School of Chemistry

73rd Irish Universities Chemistry Research Colloquium

15-16th June 2022, UCD O'Brien Centre for Science

run annually under the aegis of the **Institute of Chemistry of Ireland**

SCHEDULE AND BOOK OF ABSTRACTS

https://www.ucd.ie/chem/newsevents/the73rdirishuniversitieschemistryresearchcolloquium/

Welcome to the 73rd Colloquium! It will be the first full face-to-face meeting of chemists on the Island since the Covid pandemic. We have 40 Talks in two parallel sessions and a Poster Session with 72 Posters. The latter is combined with a hot-food reception. Our Plenary Speaker, Dr Matthew O. Kitching, Durham University. He is presently Royal Society University Research Fellow at Durham, having been briefly at Dublin City University. He came to prominence last year with the "First Enantioselective Synthesis of Ammonium Cations" (Science, 2021), which was achieved via a supramolecular recognition process that allowed a thermodynamically driven adductive crystallization. This year, with his colleague Mark A, Walsh, he has in prospect an intriguing publication on "A Potentially Limitless Chiral Pool via Conglomerate Crystallisation: Unidentified Spontaneous Resolution in the CSD" (ChemRxiv Preprint, 2022). The next pages have the Schedule, List of Presenters and Titles and the List of Abstracts. We hope you have a good time at the Colloquium and get some good ideas for your Chemistry research. But first we set out formally our Dignity and Respect Responsibilities.

Our Responsibilities. As the Organising Committee we:

- want everyone to enjoy the Colloquium and feel able to contribute
- will not share any communication on anyone's personal circumstances/experience
- will treat everyone with dignity and respect and conduct ourselves in a respectful manner
- will be kind to each other and not insult or put down other Colloquium attendees
- will ensure that all communication, online or in person, will be appropriate for a professional audience and considerate of people from different cultural backgrounds
- will contribute to discussion with a constructive and positive approach
- seek actively to exclude harassment including (but not limited to): offensive verbal comments, exclusionary jokes, deliberate intimidation, stalking, following, harassing photography or recording, sustained disruption of discussions, inappropriate physical contact and unwanted sexual attention.

Your Responsibilities. As a Colloquium Participant, you agree to:

- foster equal participation
- maintain privacy/confidentiality
- not tolerate bullying, harassment, or discrimination
- respect people's identities & experiences
- engage with kindness and respect
- keep communication professional
- consider diverse cultural backgrounds
- contribute constructively.

Declan Gilheany, Susan Wilson, Deirdre Murphy and Sean Kenny Organising Committee

Thanks to our Generous Sponsors!

We are very grateful to our Sponsors without whom the Colloquium would not have been possible:

Institute of Chemistry of Ireland
Royal Society of Chemistry
(Republic of Ireland Local Section)
Almac Pharma Services
Agilent Technologies
Mason Technology
GPE Scientific
Fluorochem

ICI Chemistry Colloquium at UCD 2022
O'Brien Centre for Science 15/16 June

Final Schedule

Wed 15th June, 9.15 AM: Welcome: Professor Pat Guiry, President, Institute of Chemistry of Ireland

	Theatre D (Agilent Sponsored)	Theatre E (Mason Technology Sponsored)
9.30 – 10.50	**Organic Synthesis (Chair: P. Byrne)**	**Materials 1 (Chair: D.G. Gilheany)**
	Cian Reid	Aisling Fleming
	Sheila Fitzgerald	Yaoguang Song
	Ashis Dhara	Nilotpal Kapuria
	Alex Gibney	Reabetswe Zwane
	Tea/Coffee, Mounting of Posters	
11.30 – 12.50	**Reaction Mechanism (Chair E McGarrigle)**	**Materials 2 (Chair: K.M. Ryan)**
	Joshua O'Donnell	Vivek Christhunathan
	Gavin Lennon	Anthony Dodd
	Lorna Doyle	Mohini Mishra
	Sadbh Byrne	Yiming Huang
	Lunch (Local Outlets)	
2.00 – 3.00	**Biological Activity (Chair P.V. Murphy)**	**Chemical Imaging (Chair: J. Lowry)**
	Eoin Hever	David Cullinane
	Mark Stitch	Colm McKeever
	Caytlin Boylan	Niamh Curtin
	Tea/Coffee, Viewing of Posters, Presentation by Almac about Careers	
4.00 – 5.00	**Dr Matthew O. Kitching,** Durham University, Theatre D	
Almac	Enantioselective Crystallographic Synthesis of Ammonium Cations	
Plenary Lecture	and a Potentially Limitless Chiral Pool via Conglomerate Crystallisation	
5.30 – 8.30	**Poster Session** with associated Hot Food and Drinks reception	
	Sponsored by the Royal Society of Chemistry, Local Section	
	5.30 – 6.30 Even-Numbered Posters; 6.30 – 7.30 Odd-Numbered Posters	

Thursday 16th June	Theatre D (Fluorochem Sponsored)	Theatre E (GPE Scientific Sponsored)
9.30 – 10.50	**Flow Chemistry (Chair: M. Baumann)**	**Medicinal Chemistry (Chair: F. Kelleher)**
	Cormac Bracken	Cathal Caulfield
	Ailbhe Ryan	Karolina Wojtczak
	Lara Nolan	Hua Tong
	Aoife Kearney	Liam Fitzgerald
	Tea/Coffee	
11.30 – 1.10	**CO_2 Chemistry (Chair J. Sullivan)**	**Therapeutic Agents (Chair: S. Bell)**
	Florian Cerpentier	Ioannis Titilas
	Kristy Stanley	Neville Murphy
	Daniel Kerr	Ashutosh Sharma
	Qi Huang	Avelino Ferreira
	Amy Bridget Lowry	Erika Mooney

1.15-1.30 **Closing:** Professor James Sullivan & **Prize Giving:** Professor Pat Guiry (Prizes ICI Sponsored)

LIST OF PhD SPEAKERS, SEMINAR TITLES and PRINCIPAL INVESTIGATORS

Theatre D Wednesday

9.30-11.0 Organic Synthesis

Cian Reid	UCD	Pat Guiry	Novel Axially Chiral P,N Ligands and their Applications within Asymmetric Catalysis
Sheila Fitzgerald	RCSI	Donal O'Shea	Chirality Through Double Click Reactions with Sondheimer Diyne
Ashis Dhara	NUIG	Paul Murphy	Design, Synthesis and Biological Evaluation of Galectin Inhibitors
Alex Gibney	DCU	Andrew Kellett	Click and Cut: Towards the Simplified Preparation of Cu(II) Chemotherapeutics

11.30-1.00 Reaction Mechanism

Joshua O'Donnell	UCC	Peter Byrne	Development of a New Rationale to Account for Selectivity in Reactions of Ambident Nucleophiles
Gavin Lennon	QUB	Paul Dingwall	Insights into the Mechanism and Origin of Selectivity in PalladiumCatalysed Carbene Insertion Cross-Coupling Reactions
Lorna Doyle	TCD	Aidan McDonald	Activation of an $Mn^{II}Mn^{III}$-Peroxide with Relevance to the Catalytic Cycle of Ib RNRs
Sadbh Byrne	UCD	Declan Gilheany	Enantioselective Grignard Reactions in Total Synthesis: Development of Asymmetric Methodology and Exploration of New Targets

2.00-3.00 Biological Activity

Eoin Hever	NUIG	Paul Murphy	Design, Synthesis and Biological Evaluation of Galactosidase Inhibitors
Mark Stitch	UCD	Susan Quinn	Combining Spectroscopic techniques to Unravel the Binding of an Osmium Polypyridyl Probe to G-quadruplex Structures in Solution
Caytlin Boylan	MU	John Lowry	Monitoring Acetylcholine and Choline using Electrochemistry

Theatre E Wednesday

9.30-11.00 Materials 1

Aisling Fleming	UCD	Kenneth Dawson	Particle Mapping by Fluorescence Microscopy: Characterizing Surface Composition and Subpopulation Heterogeneity of Bionanocomposites
Yaoguang Song	QUB	Xiaolei Zhang & Peter Nockemann	Ionic liquid-assisted Synthesis of Mesoporous Carbons for Supercapacitors
Nilotpal Kapuria	UL	Kevin Ryan	Metal Seed Chemistry to Control Growth of Multicomponent Metal Chalcogenide Nanocrystals
Reabetswe Zwane	DCU	Joaquin Klug	The Elastic Properties of Postulated Solid Forms from First Principles

11.30-1.00 Materials 2

Vivek Christhunathan	NUIG	Mingming Tong	*Ab-initio* Modelling on the Electronic and Absorption Properties of Pure and Cu-Doped $CaWO_4$
Anthony Dodd	QUB	Peter Nockemann	Multidentate Amide Ligands for the Separation of Rare Earth Elements
Mohini Mishra	UL	Kevin Ryan & Shalini Singha	Colloidal Synthesis of Copper Telluride using Diphenylditelluride as Alternative Te Source
Yiming Huang	QUB	Steven Bell	Controlling Nanoparticle Aggregates for Stable SERS

2.00-3.00 Chemical Imaging

David Cullinane	DCU	Tia Keyes	Drug Delivery Technology for Cell Permeation of Novel Luminescent Ruthenium Polypyridyl Complexes for Cell Imaging & Therapeutics
Colm McKeever	MU	Eithne Dempsey	Latent Fingerprint Enhancement on Brass Substrates with the aid of Electrochromic and Redox Polymer Deposition
Niamh Curtin	RCSI	Donal O'Shea	Exploiting Directed Self-Assembly and Disassembly for off-to-on Fluorescence Responsive Live Cell Imaging

Theatre D Thursday

9.30-11.00 Flow Chemistry

Cormac Bracken	UCD	Marcus Baumann	The Photoflow Generation and Capture of Reactive Intermediates
Ailbhe Ryan	QUB	Mark Muldoon	Development of a Continuous Flow Process for the Epoxidation of Alkenes with Peracetic Acid and a Homogeneous Manganese(II) Catalyst
Lara Nolan	QUB	Peter Knipe	Continuous Synthesis of α-Substituted Cyclic Amines via C-H Functionalization Reactions
Aoife Kearney	UCC	Stuart Collins & Anita Maguire	Using Batch and Continuous Flow for the Synthesis of α-Sulfenyl-β-chlorolactams

11.30-1.10 CO_2 Chemistry

Florian Cerpentier	DCU	Mary Pryce	The Design and Study of Novel Ruthenium Supramolecular Assemblies for Photocatalytic Hydrogen Evolution and CO_2 Reduction
Kristy Stanley	UCD	James Sullivan	New Vistas of an Old Reaction
Daniel Kerr	DCU	Brian Kelleher	A Python Based Non-Linear Regression Model to Estimate Acid-Base Characteristics of Organic Alkalinity – Pilot Study Dublin Bay
Qi Huang	QUB	Chunfei Wu	Enhanced Efficiency of a Photo Switching Metal-Organic Framework Toward Low Energy Carbon Dioxide Capture
Amy Bridget Lowry	UCC	Peter Byrne & Gerard McGlacken	Synthesis of α,β-Unsaturated Carboxylic Acids by Phosphonium Ylide-Mediated CO_2 Activation

Theatre E Thursday

9.30-11.00 Medicinal Chemistry

Cathal Caulfield	RCSI	Donal O'Shea	Synthesis and Testing of Water-Soluble Near Infrared Azadipyrromethene (NIR-AZA) Fluorophores
Karolina Wojtczak	NUIG	Joseph Byrne	Shining a Light on Bacteria: Lanthanide-Based Glycoconjugate Molecular Sensors for Lectins
Hua Tong	MU	Robert Elmes	Squaratides: A New Family of Macrocyclic Peptidomimetics with Application as Anion Recognition Scaffolds
Liam Fitzgerald	NUIG	Paul Murphy	Docking of Sialic Acid Derivatives to Influenza Hemagglutinin and Synthesis of Glycoclusters Based on a Tetraphenylethylene Scaffold

11.30-1.10 Therapeutic Agents

Ioannis Titilas	NUIG	Luca Ronconi	Metal-based Glycoconjugates for Targeted Anticancer Chemotherapy
Neville Murphy	NUIG	Pau Farràs	Metallacarboranes: a Versatile New Player in Biomedicine
Ashutosh Sharma	SETU Water	Helen Hughes	Novel Process Strategies for the Stabilization of Biopharmaceuticals for Parenteral Use
Avelino Ferreira	RCSI	Marco Monopoli	In vitro and In vivo Biological Evaluation of Functionalized Ultrasmall Gold Nanoparticles for Targeted Drug
Erika Mooney	TUD	Bernie Creaven & Fintan Kelleher	Synthetic Strategies towards Improving the Solubility Profile of Novel Antimicrobial Coumarin Derivatives

LIST OF POSTER PRESENTERS, TITLES and PRINCIPAL INVESTIGATORS

No	Name	Univ	Principal Investigator	Poster Title
1	Aaron McCormack	NUIG	Paul V. Murphy	New Prospects of Carbohydrates as Chiral Auxiliaries for Tandem Cycloaddition Reactions: Batch vs Flow
2	Aidan Cregan	UCC	Peter Byrne	H-Phosphonate-Promoted Halogenation of Alcohols using Lithium Halides
3	Aine Coogan	TCD	Yurii Gun'ko	Chiroptically Active Copper Oxide Microstructures via Post-Synthetic Treatment of Cu-Al Layered Double
4	Aisling Fleming	UCD	Kenneth Dawson	Development of an Immunogold Mapping Strategy to Unravel the Biomolecular Architecture of Bionanocomposite Materials
5	Aleksandra Krajewska	TCD	Aidan McDonald	Synthesis of Negatively Charged 2D 2H-MoS_2 and Its Functionalization
6	Alice Parkes	UL	Emmet O'Reilly & Gavin Walker	Controlling the Polymorphism of Carbamazepine by Droplet-Confinement via Spray Drying
7	Amit Upadhyay	UCC	Timothy O'Sullivan	Development of a Synthetic Route to Novel IMPDH Inhibitors
8	Andreea Cislaru	MU	Roisin O'Flaherty	Characterisation of Serum IgG Glycosylation in Cystinosis
9	Ashis Dhara	NUIG	Paul V. Murphy	Design and Synthesis of Carbohydrate Based Galectin Inhibitors
10	Cathal Kelly	QUB	Stuart James	Scrambled Macrocycles for Greener Porous Liquids
11	Ciara Davis	TUS	Peter Downey	Effects of selenium Application on Growth and Selenium Uptake in Lettuce.
12	Ciara Tyner	UCC	Stuart Collins & Anita Maguire	Studies in Intramolecular Buchner Reactions
13	Clara Evans	MU	Denise Rooney & Frances Heaney	Stability and Biological Activity of Novel Silver-based Antifungals to Avoid Antimicrobial Resistance
14	Conor Geraghty	MU	Robert Elmes	The Design and Synthesis of Ruthenium (II) Polypyridyl Complexes as Luminescent Probes for Nitroreductase

