipyridines, pyridines linked to other heterocycles can be synthesised *via* the method. Also presented here is work towards the synthesis of 3- and 4-pyridysulfonium salts, with issues relating to N- *vs*. S-selectivity in the arylation step noted.



Scheme 1. Bis-heteroaryl synthesis *via* pyridylsulfonium salts.

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The Inverted device fabricated by Electrophoretic Deposition with high luminesce and high EQE

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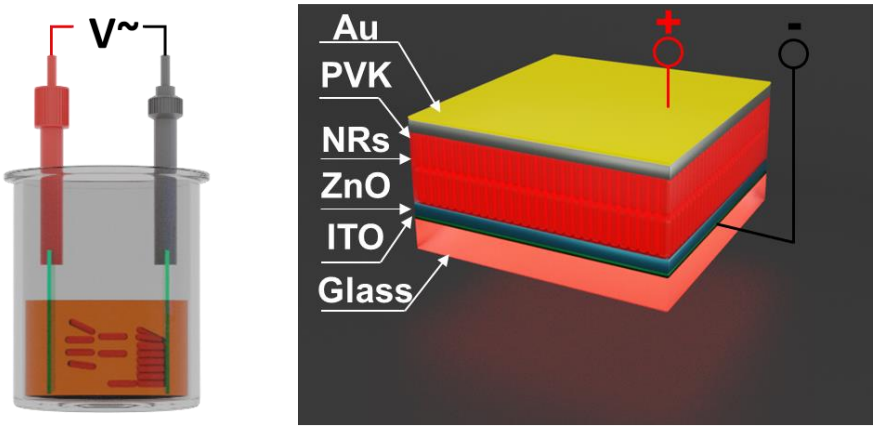
Anisotropic nanocrystals (NCs), such as semiconductor nanorods (NRs), exhibit unique optical and electrical properties arising from asymmetric quantum confinement. [1-2] Such features can be realized further at the device level thanks to ordered arrays of NRs created through directional interactions.[2-5] However, long-range assembly of colloidal anisotropic NCs into thin films with orientational and positional order has remained a challenge despite significant research efforts and advancements. Here, we achieve a vertically aligned film of NRs with high uniformity through a simple, replicable external field directed assembly approach. Afterwards, a reliable inverted LED with the ordered arrays of NRs was fabricated successfully. We realize that the vertically aligned NRs-based LED exhibits the outstanding optoelectronic performance owning to highly vertically uniform, 2-dimensional (2-D) superstructures with long-range order of quantum dots in NRs with superior properties. In particular, the LED achieves a superior value of the external quantum efficiencies (EQEs), ~0.8%, which is comparable to state-of-the-art LEDs produced by vacuum deposition. We believe that there are no fundamental obstacles to extending these techniques to differently coloured LEDs, which would lead to low-cost, large-area, high-efficiency, high-colour-quality, stable, all-solution-processed electroluminescent devices for both display and solid-state lighting technologies.



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Probing the Metal Binding Characteristics of Squaramides

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Squaramides have seen an explosion of research interest in recent years due to several favourable characteristics that provide applicability across diverse sections of the chemical and biological sciences,[1] his small organic scaffold provides ditopic hydrogen bonding units with two N-H hydrogen bond donors and two C=O hydrogen bond acceptors on a cyclobutenedione ring. Moreover, with a nitrogen lone pair capable of delocalising in to the four membered ring system, squaramides exhibit aromatic character (Hückel's rule: [4n + 2] π electrons, n = 0) that is increased when engaging in hydrogen bonding.[2] This makes squaramides highly valuable from a supramolecular chemistry perspective where these properties can be exploited in molecular recognition processes.

To date, much of the research in this regard has focused on anion recognition, however recent research suggests that squaramides may also be useful as a cation recognition scaffold. Metal cations, in particular, have several structural and functional roles and participate in a myriad of biochemical reactions.[3] Thus the design of artificial cation receptors is an active area of supramolecular chemistry research.

This poster will focus on some of our initial work on the synthesis of squaramide and thiosquaramide based cation receptors. We will also outline preliminary results on the binding behaviour of these receptors using a range of spectroscopic measurements such as NMR, absorption and IR spectroscopy.