15	Conor Shine	RCSI	Marc Devocelle	The Development of PEG-based Antimicrobial Peptidomimetics
16	Dara Curran	UCC	Peter Byrne	Phosphorus-based Reductive Etherification of Aldehydes
17	Darren Beirne	MU	Diego Montagner & Trinidad V-Torrijos	Development of Dual-action Pt(IV)-Tyrosine Kinase Inhibitor Pro-drug Conjugates Targeting Colorectal Cancer
18	David Ryan	UCC	Peter Byrne	A New Rationale to Describe Ambident Reactivity
19	Eimear Courtney	UCC	David Jones &. Gerard McGlacken	Application of a Supported Manganese Catalyst in C–H Activation and Reductive Transformations
20	Eoghain Murphy	MU	Eithne Dempsey	Dexamethasone Electroanalysis by Deposition of Copper on Glassy Carbon Electrodes with Quantitation in
21	Eoin Hever	NUIG	Paul V. Murphy	Design, Synthesis and Biological Evaluation of Galactosidase Inhibitors
22	Eoin Moynihan	MU	Diego Montagner & Trinidad V-Torrijos	Click-Pt(IV)-carbohydrate Pro-drugs for Treatment of Osteosarcoma
23	Eva Naughton	UCD	James Sullivan	Development of Cu_2O/Ag_3PO_4 Heterojunction Photocatalysts for Conversion of CO_2 into Fuels.
24	Farhad Mohammed	MU	Robert Elmes	Towards the Design and Synthesis of a New Biomimetic Code: Squaratides
25	Foteini Dimakopoulou	NUIG	Constantina Papatriantafyllopoulou	Novel Co_5 and Ni_4 Metal Clusters by the Combination of 2-Pyridyl Oximes with Polycarboxylic Ligands
26	Hannah McKeever	UL	Shalini Singh	Colloidal Synthesis of Copper Bismuth Selenide Nanocrystals as Ionic Semiconductors for Photovoltaic Absorbers
27	Hilal Kirpik	MU	Robert Elmes	A New 3-Substituted BODIPY dye: Synthesis, Crystal Structure, and Photophysical Properties
28	Hugh Mohan	DCU	Silvia Giordani	Supramolecular Functionalisation of B/N Co-doped Carbon Nano-onions for Theragnostic Applications
29	Jack Bennett	NUIG	Paul V. Murphy	Applying Continuous Flow Techniques in the Synthesis of Sugar-based Therapeutics
30	Jacqueline Smyth	RCSI	Donal O'Shea	Exfoliation and Surface Functionalisation of Graphene in Water

31	Justynne Joy Fabian	TUD	Brendan Duffy	Surface Modification of Titanium Alloys for Biomedical Applications
32	Kate Donaghy	UCD	Eoghan McGarrigle	Stereoselective Synthesis of α-Galactosides
33	Kathryn McCarthy	NUIG	Pau Farràs	Two-Dimensional Porphyrin-Based Covalent Organic Frameworks as Photosensitizers for Light-Driven CO_2 Reduction
34	Keane Mc Namee	MU	John Lowry	The Development and Characterisation of a Biosensor for the Real-time Neurochemical Monitoring of Lactate
35	Keelan Byrne	MU	Tobias Krämer	Quantum Chemical Study of Low-Valent Aluminium Compounds
36	Kishan Mandal	NUIG	Paul V. Murphy	Design and Synthesis of Sialyl Triazoles as Siglec-8 Ligands
37	Kyle Doherty	MU	Trinidad Velasco-Torrijos	Development of Norbornene-based Compounds with Proposed Synergistic Anti-biofilm and Anti-adhesion Activities
38	Laura Foley	UL	Emmett O Reilly	Developing a Roadmap to Effective Spray Drying of Biomolecules
39	Lauren Kearney	DCU	Mary T. Price	Photocatalytic & Electrocatalytic Investigation into Rhenium Tricarbonyl N-Heterocyclic Carbene Complexes for CO_2 Reduction
40	Levente Nagy	NUIG	Pau Farràs	Biphenyl Bridging Ligands as Building Blocks for Photoluminescent One-dimensional Gold Coordination Polymers
41	Lewis More O Farrell	TUD RCSI	Christine O'Connor & Darren Griffith	Next-Generation Gallium Complexes to Combat Antimicrobial Resistance
42	Liam Fitzgerald	NUIG	Paul V. Murphy	Outcome of Docking of some Simple Sialic acid Derivatives to Influenza Hemagglutinin and Synthesis of Glycocluster
43	Lorna Doyle	TCD	Aidan McDonald	Activation of a $Mn^{II}Mn^{III}$-Peroxide with relevance to the Catalytic Cycle of Ib RNRs
44	Luke Brennan	MU	Robert Elmes	A Supramolecular Approach to Anti-Microbial Resistance: Anionophores that Induce Disruption of Bacterial Chloride Homeostasis
45	Mairéad Gallagher	TUD	Fintan Kelleher	Antibiotic Metabolites: Synthesis and Characterisation of the Human Metabolites of Ciprofloxacin
46	Manting Mu	TCD	Max García-Melchor.	Mechanistic Insights into the Ferration of Aromatic Substrates via Intramolecular Sodium Mediation

47	Maria Zubair	UL	Kevin M. Ryan &. Shalini Singh	Compositionally Tunable Cu-Sb-M-S (M= Zn, Co and Ni) Nanocrystals: Synthesis and their Transport Properties
48	Marie Clara Michel	UCC	Peter Byrne & Gerard McGlacken	One Pot Tandem Wittig Hydrogenation Reactions to form $C(sp^3)$-$C(sp^3)$ in Water
49	Martina Tuberti	TUD	Fintan Kelleher	Computational Studies in Human Tau Protein Screening for Understanding the Impact in Alzheimer's disease
50	Martyna Bartusiak	DCU	Mary T. Price	A Time-Resolved Spectroscopic Analysis of Novel Porphyrins and Utilisation of their Aggregation in Dye-sensitized Solar Cells
51	Mary Hennessy	UCC	Timothy O Sullivan	Preparation of 1,2-Dioxolanes via the Enantioselective Peroxidation of γ,δ-Unsaturated-β-Keto Esters
52	Michal Bartkowski	DCU	Silvia Giordani	Smart Carbon Nano-onion Systems for Drug Delivery
53	Mona Alanazi	NUIG	Constantina Papatriantafyllopoulou	Novel Mixed-Ligand Coordination Polymers and Metal-Organic Frameworks
54	Niraj Nitish Patil	UL	Kevin M. Ryan & Shalini Singh	Tuning Polytypism in Transition Metal Disulphides by Precursor Reactivity Manipulation and Application in
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
57	Qinglu Chen & Heather McDonald	QUB	Steven Bell	SERS Analysis of Organic Extractants using 2D Hydrogel-based Nanoparticle Arrays
58	Rachel Lynch	UCC	Peter Byrne	Carbon Dioxide Utilisation for Construction of High Value CarboxylContaining Organic Products and Biologically Active Compounds
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
62	Robert Fox	DCU	Joaquin Klug	Stability of Co-crystals: a Density Functional Theory Study

63	Shan Huang	UCC	Simon Lawrence	Pharmaceutical Salts of Piroxicam and Meloxicam with Organic Counterions
64	Shane Grant	NUIG	Alan Ryder	Elemental Screening of Cell Culture Media using Microwave Plasma Atomic Emission Spectroscopy
65	Simon Poole	DCU	Andrew Kellett	Development of Holliday Junction-stabilising complexes via Click Chemistry: a new Gene Targeting Strategy for Metal-based Drugs
66	Siobhán O'Flaherty	RCSI	Marc Devocelle	Synthesis of Cholesterol-Modified Antimicrobial Peptides
67	Tara Barwa &. Yiran Luo	MU	Carmel Breslin	Development of a Bismuth Modified Molybdenum Disulfide Sensor for the Detection of Antibiotic Drugs in Water
68	Usaid Azhar	ATU Sligo	Ioannis Manolakis	Synthesis and Characterization of PEG_{400}-DOPA for Multifunctional Coatings
69	Vanessa Becker	UCD	Eoghan McGarrigle	Bis-heteroaryl Synthesis via Pyridylsulfonium Salts
70	Xuan-Manh Pham	UL	Kevin M. Ryan	The Inverted Device Fabricated by Electrophoretic Deposition with high Luminescence and high EQE
71	Xuanyang Luo	MU	Robert Elmes	Probing the Metal Binding Characteristics of Squaramides
72	Yingrui Zhang	QUB	Yikai Xu	Surface-accessible Plasmonic Pickering Emulsions as Substrates for Direct SERS Analysis in Bio-media

Novel Axially Chiral P,N Ligands and their Applications in Asymmetric Catalysis

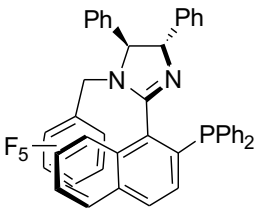
Patrick J. Guiry and Cian M. Reid

UCD Centre for Synthesis and Chemical Biology, School of Chemistry, University College Dublin, Belfield, Dublin 4, Ireland

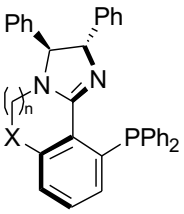
email: p.guiry@ucd.ie, cian.reid@ucdconnect.ie

Axially chiral P,N ligands are a prominent class of privileged ligand that has seen success throughout the field of asymmetric transition metal catalysis, with their success originating from their two separate donor atoms.[1] In 2017, Guiry reported the synthesis of (*S*,*S*,R_a)-UCD-Phim, an axially chiral phosphino-imidazoline P,N ligand with applications in enantioselective A^3 coupling reactions.[2] (*S*,*S*,R_a)-UCD-Phim is capable of effective asymmetric transition metal catalysis up to 40 °C, above which the ligand begins to epimerise.

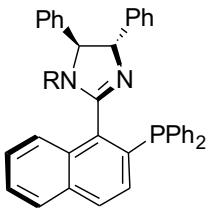
The project goal was the synthesis of axially chiral P,N ligands of the type **1** and **2** with increased barriers to rotation compared to (*S*,*S*,R_a)-UCD-Phim and therefore, capable of asymmetric catalysis at higher temperatures. Ligand **1** contains a bridged axially chiral system and ligand **2** contains increased steric bulk, both to increase the barrier to rotation. A further objective of the project is to test the ligands' catalytic activity and enantiodifferentiating ability in transition metal catalysis. Presented here is a summary of the syntheses of all ligands to date and their applications within asymmetric transition metal catalysis.



(*S*,*S*,R_a)-UCD-Phim



1



2

References:

[1] Rokade, B. V. Guiry, P. J. *ACS Catal*. **2018**, *8*, 624.
[2] Rokade, B. V. Guiry, G. J. *ACS Catal*. **2017**, *7*, 2334.

EPSPG/2019/416

Chirality Through Double Click Reactions with Sondheimer Diyne

Sheila Fitzgerald and Donal O'Shea

Department of Chemistry, RCSI, 123 St. Stephen's Green, Dublin 2
email: shfitzgerald@rcsi.ie

Strain promoted azide-alkyne [3+2] cycloadditions have become a popular route for bioconjugations due to their mild, catalyst free reaction conditions and can be used to readily functionalise biomolecules.[1] The Sondheimer diyne **1** is a unique choice of strained alkyne for cycloadditions as it reacts through a 'double click' sequence under mild rt conditions.[2]

Initial investigations during my research using benzyl azide as the cycloaddition substrate have given indications that the saddle shaped substituted tetra-arylene product **2** is chiral through NMR and DFT experiments (Figure inset). Expanding the use of these facile double cycloadditions for macrocylizations, the bis-azide substituted azadipyrromethene **3** (generated in six synthetic steps using a related published route[3]) has been reacted with **1** to yield the cyclic product **4** in good yield. NMR investigations using the chiral shift reagent (+)-camphorsulfonic acid showed clear indications of chirality. Furthermore, BF_2-chelation of **4** with $BF_3.OEt_2$ gave the highly fluorescent product **5** (λ_{max} 695 nm) which also showed related characteristics in the ^{19}F NMR. The synthesis, characterization and uses of **5** will be discussed.

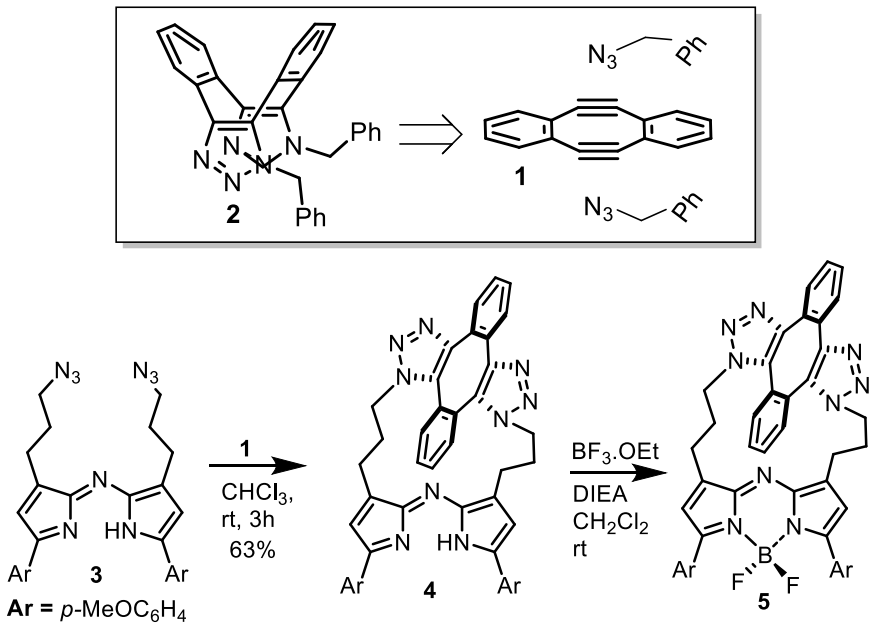


Figure 1. *Double click reactions with Sondheimer diyne and its use for macrocyclizations.*

References:

[1] Dommerholt, J.; Rutjes, F. P. J. T.; van Delft, F. L., *Top. Curr. Chem.* **2016**, *374*, 16.
[2] Yoshida, S.; Shiraishi, A.; Uekusa, H.; Hosoya, T., *Sci. Rep.* **2011**, *1*, 82.
[3] Wu, D.; Sampedro, G.; O'Shea, D.F. *Front. Chem. Sci. Eng*. **2020**, *14*, 97.

Grant Code: 2375

Design, synthesis and biological evaluation of galectin inhibitors

Ashis Dhara, and Paul V. Murphy*

School of Chemistry, National University of Ireland Galway,
University Road, Galway, Ireland. H91 TK33

E-mail: a.dhara2@nuigalway.ie; paul.v.murphy@nuigalway.ie

Galectins are galactoside binding specific subclass of lectins (carbohydrate binding proteins). This family of proteins are classified into three subfamilies based on the structure and number of carbohydrate recognition domains (CRD). Galectins involve in several cellular activities, certain cancers, infections, inflammations, fibrosis, HIV, and many other wide range of biological processes. The molecular basis for the selectivity of galectins is well documented and revolves around appropriate interactions of glycans with amino acid residues. The selectivity for galactose moiety stems largely from the hydrogen bonds (HBs) between histidine-158 (His-158)/arginine-162 (Arg-162) and the axial hydroxyl (-OH) at the 4-position. This axial hydroxyl is equatorial oriented in analogous O-linked β-glucosides. Mimetics of glycan ligands have been of interest.

We have synthesised "the clickable" intermediate (**3, 5** and **6**) from β-D-galactose and current focus is given to its modification at the C1 and C3 position with the suitable pharmacophore to increase the affinity for galectins. For example, Nilsson et al[1] reported that galactose C3-modification via click chemistry **(5)** stacked above the Arg144 sidechain, which in turn forms a water-mediated salt-bridge with Asp-148. In a variation of this strategy we have synthesised several compounds and tested them as inhibitors of galectin-8, and these compounds will be further tested against other members of the galectin family. Overall, this oral presentation will describe the synthesis and biological study of putative galectin inhibitors, mainly targeting galectin-3 and 8.

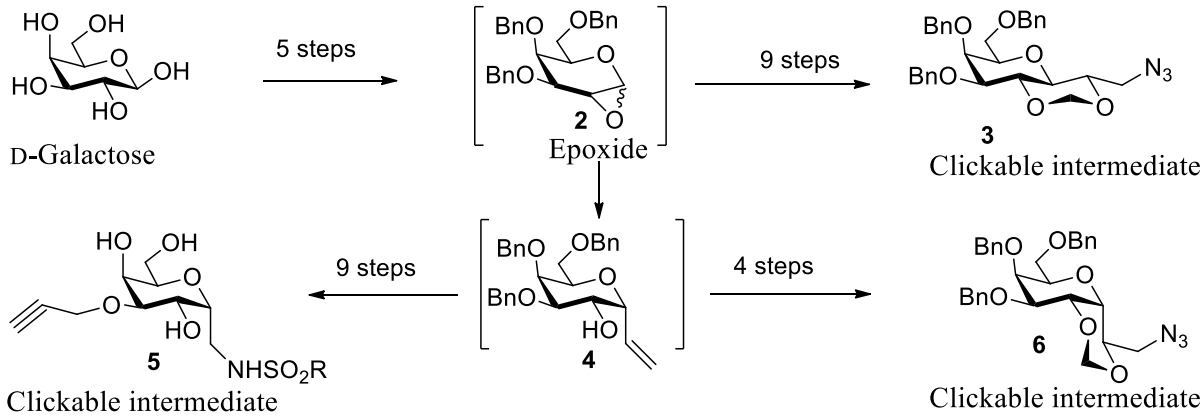


Fig: Summary of the synthesis of **3, 5** and **6**

Reference:

1) Alexander Dahlqvist, Fredrik R. Zetterberg, Hakon Leffler and Ulf J. Nilsson, *Med. Chem. Commun*., **2019**, 10, 913–925.