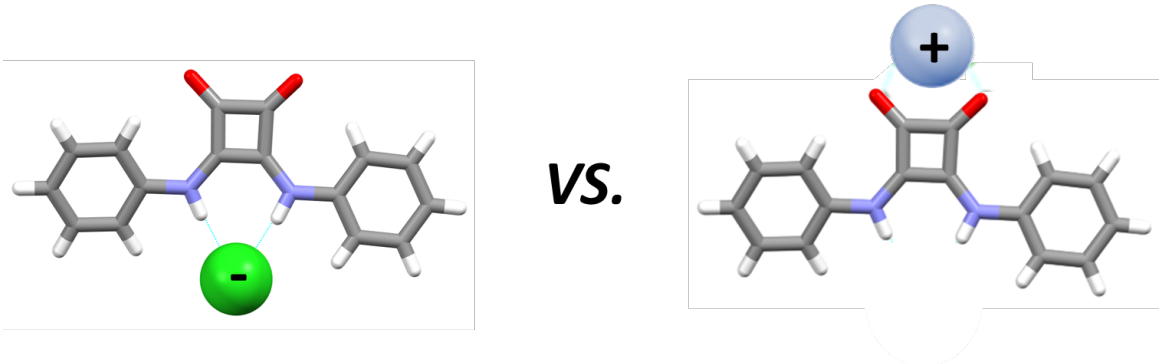

Figure 1: Schematic representation of squaramide anion recognition vs. cation recognition.

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Surface-accessible plasmonic Pickering emulsions as substrates for direct SERS analysis in bio-media

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The immense potential of plasmonic Pickering emulsions in future applications is well-recognized but hardly fulfilled. This is because there is currently no way to generate stable plasmonic Pickering emulsions without passivating the surface of the plasmonic nanoparticle building-blocks with strongly adsorbed chemical modifiers, which prevent further functionalization and/or applications.[1,2] Chemical modifiers have been irreplaceable in the synthesis of plasmonic emulsions since they are crucial to satisfying the stringent demands to the surface-chemistry properties of the plasmonic nanoparticles to form stable Pickering emulsions.[3]

Here, we demonstrate a universal and facile modifier-free approach that can be readily used to construct surface-accessible plasmonic emulsions from Ag and Au nanoparticles. The key to our approach lies in the use of "promoter" molecules, which remove interparticle electrostatic repulsion, without passivating the functional plasmonic nanoparticles. Importantly, this allowed the surface-enhanced Raman spectroscopy (SERS) analysis of small molecules which was not possible with conventional modifier-capped plasmonic emulsions, as shown in Figure 1, spectra i-iii. Moreover, the surface of the plasmonic components can be customized to introduce advanced functionalities such as self-calibration and filtration, which allows precise SERS quantitation in bio-media, as shown in Figure 1, spectrum iv. More broadly, this new approach provides a universal platform for synthesizing oil-in-water and water-in-oil Pickering emulsions carrying nanoparticles of different morphologies, compositions, surface-chemistry, and in turn, functionalities, which paves the way for the development of novel emulsion-based applications.

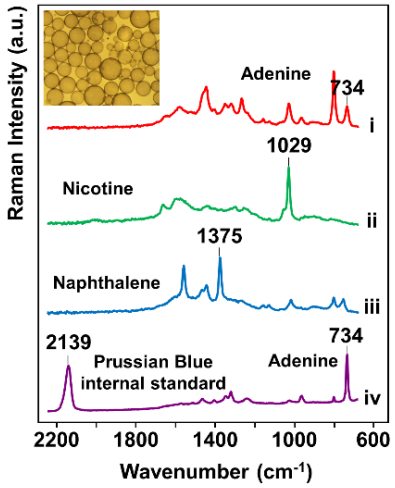

Figure 1. (i-iii) SERS signals of real-life analytes obtained using modifier-free Au Pickering emulsions. (iv) SERS signals of adenine in serum obtained using modifier-free Au Pickering emulsions functionalized with an internal standard. The intensity of the spectra has been rescaled for illustration. Inset shows optical image of the emulsions.

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