Science Foundation Ireland For what's next

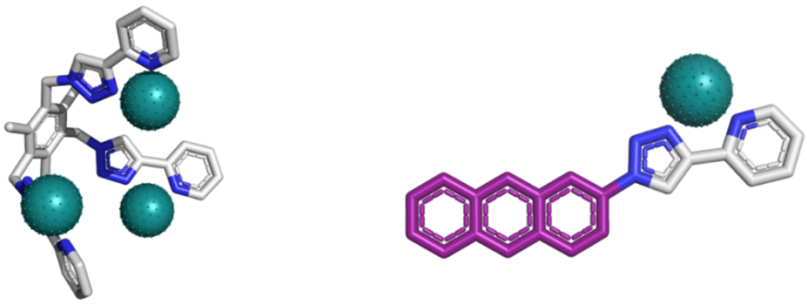
Click and Cut: Towards the Simplified Preparation of Cu(II) Chemotherapeutics

Alex Gibney[1,2], Creina Slator[1], Raphael De Paiva[1] and Andrew Kellett[1,2]

1. *School of Chemical Sciences, Dublin City University, Glasnevin, Dublin 9, Ireland*
2. *SSPC, the Science Foundation Ireland Research Centre for Pharmaceuticals, School of Chemical Sciences, Dublin City University, Glasnevin, Dublin 9, Ireland*

email: andrew.kellett@dcu.ie , alex.gibney3@mail.dcu.ie

The clinical success of transition metal complexes as therapeutic agents has long been dominated by Pt(II) drugs. The ability of Pt(II) complexes to penetrate cell membranes, via copper transport machinery, and form covalent adducts with DNA bases has allowed Pt-based agents to save, improve and/or elongate countless lives since the first clinical approval of Cisplatin. The use of such agents, however, has also become synonymous with the side effects, toxicities and resistance commonly associated with cancer chemotherapy.[1] In the effort to overcome these issues, alternative transition metals such as Cu(II) have been shown to induce oxidative cleavage of DNA.[2,3] Polynuclear Cu(II) complexes have consistently proven to be among the most potent of these artificial metallonucleases (AMNs).[4] In this work, a simplified method of preparing trinuclear Cu(II) AMNs, using the Cu(I)-catalysed alkyne-azide cycloaddition (CuAAC) is reported.[5] We demonstrate that "Tri-click" (TC) AMNs possess DNA binding and cleavage properties consistent with state-of-art marine alkaloid-based nucleases that are accessed by more complex chemistries (Figure 1A). The ability of TC complexes to induce intracellular DNA damage was investigated using single molecule imaging of cellular DNA extracts that were subject to repair using fluorescently modified deoxynucleoside triphosphates (dNTPs). Finally, the versatility of the click and cut approach is demonstrated in the repurposing of known DNA binding agents such as the triazolyl-pyridyl anthracene derivative, ACP (Figure 1B).



A B

Fig. 1 Models of Click and Cut complexes. A) $[Cu_3(TC\text{-}Pyr)]^{6+}$ B) $[Cu(ACP)]^{2+}$.

(1) Kelland, L. The Resurgence of Platinum-Based Cancer Chemotherapy. *Nat Rev Cancer* **2007**, *7* (8), 573–584. https://doi.org/10.1038/nrc2167.

(2) Kellett, A.; Molphy, Z.; Slator, C.; McKee, V.; Farrell, N. P. Molecular Methods for Assessment of Non-Covalent Metallodrug–DNA Interactions. *Chem. Soc. Rev.* **2019**, *48* (4), 971–988. https://doi.org/10.1039/C8CS00157J.

(3) *Metal-Based Anticancer Agents*; Casini, A., Vessières, A., Meier-Menches, S. M., Eds.; Metallobiology; Royal Society of Chemistry: Cambridge, 2019.

(4) Slator, C.; Molphy, Z.; McKee, V.; Long, C.; Brown, T.; Kellett, A. Di-Copper Metallodrugs Promote NCI-60 Chemotherapy via Singlet Oxygen and Superoxide Production with Tandem TA/TA and AT/AT Oligonucleotide Discrimination. *Nucleic Acids Research* **2018**, *46* (6), 2733–2750. https://doi.org/10.1093/nar/gky105.

(5) McStay, N.; Slator, C.; Singh, V.; Gibney, A.; Westerlund, F.; Kellett, A. Click and Cut: A Click Chemistry Approach to Developing Oxidative DNA Damaging Agents. *Nucleic Acids Research* **2021**, *49* (18), 10289–10308. https://doi.org/10.1093/nar/gkab817.

Funded by SSPC in collaboration with MSD Ireland

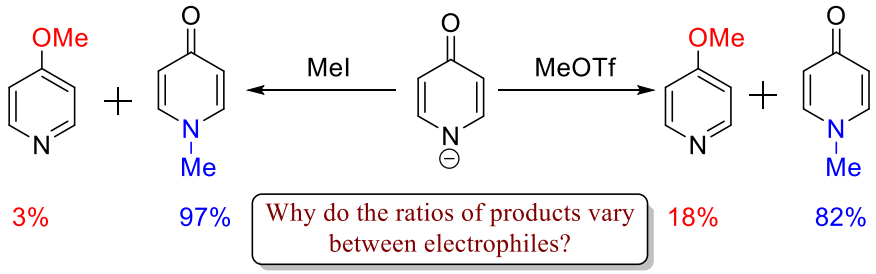
Development of a New Rationale to Account for Selectivity in Reactions of Ambident Nucleophiles

Joshua O'Donnell, Kevin Sheehy, David Ryan and Dr. Peter Byrne

School of Chemistry, University College Cork, College Road, Cork, Ireland

email: joshua.odonnell@umail.ucc.ie, peter.byrne@ucc.ie

The most widely used rationale for the understanding of reactivities of ambident species (nucleophiles and electrophiles), based on the principle of hard and soft acids and bases(HSAB principle)[1], leads to a major problem: it incorrectly predicts the products in almost 50% of all known reactions of ambident nucleophiles.[2,3]. Since the HSAB principle is not capable of reliably accounting for selectivities in reactions of ambident nucleophiles, we have set about developing a new rationale that is consistent with all experimental results from reactions of ambident nucleophiles. Our model has been shown to work for enolates, and we wanted to establish if it works for other ambident nucleophiles; 2- and 4-pyidone anions. The project involves carrying out reactions of nucleophiles with a series of different methylating and ethylating agents of differing Lewis acidity.



Scheme 1: Reactions of ambident nucleophiles with different electrophiles giving different results, why?

Specific trends were observed in carrying out alkylation reactions with both the 4-pyridone anion and 2-pyridone anion (**Scheme 1**; different counter-cations were employed). For example; reactions of 4-pyridone anion with MeI show the greatest preference for N-methylation. The proportion of N-alkylation product formed in reactions with other methylating agents decreases in the order MeI (97%), MeOTs (96%), MeOMs (94%) and MeOTf (82%).

To generate a series of Gibbs energy surface diagrams; a reaction with known $\Delta G^{\ddagger}$ value is chosen and the curvature of the parabolas is determined using computationally derived data, the parabolas can then be positioned according to the $\Delta_r G°$ (computational thermodynamic data), $\Delta G^{\ddagger}$ (experimentally determined activation energy) and $\Delta\Delta G^{\ddagger}$ (from experimentally determined product ratios) values, the remaining reactant parabolas are placed in a similar fashion by utilising the predicted $\Delta G^{\ddagger}$ and $\Delta\Delta G^{\ddagger}$ values.

References:

[1] (a) Pearson, R. G. Science **1966**, 151, 172–177; (b) Klopman, G. J. Am. Chem. Soc. **1968**, 90, 223–234; (c) Salem, L. J. Am. Chem. Soc. **1968**, 90, 543–552.
[2] Maiti, S.; Mal, P. J. Org. Chem. **2018**, 83, 1340.
[3] Mayr, H.; Breugst, M.; Ofial, A. R. Angew. Chem. Int. Ed. **2011**, 29, 6470.
[4] Sheehy, K. J.; Bateman, L. M.; Flosbach, N. T.; Breugst, M.; Byrne, P. A. Chem. Sci. **2020**, 11, 9630.

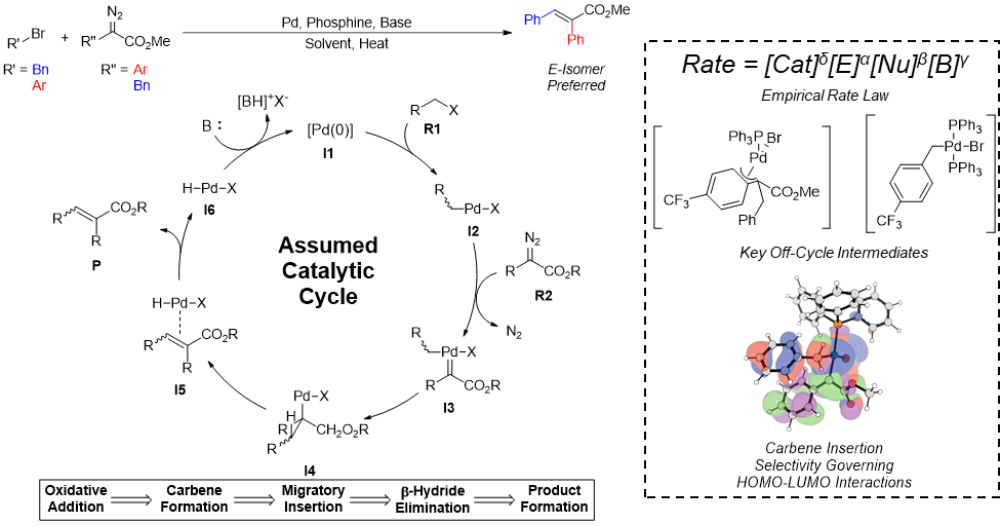
Insights into the Mechanism and Origin of Selectivity in Palladium-Catalysed Carbene Insertion Cross-Coupling Reactions

Gavin Lennon and Paul Dingwall

School of Chemistry and Chemical Engineering, Queen's University Belfast, Antrim, Ireland

email: glennon03@qub.ac.uk, p.dingwall@qub.ac.uk

The need for a first principles understanding of any catalytic cycle is paramount for the rational design of catalyst architecture and synthetic routes. Palladium-catalysed carbene insertion cross-coupling reactions, despite being an ever-evolving class of catalytic transformations, remain a mechanistic ambiguity.[1],[2] Here, we will discuss an in-depth study into their mechanism and the origins of selectivity for 1,1,2-trisubstituted olefin formation.[3],[4]



The intrinsic reaction kinetics were determined using the VTNA graphical rate equation method[5] while NMR spectroscopy and high resolution mass spectrometry were employed to identify multiple catalyst resting states and parasitic species. Theoretical investigations relied on DFT calculations with energy span and degree of TOF control analyses[6] reinforcing our experimental observations. The origin of selectivity is suggested to arise from bifurcation of the catalytic cycle during migratory insertion, rather than the widely assumed β-hydride elimination, with this novel model for selectivity appearing generally applicable to other ambiguously selective palladium carbene insertion reactions in the literature.

References:

[1] K. L. Greenman, D. S. Carter, D. L. Van Vranken, *Tetrahedron* **2001**, *57*, 5219-5225.
[2] K. L. Greenman, D. L. Van Vranken, *Tetrahedron* **2005**, *61*, 6438-6441.
[3] W.-Y. Yu, Y.-T. Tsoi, Z. Zhou, A. S. C. Chan, *Org. Lett.* **2009**, *11*, 469-472.
[4] C. Peng, G. B. Yan, Y. Wang, Y. B. Jiang, Y. Zhang, J. B. Wang, *Synthesis-Stuttgart* **2010**, 4154-4168.
[5] J. Burés, *Angew. Chem. Int. Ed.* **2016**, *55*, 16084-16087.
[6] S. Kozuch, S. Shaik, *Acc. Chem. Res.* **2011**, *44*, 101-110.

Engineering and Physical Sciences Research Council

Grant Code: GL – EP/N509541/1

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

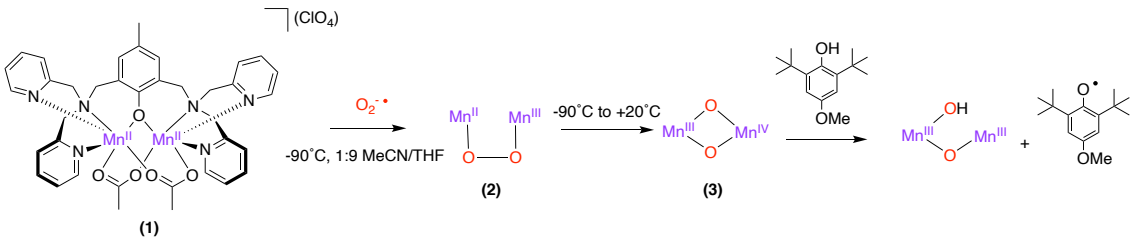
Lorna M. Doyle[a], Shuangning Xu[b], Lawerence Que Jr[b], Aidan R. McDonald[a]

[a]School of Chemistry, Trinity College Dublin, the University of Dublin, (Ireland); [2]Department of Chemistry and Center for Metals in Biocatalysis, University of Minnesota, Minneapolis, Minnesota, (United States)

email: ldoyle8@tcd.ie

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.



References:

[1] Cotruvo, J.A.; Stubbe, J. *Ann. Rev. Biochem.* **2011**, *80* (1),733.
[2] Cotruvo, J. A.; Stich, T. A.; Britt, R. D.; Stubbe, J., *J. Am. Chem. Soc.* **2013**, *135* (10), 4027.
[3] (a) Suzuki, M.; Mikuriya, M.; Murata, S.; Uehara, A.; Oshio, H.; Kida, S.; Saito, K., *Bull. Chem. Soc. Jpn.* **1987**, *60* (12), 4305 (b) Blanchard, S.; Blondin, G.; Rivière, E.; Nierlich, M.; Girerd, J.-J., *Inorg. Chem.* **2007**, *42* (15), 4568.
[4] Magherusan, A. M.; Kal, S.; Nelis, D. N.; Doyle, L. M.; Farquhar, E. R.; Que, L.; McDonald, A. R., *Angew. Chem. Int. Ed.* **2019**, *58* (17), 5718–5722.

Fondúireacht Eolaíochta Éireann Dá bhfuil romhainn

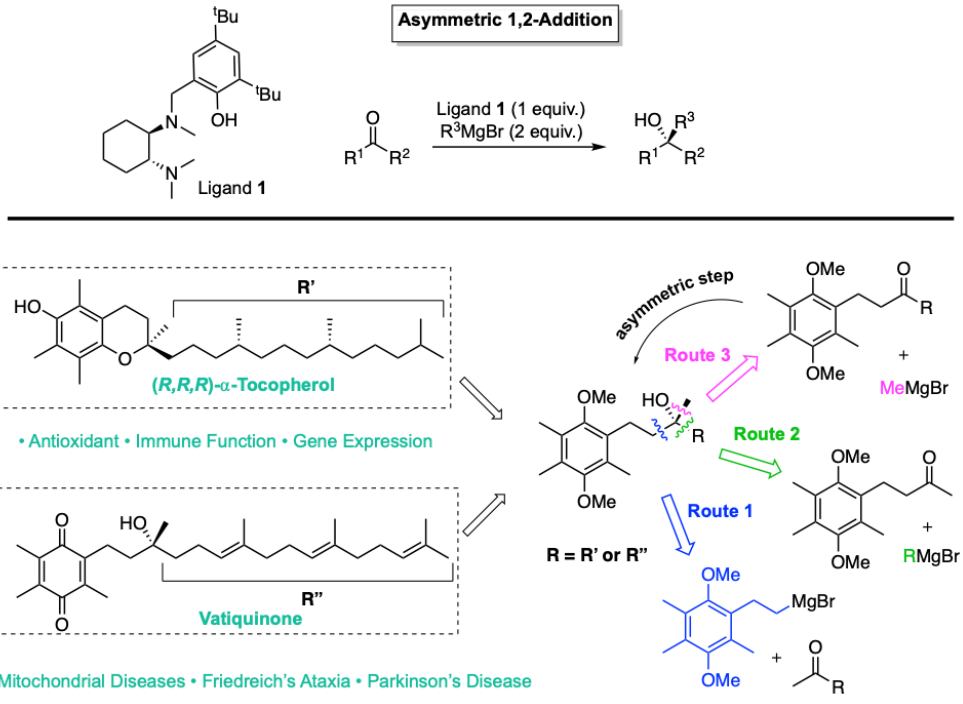
Enantioselective Grignard Reactions in Total Synthesis: Development of Asymmetric Methodology and Exploration of New Targets

Declan G. Gilheany and Sadbh E. Byrne
UCD Centre for Synthesis and Chemical Biology, School of Chemistry, University College Dublin, Belfield, Dublin 4, Ireland
email: declan.gilheany@ucd.ie, sadbh.byrne@ucdconnect.ie

Grignard reagents have been widely used across academia and industry to enable C-C bond formation for over a century. In the presence of a chiral additive, direct 1,2-addition of a Grignard reagent to a ketone is an efficient way of synthesizing chiral tertiary alcohols, a common structural motif in natural and synthetic products. Our asymmetric Grignard method involves the use of an inexpensive chiral tridentate phenol/diamine-type (NNO) ligand, which can be easily recovered and reused.[1,2] The identity of the halogen, order of addition and equivalents of Grignard reagent were examined to discover more enantioselective and efficient ways of performing this asymmetric transformation.

The naturally occurring stereoisomer of vitamin E, (*R,R,R*)-*α*-tocopherol exhibits the highest activity but still lacks an economic total synthesis. Over 30,000 tonnes of synthetic all-rac vitamin E are produced per annum. This material contains a mixture in equal parts of all 8 stereoisomers. A synthesis to the active *RRR* stereoisomer is highly desired to cut production of the other 7 stereoisomers which lack bioactivity. Our asymmetric Grignard methodology has been applied to the total synthesis of (*R,R,R*)-*α*-tocopherol.[3] Using a three-way disconnection approach, the key tertiary alcohol precursor was synthesised asymmetrically via three different routes. The methodology was further applied to the total synthesis of vatiquinone, a stage 2/3 clinical therapeutic against several rare mitochondrial diseases.

Furthermore, we have explored other uses of our NNO-type ligands and successfully applied our Grignard methodology in transition metal-free enantioselective 1,4-conjugate addition reactions, obtaining > 90% *ee*.



[1] B. Bieszczad, D. G. Gilheany, *Angew. Chem. Int. Ed.* **2017**, *56*, 4272–4276.
[2] C. Monasterolo, R. O'Gara, S. Kavanagh, S. E. Byrne, B. Bieszczad, O. Murray, M. Wiesinger, R. Lynch, K. Nikitin, D. G. Gilheany, *Chem. Sci.* **2022**, Advance Article.
[3] B. Bieszczad, D. G. Gilheany, *Org. Biomol. Chem.* **2017**, *15*, 6483–6492.

IRISH RESEARCH COUNCIL
An Chomhairle um Thaighde in Éirinn
Grant code: GOIPG/2018/2256

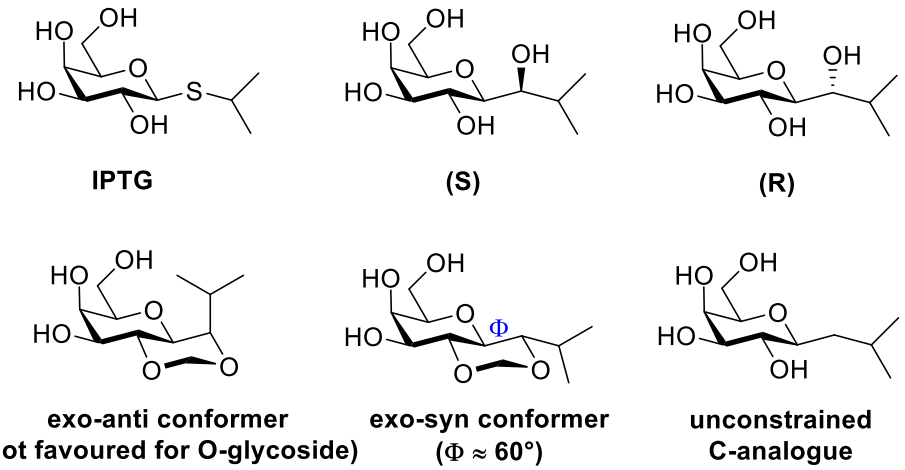
Design, Synthesis and Biological Evaluation of Galactosidase Inhibitors

Paul V. Murphy and Eoin Hever

School of Chemistry, National University of Ireland Galway, University Road, Galway, Ireland. H91 TK33

email: e.hever2@nuigalway.ie; paul.v.murphy@nuigalway.ie

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.

References:

(1) Ko, K.-S.; Kruse, J.; Pohl, N. L. Synthesis of Isobutyl-C-Galactoside (IBCG) as an Isopropylthiogalactoside (IPTG) Substitute for Increased Induction of Protein Expression. *Org. Lett.* **2003**, *5*, 1781–1783.

Combining Spectroscopic techniques to Unravel the Binding of an Osmium Polypyridyl Probe to G-quadruplex Structures in Solution

Mark Stitch,[a] Kateřina Peterková,[b] Rayhaan Boota,[c] Alannah S. Chalkley,[d] Jeremy C. Simpson,[d] Peter Podbevšek,[b] Janez Plavec,[b] Paul A. Scattergood,[c] Paul I. P. Elliot,[c] and Susan J. Quinn[a]

(a) School of Chemistry, University College Dublin, Belfield, Dublin 4, Ireland
(b) Slovenian NMR Center, National Institute of Chemistry, Hajdrihova 19, 1000, Ljubljana, Slovenia
(c) Department of Chemical Sciences, School of Applied Sciences University of Huddersfield, UK
(d) School of Biology & Environmental Science, University College Dublin, Dublin 4, Ireland.

email: susan.quinn@ucd.ie, mark.stitch@ucdconnect.ie

Luminescent probes of different DNA sequences and structures are critical diagnostic tools. Quadruplex DNA (G4), formed by guanine(G)-rich sequences, which are over-expressed in oncogene promoter regions, is an important target structure.[1] The Quinn group has previously studied G4 binding of a ruthenium polypyridyl complexes containing an intercalating dppz (dipyrido[3,2-a:2',3'-c]phenazine) ligand.[2] In this work the preparation of related osmium complex, $[Os(TAP)_2(dppz)]$ [**1**] (Figure 1a) is reported, which absorb red light, allowing deeper tissue penetration while the NIR emission at 750 nm avoids autofluorescence, enabling improved cellular detection.

The emission of **1** is enhanced in the presence of DNA, with greater enhancement for AT than GC regions and shows a sensitivity to TA over AT steps in model DNA sequences.[2] Additionally, **1** is found to bind strongly to G4 structures formed in the cMYC promoter region, with enantiomeric luminescence sensitivity (Figure 1b). Results from Time resolved Infrared (TRIR) provide a detailed picture of excited state dynamics on an ultrafast timescale. TRIR also reports the DNA bases (region 1600-1800 cm^{-1}) affected by the excited state, which combined with solution NMR studies indicates binding at the terminal guanine base stack (Figure 1c). [4]

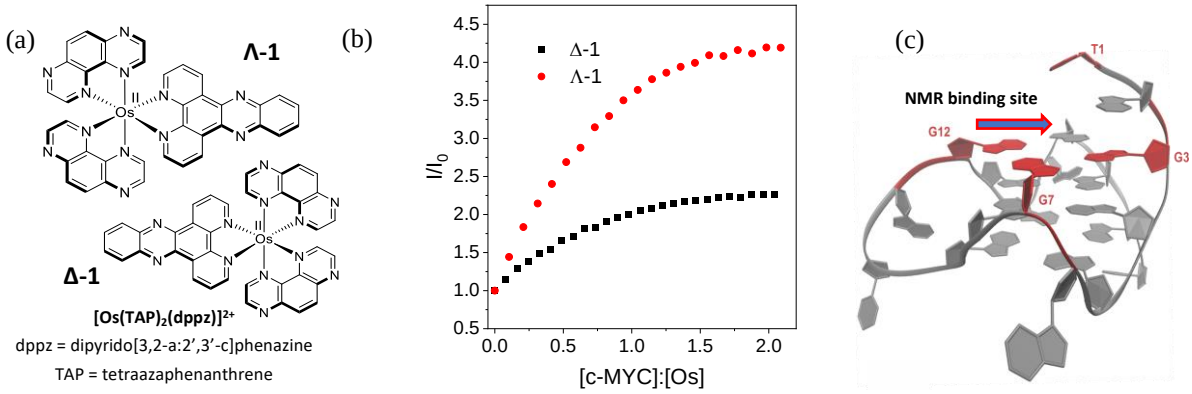


Figure. 1 (a) Complex used in study, (b) [**1**] enantiomeric luminescence enhancement upon binding to (cMYC) G4 and (c) NMR determined binding site of [**Λ-1**] binding to (cMYC) G4 highlighted in red.

References

[1] S. Neidle, J. Med. Chem. 2016, 59, 5987−6011.
[2] S. Devereux, *et al., Chem. Eur. J.*, 2020, 10, 2165.
[3] M. Stitch, R. Boota, A. S. Chalkley, J. C. Simpson, P. A. Scattergood, P. I. Elliott, S. J. Quinn, *Inorg. Chem., (under review).*
[4] K. Peterková, M. Stitch, R. Boota, P. A. Scattergood, P. I. Elliott, P. Podbevšek, J. Plavec, S. J. Quinn, *(to be submitted to Angew. Chemie).*

Light DyNAmics
Project No. 765266

Monitoring Acetylcholine and Choline using Electrochemistry

C. Boylan and J.P. Lowry

Neurochemistry Group, Department of Chemistry, Maynooth University, Co Kildare, Ireland.

Email: caytlin.boylan@mu.ie

Acetylcholine is the main neurotransmitter of the cholinergic system and is associated with many higher brain functions such as memory and learning. Malfunctions within this system have been associated with a number of disorders and diseases such as schizophrenia, Alzheimer's disease, and Parkinson's disease. Current pharmaceutical approaches are limited to treating the symptoms of brain diseases and disorders, with no cure in sight. Even diagnosis is troublesome, and with over a billion people worldwide suffering from these illnesses, more attention is needed. Treatments, cures, and appropriate diagnostic techniques will remain limited until the brain is more fully understood. We address this challenge by developing and implanting *in-vivo* electrochemical sensors.

Acetylcholine cannot be measured directly but its metabolite choline can be used as an index of its changes. However, neither can be detected using traditional electrochemistry. The purpose of this project is to develop a dual electrochemical biosensor system that can track acetylcholine (ACh) and choline (Cho) changes in the brain in real-time with the aim of more fully understanding the cholinergic system, its functions, and malfunctions. By immobilising a biological recognition element, such as an enzyme, onto the surface of the electrode, non-electroactive species like acetylcholine and choline can be monitored. This system consists of two biosensors, one selective to choline (Sensor 2) and the other selective to both choline and acetylcholine (Sensor 1) and utilises the enzymes acetylcholinesterase (AChE) and choline oxidase (ChOx). Enzyme action converts these analytes of interest to hydrogen peroxide facilitating electrochemical monitoring through the oxidation of the latter.

Sensor 1:

(Cho & ACh)

$$ACh + H_2O \xrightarrow{AChE} ChO + \text{acetic acid} \quad (1)$$

$$ChO + 2O_2 + H_2O \xrightarrow{ChOx} \text{betaine} + 2H_2O_2 \quad (2)$$

$$2H_2O_2 \rightarrow 2O_2 + 4H^+ + 4e^- \quad (3)$$

Sensor 2:

(Cho)

$$ChO + 2O_2 + H_2O \xrightarrow{ChOx} \text{betaine} + 2H_2O_2 \quad (1)$$

$$2H_2O_2 \rightarrow 2O_2 + 4H^+ + 4e^- \quad (2)$$

Choline is monitored using sensor 2 and acetylcholine is monitored by subtraction at an applied potential of + 700 mV.

To date, this monitoring system has been developed and characterised fully *in-vitro* in terms of sensitivity, selectivity, and stability/biocompatibility. It has also been implanted in the striatum and prefrontal cortex of freely moving, conscious rodents and preliminary validation experiments performed, the results of which suggest reliable simultaneous monitoring of both ACh and Cho, making it completely novel.

Particle-by-Particle Mapping by Fluorescence Microscopy: Characterizing the Surface Composition and Subpopulation Heterogeneity of Bionanocomposite Materials

Aisling Fleming, Koen Evers, Alexandria Lawless, Wei Zhang, Yuchen Lin, Laurent Adumeau, Yan Yan, Kenneth A. Dawson.

Centre for BioNano Interactions, School of Chemistry, University College Dublin, Belfield, Dublin 4, Ireland.

email: aisling.fleming@cbni.ucd.ie, kenneth.a.dawson@cbni.ucd.ie

There is great optimism that nanomedicine holds the potential to revolutionize the diagnosis, monitoring and treatment of disease. The integration of nanotechnology in medicine has been accompanied by the emergence of a range of bionanocomposite materials, which may be spontaneously or synthetically derived. It is a firm belief within our group that the biological recognition and behaviour of these bionanocomposites is, in part, controlled by the precise composition of their surface biomolecular architecture.[1,2] The biomolecular architecture, adsorbed or conjugated on the nanomaterial surface, constitutes a major element of the bionanocomposite's biological identity, mediating interactions with cells and biological barriers.[3,4] Gaining a comprehensive understanding of bionanocomposite surface composition is challenged however by a lack of techniques capable of characterizing the biomolecular architecture *in situ*, directly on the nanomaterial surface, on a particle-by-particle basis.

To this end, we introduce a characterization strategy based on confocal laser scanning microscopy which permits such analysis. The technique relies on the incorporation of fluorescent tags into proteins of interest prior to preparation of the bionanocomposite, to enable tracking of the protein's integration within the surface architecture. Confocal laser scanning microscopy allows for the visualisation of individual fluorescent nanoparticles, and thus, on a particle-by-particle basis, determination as to whether or not the protein of interest has been incorporated within the bionanocomposite surface architecture. In conjunction with analytical image processing software, the strategy allows for the characterization of thousands of particles, providing statistically robust results. The technique may be complemented through the use of external fluorescent immunolabels, which probe the presence of both the protein and incorporated fluorescent tag on the nanomaterial surface. We demonstrate the utility of this fluorescence mapping strategy in characterizing the surface composition of bionanocomposites, highlighting it's potential to unveil heterogeneities in the biomolecular architecture and to identify distinct subpopulations within the suspension.

References

1. K. A. Dawson, Y. Yan, *Nature Nanotechnol.*, **2021**, *16*, 229.
2. A. Fleming, L. Cursi, J. A. Behan, Y. Yan, Z. Xie, L. Adumeau, K. A. Dawson, *Bioconjug. Chem.*, **2022**, *33*, 429,
3. D. Walczyk, F. Baldelli Bombelli, M. P. Monopoli, I. Lynch, K. A. Dawson, *J. Am. Chem. Soc.*, **2010**, *132*, 5761.
4. M. P. Monopoli, C. Åberg, A. Salvati, K. A. Dawson, *Nature Nanotechnol.*, **2012**, *7*, 779.

Ionic liquid-assisted Synthesis of Mesoporous Carbons for Supercapacitors

Yaoguang Song,[a] Fraser Norris,[b] Daryl Hinchcliffe,[a] Xiaolei Zhang,[*b] and Peter Nockemann[*a]

[a]*The QUILL Research Centre, School of Chemistry and Chemical Engineering, Queen's University Belfast, BT9 5AG, Belfast,UK*
[b]*Department of Chemical and Process Engineering, University of Strathclyde, G1 1XJ, Glasgow, UK*

email: ysong17@qub.ac.uk, xiaolei.zhang@strath.ac.uk, p.nockemann@qub.ac.uk

Mesoporous carbons (MCs) have drawn huge attention for energy storage as electrode materials in supercapactiors. Soft-templating synthesis is one of the most adopted strategies to fabricate MCs for being more effective than other methods in tuning nanostructures.[1–5] However, the non-recyclability of widely used soft templates, block copolymers, has limited the production of MCs at a lab scale. Therefore, it is imperative to seek promising alternatives that have excellent recyclability without sacrificing templating effectiveness.

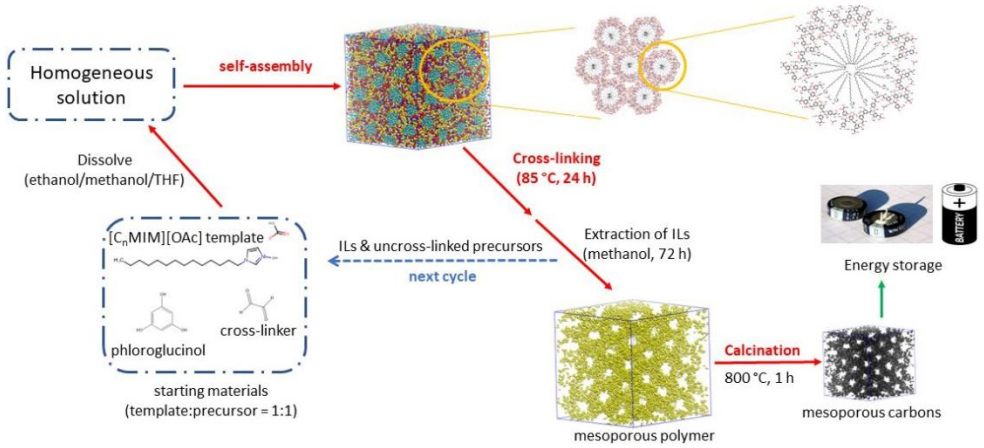


Figure 1. IL-assisted synthesis of MCs for supercapacitors.

This work investigated the employment of long-chain ionic liquids (ILs) as recyclable templates to prepare MCs for supercapacitors. For the successful implement, both experimental techniques and multi-scale modelling were employed to study the self-assembly mechanism with special emphasis on two crucial factors: the morphology of IL templates and template-precursor spatial correlations. Then, various typical cross-linking reagents were chosen to study the role of cross-linking of carbon precursors in the nanostructures and surface functionalities of as-made MCs, which ultimately lead to different electrochemical performance. Finally, the preparation of MCs with IL templates and template removal/recycling were investigated with the electrochemical performance of as-made MCs tested on symmetric Swagelok type supercapacitor cells.

Reference

1 Y. Meng, D. Gu, F. Zhang, Y. Shi, L. Cheng, D. Feng, Z. Wu, Z. Chen, Y. Wan, A. Stein and D. Zhao, *Chem. Mater.*, 2006, **18**, 4447–4464.
2 X. Zhang and A. Lu, in *Materials for Carbon Capture*, Wiley, 2020, pp. 29–95.
3 C. Liang, Z. Li and S. Dai, *Angew. Chemie - Int. Ed.*, 2008, 47, 3696–3717.
4 A. Eftekhari and Z. Fan, *Mater. Chem. Front.*, 2017, 1, 1001–1027.
5 D. Wu, F. Xu, B. Sun, R. Fu, H. He and K. Matyjaszewski, *Chem. Rev.*, 2012, 112, 3959–4015.

The Elastic Properties of Postulated Solid Forms from First Principles

Reabetswe Zwane[1]; Andrew Kellett[1]; Damien Thompson[2]; Anthony Reilly[1]; Joaquin Klug[1]

1. *School of Chemical Sciences, Dublin City University; Synthesis and Solid-State Pharmaceutical Centre*
2. *University of Limerick; Synthesis and Solid-State Pharmaceutical Centre*

email: reabetswe.zwane2@mail.dcu.ie

Understanding the nature of crystal energy landscapes, obtained from crystal structure prediction (CSP) calculations, can greatly aid drug development. Beyond crystal structure prediction, the analysis of a crystal energy landscape in a pharmaceutical setting can highlight the preferred crystal packing of an active pharmaceutical ingredient or structural motifs. Identifying these distinctive structural features can then be useful for establishing structure-property relationships for crystal engineering or drug design. For structure-mechanical response relationships (see figure below), the mechanical properties of a set of low putative solid forms from a CSP study can be predicted, and therefore potentially assist in identifying mechanical properties accessible to an API, within a specific energy range of interest. In this contribution, elastic properties of postulated solid forms of 2-((4-(3,4-Dichlorophenethyl)phenyl)amino)benzoic acid DPAB, a former drug candidate for the treatment of Alzheimer's disease and the XXIIIth molecule in the sixth CSP blind test,[1-2] are characterized using Density Functional theory (DFT). The assessment of mechanical stability, elastic moduli and the anisotropy of the elastic moduli of DPAB will potentially enable the screening of putative solid forms for polymorphs that exhibit improved compression properties.

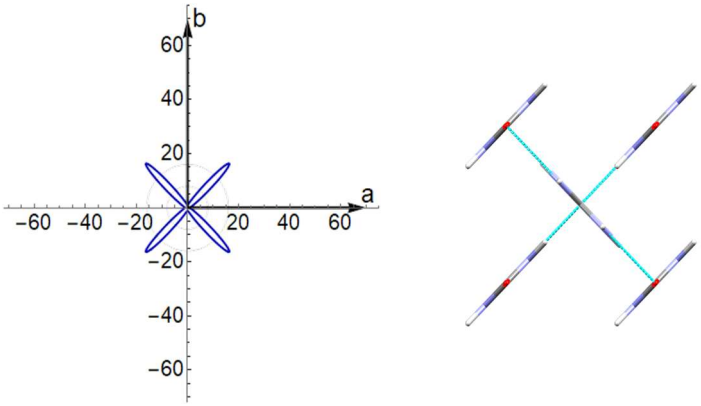


Figure 1 (left) The 2-dimensional spatial dependence of the Young's modulus of urea in the ab crystallographic plane and (right) the N-H···O hydrogen bond arrangement in the ab crystallographic plane. The direction of the largest resistance of the Young's modulus aligns with the N-H···O bonds.

References:

[1] 1. L. Simons, B. Caprathe, M. Callahan, J. Graham, T. Kimura, Y. Lai, H. LeVine, W. Lipinski, A. Sakkab, Y. Tasaki, L. Walker, T. Yasunaga, Y. Ye, N. Zhuang and C. Augelli-Szafran, Bioorganic & Medicinal Chemistry Letters, 2009, 19, 654-657..

[2] 2. C. Groom and A. Reilly, Acta Crystallographica Section B Structural Science, Crystal Engineering and Materials, 2014, 70, 776-777.

Exploiting the metal seed chemistry to control morphologies and compositions of multicomponent metal chalcogenide nanocrystals

Nilotpal Kapuria, Sumair Imtiaz, Micelle Conroy, Temilade Esther Adegoke, Abinaya Sankaran, Vasily A. Lebedev, Andreu Cabot, Shalini Singh, and Kevin M Ryan

Department of Chemical Sciences and Bernal Institute, University of Limerick, V94T9PX Limerick, Ireland

email: Nilotpal.Kapuria@ul.ie, Kevin.M.Ryan@ul.ie

Regulation of morphology and composition of multicomponent metal chalcogenide nanocrystals inculcate distinct chemical and physical properties enabling significant advances in energy storage applications.[1,2] In multicomponent systems, the subtle reactivity balance of multiple precursors, allows metal-semiconductor heterostructure formation from pre-formed metal seeds. Also, the monophasic multicomponent metal chalcogenide nanocrystals develop dynamically from the binary metal chalcogenide seeds with the subsequent incorporation of additional metal cations from solution during the growth process.[3,4] Therefore, exploiting the seed formation chemistry in solution will further permit greater control of the reaction mechanism to achieve various morphologies and compositions in multicomponent systems. Catalyst assisted growth is an embodiment of such systems where changing the nature of the catalyst seed (Bi, In, and Sn) can regulate the NC growth kinetics.[5] We demonstrate that controlling the in situ formed Bi seedin a liquid or solid form and the influx rate of the Cu^+ can alter the number of pod formation during heteronucleation of Bi seeded $Cu_{2-x}S$ heterostructures (Figure **1a**). The ex situ mechanistic investigation of the growth process reveals that modulating the amount of diphosphonic acid can effectively tune the stability of the reaction intermediate (Cu-thiolate complex, **1**) upon thiol injection. Increased stability of the Cu thiolate reduces the free Cu^+ concentration and increases the Cu^+ induction time during solution-liquid-solid growth, resulting in a morphology variation based on the number of $Cu_{2-x}S$ pod formation (**2**). We also exploit the metal seed for the first time as active alloying nuclei to form colloidal Cu–Bi–Zn–S nanorods (NRs) from Bi-seeded $Cu_{2-x}S$ heterostructures (Figure **1b**). The evolution of these homogeneously alloyed NRs is driven by the dissolution of the Bi-rich seed and recrystallization of the Cu-rich stem into a transitional segment (**3**), followed by incorporation of Zn^{2+} to form the quaternary Cu-Bi-Zn-S composition (**4**). The present study also reveals the importance of morphological modulation of Bi-$Cu_{2-x}S$ heterostructures in potassium ion storage and the effect of compositional modulation on thermoelectric properties of Cu-Bi-Zn-S nanorods.

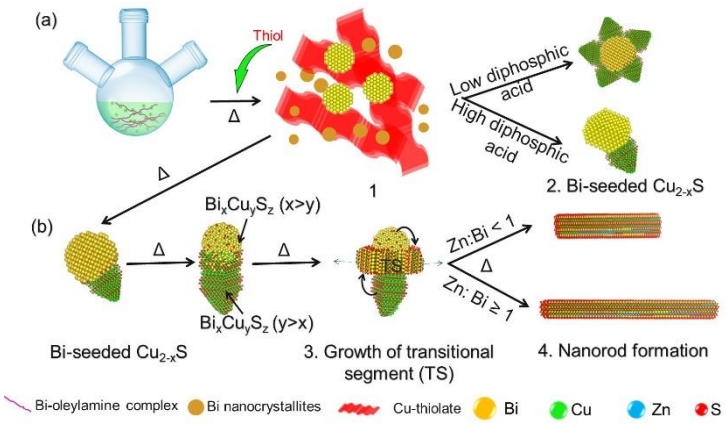


Figure 1. Schematic depiction of the evolution sequence of the multicomponent (a) Bi-$Cu_{2-x}S$ heterostructures and (b) Cu-Bi-Zn-S nanorods

References:

[1] Singh, A.; Singh, S.; Levcenko, S.; Unold, T.; Laffir, F.; Ryan, K. M. *Angew. Chem., Int. Ed.* **2013**, *52*, 9120.

[2] Yuan, L; Geng, Z; Xu, J; Guo, F; Han, C. *Adv. Funct. Mater.* **2021**, *31*, 2101103.

[3] Kapuria, N.; Conroy, M.; Lebedev, V.A.; Adegoke, T.E.; Zhang, Y; Amiinu, I.S.; Bangert, U.; Cabot, A.; Singh, S.; Ryan, K.M. *ACS Nano*, ***2022***.

4] Just, J.; Coughlan, C.; Singh, S.; Ren, H.; Müller, O.; Becker, P.; Unold, T.; Ryan, K. M. *ACS Nano*, **2021**, 15, 6439.

[5] Afik, N.; Shreteh, K.; Fridman, H.; Volokh, M.; Ezersky, V.; and Mokari, T. *Chem. Mater.* ***2021***, 33, 9326.

UNIVERSITY OF LIMERICK OLLSCOIL LUIMNIGH | Bernal Institute

IRISH RESEARCH COUNCIL An Chomhairle um Thaighde in Éirinn

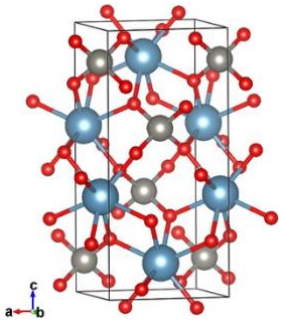
Ab-initio modelling on the electronic and absorption properties of pure and Cu-doped $CaWO_4$.

Vivek Christhunathan[1,4], Wenming Tong[2,4], Pau Farràs[2,4], Mingming Tong[1,3,4]

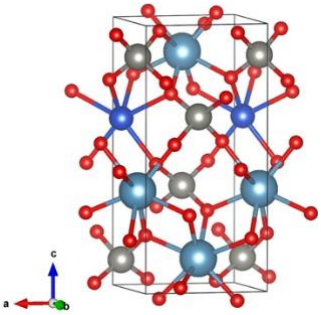
[1] *Mechanical Engineering, School of Engineering, College of Science and Engineering, National University of Ireland Galway, University Road, Galway, Ireland.*
[2] *School of Biological and Chemical Sciences, National University of Ireland Galway, University Road, Galway, Ireland.*
[3] *I-Form, SFI Research Centre for Advanced Manufacturing, Ireland.*
[4] *Ryan Institute for Environmental, Marine and Energy Research, National University of Ireland Galway, University Road, Galway, Ireland.*

email: v.christhunathan1@nuigalway.ie, wenming.tong@nuigalway.ie, pau.farras@nuigalway.ie, and mingming.tong@nuigalway.ie

This study involves designing an advanced photocatalyst that can more effectively generate e^--h^+ pairs for the purpose of degrading organic wastes by using computational modelling. The chemical modifications on $CaWO_4$ was performed, such as doping $CaWO_4$ with 25 at.% of Cu cations to change the band edges of pure $CaWO_4$. The photocatalytic properties of Cu-doped $CaWO_4$ (such as lattice structure, electronic band structure, total density of states, partial density of states and absorption spectra) were computationally predicted using ab-initio calculations based on density function theory (DFT[1]) to have a deeper insight into how related chemical modification can affect $CaWO_4$'s photocatalytic activity.



Pure $CaWO_4$ (**1**)



25 at.% Cu-doped $CaWO_4$ (**2**)

The Cu-doped $CaWO_4$ (**2**) was found to have considerably narrower band-gap compared to $CaWO_4$ (**1**), from 4.24 to 3.07 eV, resulting in e^--h^+ pair generation extended into the visible-light region. For the Cu-doped $CaWO_4$, the maximum absorption was found to be at ~158 nm, and its absorption band edge was found to be between 290 to 410 nm, resulting on a red shift in its absorption spectrum. The Quantum Espresso code[2], which is based on the projector augmented wave (PAW) method, was used to implement the modelling calculation.

References:

[1] Perdew, J. P.; Burke, K.; Ernzerhof, M. Phys. Rev. Lett., 1996, 77 (18), 3865.
[2] Giannozzi, P.; Baseggio, O.; Bonf`a, P.; Brunato, D.; Car, R.; Carnimeo, I.; Cavazzoni, C.; de Gironcoli, S.; Delugas, P.; Ferrari Ruffino, F.; Ferretti, A.; Marzari, N.; Timrov, I.; Urru, A.; Baroni, S.; J. Chem. Phys., 2020, 152, 154105.

NUI Galway OÉ Gaillimh
Grant code: D3800

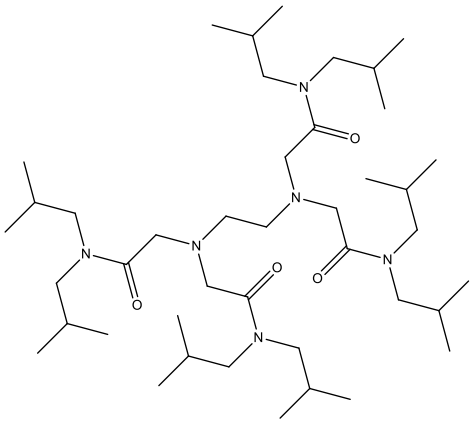
Multidentate amide ligands for the separation of rare earth elements

Peter Nockemann and Anthony Dodd

School of Chemistry and Chemical Engineering, Queen's University Belfast, University Road, Belfast

email: p.nockemann@qub.ac.uk, adodd01@qub.ac.uk

The rare earth elements (REEs) are a set of 17 chemically similar elements consisting of the 15 lanthanides plus scandium and yttrium. Due to their unique optical, electrical and magnetic properties the rare earths are widely used in electronics, magnets, advanced weapons and renewable energy.[1] However due to their similar ionic radii, charge and coordination the separation of these elements is still a significant challenge.[2] Currently solvent extraction has been the most efficient method for separation with a wide range of extractants being studied including phosphoric acid reagents[3], amides[4] and ionic liquids.[5] Phosphoric acid reagents have been demonstrated the ability to effectively extract and separate the rare earths however they have many disadvantages such as low stability and recyclability, requiring strict pH control and saponification producing massive amounts of chemical waste water. Compared to this amide extractants are considered promising alternatives due to their simple synthesis process, low cost and limited waste.[6]



EDTDBA

This project focuses on the synthesis and application of the multidentate amide ligand EDTDBA for the separation of the rare earth elements as an alternative to traditional phosphoric acid reagents. Presented here is a summary of the work to date looking at the design and synthesis of the ligand, its ability to extract the rare earth elements and characterising its coordination chemistry to help develop the next generation of extractants.

References:

[1] S. Riano, K. Binnemans, *Green Chem*., 2015, **17**, 2931-2942
[2] P. Sun, K. Huang, H. Liu, *Hydrometallurgy*, 2019, **189**, 105136
[3] A. Rout, K. Binnemans, *Dalton Trans*., 2015, **44**, 1379-1387
[4] D. Schadle, R. Anwander, *Chem. Soc. Rev*., 2019, **48**, 5752-5805
[5] A. Rout, K. Binnemans, *Dalton Trans*., 2014, **43**, 3186-3195
[6] C. Platas-Iglesias, D. M. Corsi, L. V. Elst, R. N. Muller, D. Imbert, J. C. G. Bunzil, E. Toth, T. Maschmeyer, J. A. Peters, *Dalton Trans*., 2003, **4**, 727-737

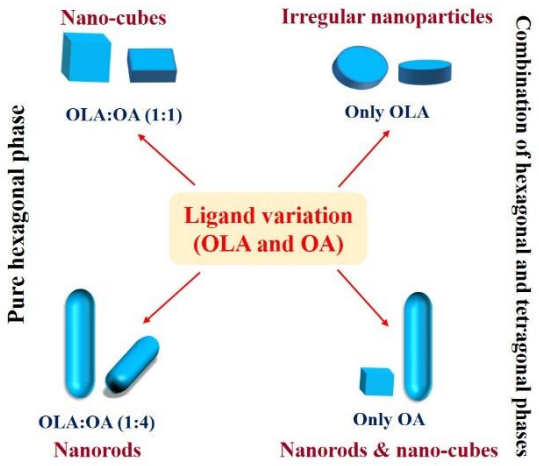
Colloidal synthesis of copper telluride 1-D and 2-D shaped nanocrystals using Dipehylditelluride (DPDTe) as an air-stable and highly-reactive alternative source of tellurium.

Mohini Mishra[a], Niraj Nitish Patil[a], Maria Zubair, Nilotpal Kapuria[a], Vasily Lebedev[a], Temilade Esther Adegoke[a], Kevin M. Ryan[a]* and Shalini Singh[a]

a Department of Chemical Sciences and Bernal Institute, University of Limerick, Limerick, Ireland

Email:mohini.mishra@ul.ie, Shalini.Singh@ul.ie, kevin.m.ryan@ul.ie

Copper telluride ($Cu_{2-x}Te$) has a complex phase diagram with numerous stoichiometries and crystal morphologies, resulting in a wide range of applications with a composition tunable direct bandgap of 1.1 to1.7 eV[1]. Due to stoichiometry deviations in the Cu–Te phase diagram compared to sulphur and selenide analogues[2–8], control over shape, size, and phase in $Cu_{2-x}Te$ nanocrystal synthesis is difficult to achieve. Here, we developed a "phosphine-free" approach for synthesising copper telluride nanocrystals with different shapes, sizes and crystal phases, using diphenyl ditelluride (DPDTe) as an air-stable, feasible and commercially accessible tellurium source. The DPDTe is shown to have optimal reactivity for the colloidal synthesis of Cu_2Te, allowing optimal control over the phase and morphology due to its solution stability and compatibility with Cu^{2+} precursors for copper telluride synthesis.



1-D nanorods of hexagonal phase (Cu_2Te) were synthesised at a moderate temperature of 180 °C using this unexplored Te precursor. $Cu_{2-X}Te$ nanocrystals of various forms (1-D nanorods and 2-D nanoplates), sizes, and crystal phases emerge as a result of careful control over crucial parameters in this system (hexagonal Cu_2Te nanorods and orthorhombic $Cu_{1.43}Te$ nanoplates). We also observed optical properties of synthesised hexagonal Cu_2Te nanorods and orthorhombic $Cu_{1.43}Te$ nanoplates with UV-visible absorption at room temperature.

Controlling Nanoparticle Aggregates for Stable SERS

Yiming Huang, Yikai Xu and Steven E. J. Bell

School of Chemistry and Chemical Engineering, Queen's University Belfast, Belfast, Northern Ireland

email: yhuang30@qub.ac.uk, Yikai.Xu@qub.ac.uk, S.Bell@qub.ac.uk

Surface electron oscillations on Au and Ag nanoparticles can be excited by light to generate an electromagnetic field (surface plasmon), which can be utilized for various applications including surface-enhanced Raman spectroscopy (SERS). To achieve optimal SERS enhancement, the Ag/Au nanoparticles generally need to be assembled into tightly packed structures to form interparticle nano-junctions which support electromagnetic hot-spots.[1] In practice, this is often achieved by salt-induced aggregation of Ag/Au colloids. Although this method is extremely effective and straightforward, a crucial disadvantage of this approach is that the aggregates are only dynamically stable, lasting only minutes to hours, which hinders their wider applications.

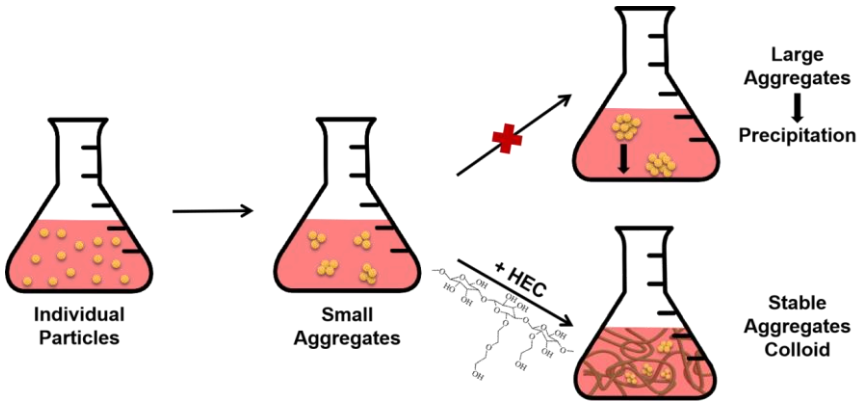


Figure 1. Schematic illustration of the formation of conventional aggregates and HEC-stabilized aggregates colloid.

Hydroxyethyl cellulose (HEC) is a nonionic water-soluble polymer derived from cellulose which is largely used as water-binder and thickening agent in many applications including personal care products, pharmaceutical formulations.[2][3] Here, we show that HEC can be used to halt aggregation at the optimum point and then stabilise these colloidal aggregates so that they can be stored for months without degradation of their plasmonic properties. Importantly, we show that HEC stabilizes the aggregates without adsorbing directly to their surfaces which leaves them active for further applications, including SERS. In addition, we show that the method can be universally applied to stabilize various types of Ag/Au colloidal aggregates regardless of their surface-chemistry and particle morphology.

References:

[1] Israelsen, N.; Hanson, C.; Vargis, E. *The Scientific World Journal* **2015**, *2015*.

[2] Su, X.; Lian, Z.; Yuan, Y. *Geofluids* **2019**, 2019.

[3] Di Giuseppe, E. *Reference Module in Earth Systems and Environmental Sciences*. **2018**.

Exploiting drug delivery technology to enable cell permeation of novel luminescent ruthenium polypyridyl complexes for application as cell imaging and therapeutic agents.

D. Cullinane, K. Gkika, A. Byrne, S. Ghosh, P. Morgenfurth, A. Prabhakaran, C. Long and T.E. Keyes.

School of Chemical Sciences, National Centre for Sensor Research, Dublin City University, Dublin 9, Ireland
email: david.cullinane5@mail.dcu.ie, tia.keyes@dcu.ie

Luminescent ruthenium polypyridyl complexes are emerging as robust bioimaging agents for intracellular sensing and (photo)therapeutics.[1] Further work however is required, to drive the emission of ruthenium complex probes into the NIR where light is most penetrative through cells and tissue, whilst maintaining photostability. And to overcome the problematic inability of certain metal complexes to cross the cell membrane without cell permeabilizing agents such as DMSO.

In this contribution, our efforts to shift the typically red emission of ruthenium polypyridyl complexes into the NIR to coincide with the photobiological optical window (700-950 nm) are described.[2] A photostable bis heteroleptic Ru(II)-biquinoline complex (λ_{em}=786 nm) stabilized with an anionic triazolate ligand was synthesised.[3, 4] To promote cell membrane permeation, the complex was conjugated to both cell penetrating and signal peptides sequences. To overcome the observed cytotoxicity of the complex in cells, a polyethyleneglycol chain (PEG) was conjugated to the complex which was highly effective in reducing cytotoxicity whilst maintaining cell permeation.

The second part of this talk will discuss the development of a series of light switch ruthenium phendione complexes motivated by their reported ability to photocleave DNA via proton coupled electron transfer (PCET) an approach attractive for the treatment of hypoxic tumour tissue.[4] The complexes were cell impermeable which motivated the use of liposome technology as a cell delivery mechanism. The complexes were successfully incorporated into functionalised liposomes that allowed them to traverse the cell membrane of live cells. The uptake and distribution of the complexes in cells as well as their cytotoxicity will be discussed.

References:

[1] F. E. Poynton, S. A. Bright, S. Blasco, D. C. Williams, J. M. Kelly and T. Gunnlaugsson, Chem. Soc. Rev., 2017, 46, 7706–7756.
[2] T. E. Keyes, J. G. Vos, J. A. Kolnaar, J. G. Haasnoot, J. Reedijk and R. Hage, Inorganica Chimica Acta, 1996, 245, 237–242.
[3] D. Cullinane, K. S. Gkika, A. Byrne and T. E. Keyes, Journal of Inorganic Biochemistry, 2020, 207, 111032.
[4] S. A. Poteet, M. B. Majewski, Z. S. Breitbach, C. A. Griffith, S. Singh, D. W. Armstrong, M. O. Wolf and F. M. MacDonnell, J. Am. Chem. Soc., 2013, 135, 2419–2422.

Science Foundation Ireland For what's next

Grant code: [19/FFP/6428] and [12/RC/2276_P2]

Latent Fingerprint Enhancement on Brass Substrates with the aid of Electrochromic and Redox Polymer Deposition

Colm McKeever and Eithne Dempsey

Department of Chemistry, Kathleen Lonsdale Institute for Human Health, Maynooth University, Maynooth Co. Kildare, Ireland.
email: colm.mckeever.2020@mumail.ie, eithne.dempsey@mu.ie

Fingerprints are one of the most commonly sought-after forms of forensic evidence for scenes of crime professionals. Friction ridges on the fingerprints and hands are unique to the individual and used for identification purposes, requiring chemical or physical treatment to render them visible. Latent (colourless) prints are formed from contact with the skin of the finger and a surface, with material transfer resulting from residue arising from skin's natural secretions including amino acids, proteins and fatty acids. Many visualisation methods have used these secretions as an anchor point (e.g. powdering, cyanoacrylate fuming and chemical methods such as ninhydrin), providing resolved fingerprints suitable for tape lifts or photography. In this work, electrochemically driven visualisation enhancement of latent prints on non-porous conducting surfaces (ITOs and brass), is the key focus, particularly for those substrates which have been subjected to high temperatures. Success in the development of latent fingerprints on discharged cartridge cases has been a significant challenge for forensic investigators where due to the nature of the firing process, prints and DNA/protein evidence are destroyed by the extreme temperatures and abrasive forces involved. The methods proposed here exploit localised changes in electrical and optical properties of a metal surface due to chloride driven corrosion due to eccrine gland hand secretions. Our work advances this via electrochemical means (Figure 1a) following the work of Sapstead et al. [1] on steel, with an enhancement which can be controlled by the conditions, electrolyte and timescale of the experiment. Controlled electrochemical deposition of semiconducting/electrochromic polymers such as poly(3,4-ethylenedioxythiophene (PEDOT)) (homo or co-polymerisation) enable a negative print to be developed due to their growth on the conducting "valley" region between the ridge lines (Figure 1b) with the polymer thickness not exceeding that of the fingerprint. Fine tuning of contrast exploits the colours of different oxidation states via a post deposition applied potential. Further advancement includes the use of phenothiazine dyes (e.g. amine derivatives such as thionine) which form redox active films when co-deposited during EDOT [2] or 3-methyl thiophene polymerisation, realising purple poly(thionine)/thiophene deposition. Imaging is possible using photography and reflectance microscopy, allowing grading according to second/third level detail, being consistent with legal identification of an individual.

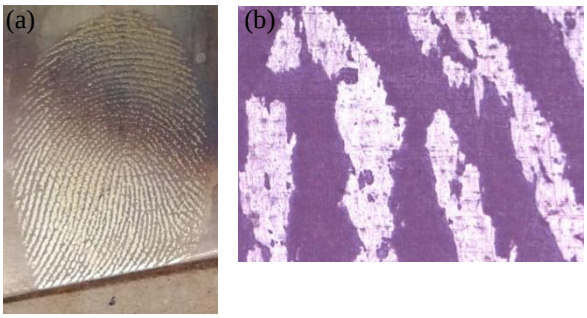


Figure 1. Latent print deposited at (a) brass surface following electrochemical enhancement by potential sweeping in 2 mM EDOT with 1 mM thionine acetate in 0.1 M $NaNO_3$ over the range -0.2 to 0.5 at 50 $mV.s^{-1}$ for 3 cycles. (b) Core of latent print under x1000 magnification with visible pores.

References:

1. Sapstead, R.M., N. Corden, and A. Robert Hillman, *Latent fingerprint enhancement via conducting electrochromic copolymer films of pyrrole and 3,4-ethylenedioxythiophene on stainless steel.* Electrochimica Acta, 2015. **162**: p. 119-128.
2. Murphy, B., et al., *Phenothiazine Redox Active Conducting Polymer Films at Nanocomposite Surfaces.* Journal of the Electrochemical Society, 2020. **167**(2).

IRISH RESEARCH COUNCIL
An Chomhairle um Thaighde in Éirinn

Funded under: Irish Research Council 2021 Government of Ireland Postgraduate Scholarship (GOIPG/2021/250)

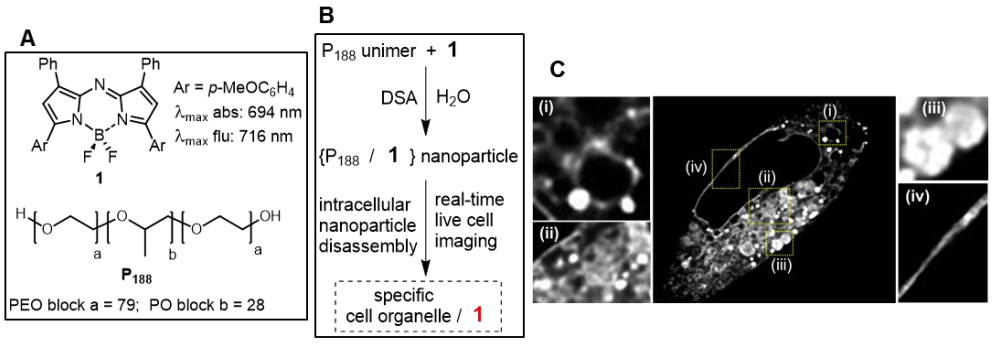
Exploiting Directed Self-Assembly and Disassembly for *off-to-on* Fluorescence Responsive Live Cell Imaging

Donal O'Shea and Niamh Curtin

Royal College of Surgeons in Ireland, 123 St. Stephens Green, Dublin 2, Ireland

email: donalfoshea@rcsi.ie, ncurtin@rcsi.ie

Directed self-assembly (DSA) is the spontaneous organisation of two or more components into ordered structures that occurs due to specific interactions (Van der Waals, hydrophobic, hydrophilic, π-π interactions etc.) occurring through their environment. In this work an NIR-fluorescence responsive nanoparticle is formed by DSA of a triblock co-polymer P_{188} with a hydrophobic NIR-AZA fluorophore in water.[1] The assembly of the nanoparticle and its ability to deliver the fluorophore into lipophilic environments were its fluorescence switches from off to on was investigated. Cellular uptake of nanoparticles occurred within minutes with selective emission seen first inside lipid droplets[2] at 1 hr followed by other membrane regions at 24 hr (Figure). The fluorophore was photostable inside the cell allowing for prolonged continuous imaging of the motion of these lipid droplets over time.



(**A**) Structure and spectroscopic characteristics of fluorophore **1** and P_{188} used in this study. (**B**) Use of the fluorescence functional response of NP**1**P_{188} in complex aqueous systems. (**C**) CLSM image showing an MDA MB 231 cell following 24 h incubation with NP**1**P_{188}. (i) LDs in close proximity to the extended branching ER network; (ii) central ER network with LDs; (iii) large vacuoles; (iv) nuclear membrane.

References:

1. Cheung, S.; O'Shea, D. F. Nat Commun 2017, 8, 1885.
2. Martin, S.; Parton, R. G., Lipid droplets: a unified view of a dynamic organelle. Nature reviews Molecular cell biology 2006, 7 (5), 373-378.

RCSI Leading the world to better health
Apjohn Scholar

Grant code 2399

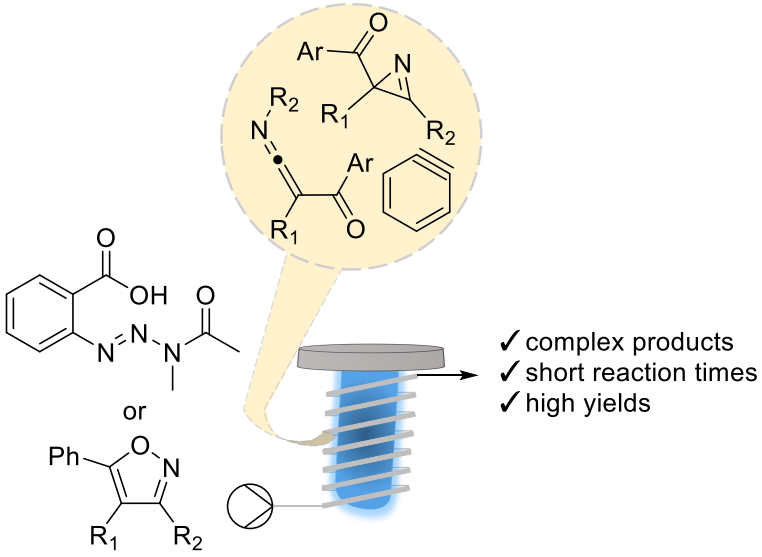
THE PHOTOFLOW GENERATION AND CAPTURE OF REACTIVE INTERMEDIATES

Marcus Baumann and Cormac Bracken

UCD Centre for Synthesis and Chemical Biology, School of Chemistry, University College Dublin, Belfield, Dublin 4, Ireland.

email: marcus.baumann@ucd.ie, cormac.bracken@ucdconnect.ie

Photoflow chemistry has come to the fore as an enabling technology whereby microflow parameters allow uniform irradiation of a solution, and consequently more precise control over reaction conditions.[1] Photochemistry has become increasingly popular as an alternative energy source when it is used concurrently with modern flow technology, providing us with a reliable means for generating reactive intermediates via photochemical pathways and subsequently capturing them. Typically, many of these photochemical pathways suffer from poor efficiency under batch conditions, primarily explained by limitations contained within the Beer-Lambert law. The ultraviolet irradiation, when combined with the microfluidic benefits of augmented heat and mass transfer, gives a photoflow process that is a unique, continuous synthesis and which otherwise may not be viable in batch.[2] Photoflow chemistry is therefore an attractive and alternative platform for low efficiency photochemical reactions.



This research talk details the development of continuous flow protocols for efficient flow generation of reactive intermediates and their subsequent capture, providing biologically useful heterocycles. These intermediates were generated under UV irradiation, where the microflow systems catered to a range of various UV energy sources which were specific to the substrates in question. These reactive intermediates consequently underwent photoisomerisation and/or electrocyclisation reactions in flow, affording the desired heterocyclic targets in high yields and short reaction times.[3,4] Current work is focusing on expanding this series of heterocycles to include more complex ring systems in multi-step telescoped flow processes.

References

[1] D. Cambié; C. Bottecchia; N. J. W. Straathof; V. Hessel and T. Noël. *Chem. Rev*. **2016**, 116, 10276−10341.

[2] M. Di Filippo, C. Bracken and M. Baumann. *Molecules*, **2020**, 25, 2, 356.

[3] C. Bracken and M. Baumann. *J. Org. Chem*, **2020**, 85, 2607−2617.

[4] C. Bracken, A. S. Batsanov and M. Baumann. *SynOpen*, **2021**, 5, 29–35.

Development of a continuous flow process for the epoxidation of alkenes with peracetic acid and a homogeneous manganese(II) catalyst

Ailbhe Ryan[1], Karen Fahey,[2] Tom S. Moody,[2] Scott Wharry,[2] Megan Smyth,[2] Jillian M. Thompson,[1] Peter C. Knipe[1] Mark J. Muldoon[1*]

1 Queen's University Belfast

2 Arran Chemical Company / Almac Group

**corresponding author: m.j.muldoon@qub.ac.uk*

Oxidations are valuable reactions in the synthesis of a wide range of pharmaceutical, agrochemical and fragrance compounds. Using oxidants in the presence of flammable organic solvents is a challenge on large-scale, with the risk of fire or explosion often prohibitive.[1] Continuous flow has been highlighted as a solution to allow oxidations to be carried out safely on-scale.[2] The smaller dimensions of a flow reactor mean that a significantly reduced volume of the reaction is occurring at any one time when compared to batch reactors, reducing the severity of any potential adverse event. Continuous flow also allows for highly reactive or hazardous reagents to be synthesized *in-situ*, removing the risk associated with their handling and storage. The increased control over reaction parameters due to increased heat and mass transfer allows for greater reproducibility between runs and reduced risk of runaway reactions.

There is a desire to develop more sustainable oxidation systems. The use of manganese catalysts is an attractive option, as manganese is a non-toxic, earth abundant metal. Peracetic acid (PAA) is an inexpensive strong oxidant which results in acetic acid, oxygen, and water as decomposition products. Stack and co-workers published an epoxidation procedure, using manganese triflate with the commercially available 2-picolinic acid ligand and peracetic acid as the terminal oxidant. Stack and co-workers demonstrated a broad range of alkene substrates which could be oxidised under these conditions, with challenging model substrates.[3]

Our initial studies, carried out in batch, confirmed the reproducibility of the Mn(II)/2-picolinic acid epoxidation system reported by Stack and co-workers.[3] We also found that the use of the cheaper, more sustainable manganese acetate in place of the reported manganese triflate produced comparable results and we worked towards using this in our flow studies.

This talk will describe the design and optimization of a continuous flow process for carrying out an epoxidation with a homogenous manganese catalyst at 0.05 mol% $Mn(OAc)_2$ loading. In this process, peracetic acid is generated *in-situ* and telescoped directly into the epoxidation reaction, thus removing the risks associated with its handling and storage. Through optimization studies, it was found that controlling the speciation of manganese species by varying the ligand: Mn ratio is key to the performance of the reaction under flow conditions. The resultant continuous flow process offers a scalable route to the oxidative synthesis of epoxides from alkenes, overcoming the safety concerns often associated with these reactions.

References

1 S. Caron, R. W. Dugger, S. G. Ruggeri, J. A. Ragan and D. H. Brown Ripin, *Chem. Rev.*, 2006, **106**, 2943–2989.

2 H. P. L. Gemoets, Y. Su, M. Shang, V. Hessel, R. Luque and T. Noël, *Chem. Soc. Rev.*, 2016, **45**, 83–117.

3 R. A. Moretti, J. Du Bois and T. D. P. Stack, *Org. Lett.*, 2016, **18**, 2528–2531.

Acknowledgements

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No. 813394

Continuous Synthesis of α-Substituted Cyclic Amines *via* C-H Functionalization Reactions

Lara J. Nolan[1,2,3], Megan Smyth[2], Thomas S. Moody[2,3], Scott Wharry[2], Karen Fahey[3] and Peter Knipe[1]

[1]School of Chemistry and Chemical Engineering, Queen's University Belfast, Belfast.[2] Almac Sciences, 20 Seagoe Industrial Estate, Craigavon, Northern Ireland. [3] Arran Chemical Company, Unit 1 Monksland Industrial Estate, Athlone, Ireland.

email: lnolan03@qub.ac.uk, P.Knipe@qub.ac.uk

The development of the α-C-H functionalization of pyrrolidines and piperidines en route to the preparation of Active Pharmaceutical Ingredients under a continuous flow operation has been successfully demonstrated. Functionalized nitrogen-containing heterocycles are key structural moieties in a plethora of natural products and small molecule APIs. Typical routes towards these structures required laborious, multi-step protection-functionalization-deprotection strategies rendering them unappealing to the modern pharmaceutical industry. Comparatively, in 2018 a facile preparation of a-functionalized cyclic amines involving an intermolecular hydride transfer to form an imine intermediate which is subsequently captured by an organolithium nucleophile was reported (1) – however the protocol suffered from the need for cryogenic temperatures and poor scalability due to handling of large quantities of pyrophoric compounds. These issues may be overcome on transference of this protocol from batch to continuous flow. The use of organolithium compounds as nucleophilic addition reagents and strong bases are staple protocols in organic synthesis. However, due to the highly reactive nature of these entities, their use is often challenging in industrial batch-type chemistry due to the associated safety risks. The advent of flow chemistry has allowed for a safe and scalable approach for the use of reactive organometallic compounds.

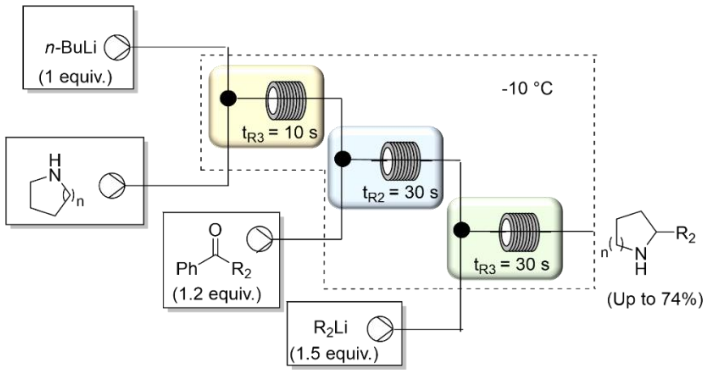


***Figure 1**. The α-CH functionalization reaction under continuous flow conditions*

Proof-of-concept transference of this elegant protocol into a continuous approach has been successfully demonstrated. Preliminary results have shown that cryogenic temperatures can be circumvented operating under relatively mild conditions with little-to-no detriment on reaction efficacy. The hyper-reactive nature of the organolithium reagents is also recognized relative to batch by significantly reduced reaction times resulting from improved reaction mixing ultimately providing maximal space-time-yields. Finally, the incorporation of an in-situ lithium halogen exchange has been achieved, unlocking an array of organolithium nucleophiles resulting in a diverse substrate scope.

References:

1. W. Chen, L. Ma, A. Paul and D. Seidel, Nat. Chem., 2018, 10, 165–169.

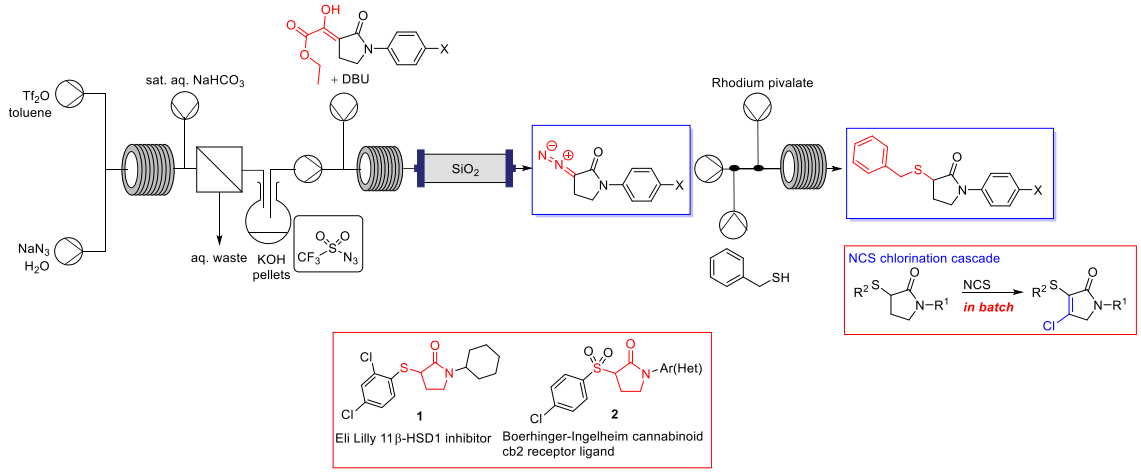
This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No. 813394

Utilising Batch and Continuous Flow in the Synthesis of α-Sulfenyl-β-chlorolactams

Aoife M. Kearney, Stuart G. Collins, Anita R. Maguire
School of Chemistry, ABCRF, University College Cork

email: a.maguire@ucc.ie, stuart.collins@ucc.ie, aoife.kearney@ucc.ie

To-date in the Maguire-Collins group, a NCS chlorination cascade has been studied in linear, acyclic systems originally with amides, and then more recently extended to ketones.[1,2] The current work extends this methodology to cyclic derivatives in the form of α-sulfenyl lactams, posing the interesting question of whether this chlorination cascade would proceed in the constrained cyclic system. The cyclic α-sulfenyl amide precursors are synthesised via α-diazolactams,[3,4] which display remarkable synthetic versatility in organic chemistry. Use of α-diazocarbonyl compounds at-scale has been impacted by the safety concerns associated with their use, particularly their precursors, such as sulfonyl azides and diazoalkanes.[5] Flow chemistry has enabled the use of these hazardous compounds in organic synthesis as it facilitates in-line reaction monitoring, efficient transfer of heat and mass and automation, among other benefits.[6] Coupled with the biological importance of the α-sulfenyl lactam scaffold, as seen by its presence in many APIs such as Eli Lilly's 11β-HSD1 inhibitor **1**[7] and Bristol—Myers–Squibb's melanin hormone receptor-1 agonist **2**,[8] the opportunity to develop a telescoped continuous process combining the *in-situ* generation of hazardous triflyl azide, diazo transfer and rhodium-catalysed S–H insertion was an exciting prospect. This talk outlines this recently developed telescoped sequence, as well as the subsequent NCS chlorination cascade with the novel library of α-sulfenyl lactam scaffolds.[9,10] The biological activity of some of the unsaturated α-sulfenyl-β-chlorolactams was evaluated at the National Cancer Institute in Maryland, USA.



References:

1. M. Kissane, A.R. Maguire, *Synlett*, 9, **2011**, 1212-1232.
2. A.M. Kearney, L. Murphy, C.C.Murphy, K.S. Eccles, S.E. Lawrence, S.G. Collins, A.R. Maguire, *Tetrahedron*, **2021**, 132091.
3. D. Zhukovsky, D. Dar'in, G. Kantin, M. Krasavin, *Eur. J. Org. Chem.*, 13, **2019**, 2397-2400.
4. D. Barkhatova, D. Zhukovsky, D. Dar'in, M. Krasavin, *Eur. J. Org. Chem.*, 33, **2019**, 5798-5800.
5. F.W. Bollinger, L.D. Tuma, *Synlett*, 5, **1996**, 407-413.
6. I.R. Baxendale, L. Brocken, C.J. Mallia, *Green Process Synth.*, 2, **2013**, 211-230.
7. T.D. Aicher, M.J. Chicarelli, R.J. Hinklin, H. Tian, O.B. Wallace, Z. Chen, T.E. Mabry, J.R. Mccowan, N.J. Snyder, L.L.J. Winneroski, J.G. Allen, US Patent, WO2006/049952, **2006**.
8. G. S. Z. Ahmad, W. N. Washburn, US Patent, WO 2014/0394, **2014**.
9. D.C. Crowley, T.A. Brouder, A.M. Kearney, D. Lynch, A. Ford, S.G. Collins, A.R. Maguire, *J. Org. Chem.*, 86, **2021**, 13955.
10. A.M. Kearney, D. Lynch, S.G. Collins, Maguire, *Tetrahedron Lett.*, 83, **2021**, 153438-153442.

IRISH RESEARCH COUNCIL
An Chomhairle um Thaighde in Éirinn

The design and study of novel ruthenium supramolecular assemblies for photocatalytic hydrogen evolution and CO_2 reduction

Florian J.R. Cerpentier, Michael P. Brandon, Joshua Karlsson, Elizabeth A. Gibson and Mary T. Pryce

School of Chemical Sciences, Dublin City University, Dublin, Ireland.
Energy Materials Laboratory, Department of Chemistry, School of Natural and Environmental Science, Newcastle University, Newcastle upon Tyne, United Kingdom
email: Florian.cerpentier2@mail.dcu.ie

Our ever increasing demands for energy, together with the escalation in global warming have created the need for large scale production and storage of renewable energy.[1] Photocatalytic systems capable of reducing low energy substrates such as water and CO_2 to higher energy products including hydrogen gas and CO are viable candidates for this large scale energy transition.[2] Supramolecular ruthenium complexes, in which a ruthenium-based light harvester is coupled to a hydrogen evolution catalyst, or a CO_2 reduction catalyst, have been extensively studied due to their stability, strong light absorption in the visible region and long-lived charge separated states.[3] The properties of these complexes can be tuned easily through modification of the various ligands on the ruthenium centre. Importantly, anchoring groups can be attached to the peripheral ligands to enable immobilization onto semiconductor surfaces.[4]

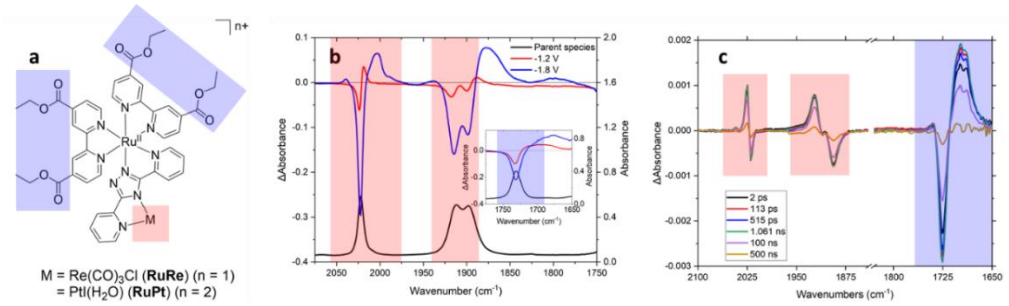


Figure 1a) The novel supramolecular assemblies. b) infrared spectroelectrochemistry for the ruthenium-rhenium assembly. c) picosecond time-resolved infrared spectrum for the ruthenium-rhenium assembly.

In this project, two novel supramolecular systems were synthesized in which a ruthenium light harvesting moiety was connected to a platinum or rhenium metal centre for hydrogen evolution or CO_2 reduction, respectively. The peripheral ligands were functionalized with ester functional groups to enable immobilization onto a NiO semiconductor surface. The complexes were studied using a combination of electrochemical, spectroscopical and spectroelectrochemical approaches, including time resolved studies on the picosecond timescale. Finally, the activity of these systems in solution and on a NiO surface for photocatalytic hydrogen evolution or CO_2 reduction was investigated.

References:

[1] Pörtner, H. O.; Roberts, D. C.; Adams, H.; Adler, C.; Aldunce, P; Ali, E.; Ara Begum, R; Betts, R; Zelina Zaiton, I. *Climate Change 2022 Impacts, Adaptation and Vulnerability*. **2022**
[2] Hunt, J.D; Nascimento, N.; Vieira, L.W.; Romero, O.J. *Renew. Sustain. Energy Rev.* **2022**, *160*, 112291.
[3] Kalyanasundaram, K.; Kiwi, J.; Grätzel, M. *Hel. Chim. Acta*, **1978**, 2720.
[4] Singh Bindra, G.; Schulz, M.; Paul, A.; Groarke, R.; Soman, S.; Inglis, J.L.; Browne, W.R.; Pfeffer, M.G.; Rau, S.; Maclean, B.J.; Pryce, M.T.; Vos, J.G. *Dalt Trans.* **2012**, *41*, 13050.

The SEAI National Energy Research, Development & Demonstration Funding Programme 2018 Grant number 18/RDD/282,

NEW VISTAS OF AN OLD REACTION

James A. Sullivan[1], Sean Kelly[2] and Kristy Stanley[1]
[1]*UCD Environmental and Sustainable Catalysis Lab, School of Chemistry, University College Dublin, Belfield, Dublin 4, Ireland*
[2]*School of Biosystems and Food Engineering, University College Dublin, Belfield, Dublin 4, Ireland*

email: james.sullivan@ucd.ie, kristy.stanley@ucdconnect.ie

Climate change and fossil fuel shortage are two of the biggest challenges currently facing our society. With atmospheric CO_2 levels exceeding 410 ppm, to avoid irreversible climate damage the IPCC have stated that 70-85% of the world's energy must come from renewables by 2050[1]. Currently this is only 10 %, meaning research and investment into renewable energy is urgent. However, renewable energy, such as wind and solar, come with their own drawbacks, namely transience. The potential to harness all of our energy needs is possible but storage during times of excess (for use in times of low production) is a major challenge. One possible solution are solar fuels, by using excess electricity to power endothermic chemical processes, the products of which can be easily stored then back-reacted to produce heat when energy generation is low, creating a thermochemical heat pump. The dry reforming of methane (DRM) is one such chemical process, reacting two harmful greenhouse gases, CO_2 and CH_4 to produce CO and H_2.

$$CO_2 + CH_4 \rightleftharpoons 2CO + 2H_2$$

This rection also comes with problems, expensive noble metal catalysts and temperatures exceeding 1000 ºC are required for meaningful conversion[2], catalysts are prone to severe deactivation through coking and the reaction is equilibrium limited. To overcome this, it is possible to use cheap transition metal catalysts under the promotion of non-thermal spark-discharge plasma (NTP)[3]. NTP reactions are instantaneous, removing the need for long warm-up times and maintaining high temperatures. This makes them ideal for solar fuel production as excess electricity can be used as and when it is available.

In this work a range of Ni nanoparticles with differing morphologies were synthesised and deposited onto Al_2O_3 supports. These catalysts were characterised *via* XRD, SEM/EDX, TEM and FTIR and UV-Vis spectroscopies. Their catalytic activity was analysed in the (DRM) reaction with NTP as the promotor, the reactions were monitored *via* GC and mass spectrometry. To our knowledge, work on catalysts of this nature in the NTP-promoted DRM reaction have yet to be published.

References:

[1] IPCC. *Renewable Energy and Climate Change Mitigation Report Summary for Policymakers*. 2019
[2] D. Pakhare, J. Spivey, *Chemical Society Reviews*, 2014. 43(22): p. 7813-7837.
[3] W.C. Chung,M.B. Chang, *Renewable and Sustainable Energy Reviews*, 2016. 62: p. 13-31.

IRISH RESEARCH COUNCIL
An Chomhairle um Thaighde in Éirinn

GOIPG/2018/2880

A Python Based Non-Linear Regression Model to Estimate Acid-Base Characteristics of Organic Alkalinity – Pilot Study Dublin Bay.

Daniel E. Kerr[1], Charles Turner[2], Anthony Grey[1], Brian P. Kelleher[1*]

[1] *Organic Geochemical Research Laboratory, School of Chemical Science, Dublin City University, Ireland*
[2] *Ocean and Earth Science, National Oceanography Centre Southampton, University of Southampton, Southampton, UK.*

[*] *Corresponding author email: brian.kelleher@dcu.ie*

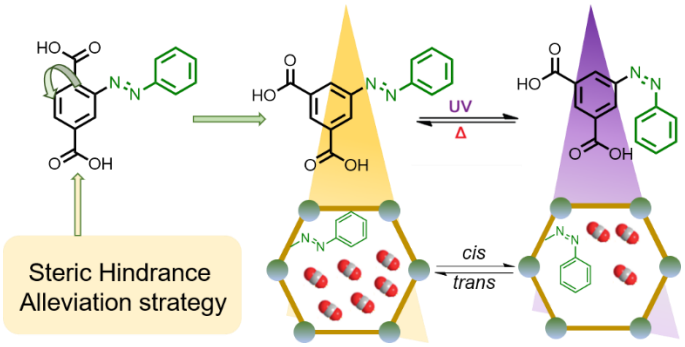
Accurate analysis of carbonate system parameters is paramount in tracking phenomena resulting from anthropogenic CO_2 emission such as ocean acidification. Total alkalinity (TA) is a widely utilised parameter in the calculation of pH and acidification trackers such as aragonite saturation state. Organic alkalinity (OrgAlk) is the fraction of TA that is associated with organic charge groups present on dissolved organic matter and is typically unaccounted for in TA values used in carbonate system calculations. This can lead to the propagation of errors in calculated carbonate parameters and key carbonate system descriptors. Quantification of OrgAlk and estimation of its acid-base characteristics can aid in reducing the magnitude of propagated errors. This study evaluated OrgAlk variability and acid-base characteristics in Dublin Bay and its associated transitional waters across a 9-month period. Back titrations carried out with readily available Global Ocean Acidification Observing Network apparatus coupled with a bespoke Python based regression model allowed for the quantification of OrgAlk and identification of the main charge groups. OrgAlk varied from 64 – 248 $\mu mol.kg^{-1}$ with larger values reported in more saline waters. 2 main charge groups were identified, both indicative of carboxylic groups. OrgAlk was found to be a significant portion of TA in transitional waters, highlighting the importance of its inclusion in subsequent carbonate system calculations.

iCRAG
SFI RESEARCH CENTRE
IN APPLIED GEOSCIENCES

Enhanced Efficiency of Photo Switching Metal-Organic Framework Toward Low Energy Carbon Dioxide Capture

Qi Huang, Chunfei Wu*
School of Chemistry and Chemical Engineering, Queen's University Belfast, Belfast, BT7 1NN, UK
*email: qhuang05@qub.ac.uk, *email:C.Wu@qub.ac.uk*

In the recent decades, many technologies (CCS and CCU) have been attempted to reduce the rising global 2- level. Although some progress had been made, the current state of carbon capture technologies is still relatively expensive and energy intensive. metal organic frameworks (MOFs) because of the high surface area, have been widely reported as adsorbents for gas storage. Photo-switching MOFs are commonly fabricated by incorporating photo-switchable units into MOF material since they can reversibly change their molecular structure and electronic state through light exposure, such as azobenzene, diarylethene and spiropyran. More importantly, photo switching MOFs prepared via integrating MOF frameworks with photochromic units, can realize the adsorbents regeneration process simply through remote light triggering, which greatly saves the energy cost for MOF adsorbents regeneration. [1]



Herein, we present a strategy to tailor the photo switching efficiency of azobenzene functionalized MOFs via a steric hindrance alleviation approach, which contributed to about 34% enhancement of CO_2 switching efficiency. Thereby, a promising strategy for optimizing the switching efficiency of present photo responsive MOF is explored and verified.[2]

References:

[1] Q. Huang, C. Wu, *Materials Today Sustainability*, 2022, 18, 100149.
[2] Q. Huang, J. Mu, Z. Zhan, F. Wang, S. Jin, B. Tan and C. Wu, *Journal of Materials Chemistry A*, 2022,10, 8303-8308.

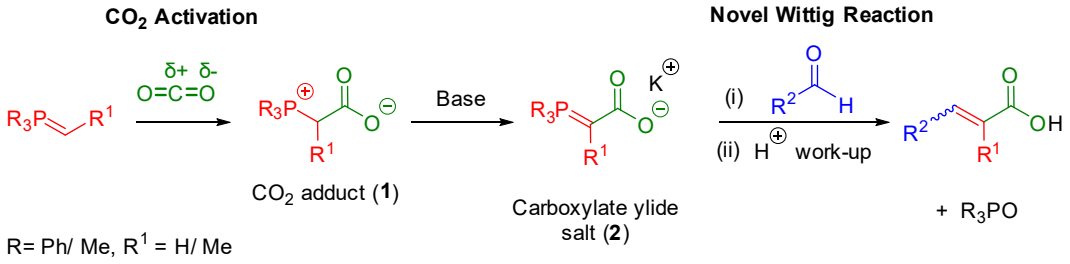
Synthesis of α,β-Unsaturated Carboxylic Acids by Phosphonium Ylide-Mediated CO_2 Activation

Amy Lowry, Dr Peter Byrne, and Dr Gerard McGlacken

School of Chemistry, University College Cork, Cork, Ireland.
Analytical and Biological Chemistry Research Facility, University College Cork, Cork, Ireland.

email: peter.byrne@ucc.ie, 114317296@umail.ucc.ie

Carbon dioxide utilisation continues to capture the attention of chemists due to its ever-increasing levels and the negative effects of global warming.[1-2] However, CO_2 is a valuable and environmentally friendly C_1 building block for the synthesis of various value-added chemicals. CO_2 has an inherently low reactivity due to its stability, therefore must be activated before it can be converted into synthetically useful products.[3] Many medicinally important compounds contain the elements of CO_2 within their structure, including α,β-unsaturated carboxylic acids and enoates. Some common approaches to the construction of α,β–unsaturated carboxyl compounds include ylide-mediated Wittig and Horner-Wadworth-Emmons reactions, and others such as Heck, Perkin, Knoevenagel, and Claisen-Schmidt reactions. Many of these synthetic routes require hydrolysis of the ester product to the corresponding acid. In contrast, we report a novel application of the Wittig reaction, enabling direct installation of the carboxyl group, and importantly, achieving CO_2 incorporation.



In the methodology herein reported, CO_2 is activated by reaction with a phosphonium ylide, generating a carboxyl-containing phosphonium salt (**1**). Deprotonation of adduct **1** generates a novel entity (carboxylate ylide **2**). This has been demonstrated to undergo Wittig reactions with a range of aldehydes to form α,β-unsaturated carboxylic acids. Using this novel strategy, a variety of α,β-unsaturated carboxylic acids have been generated and separated from phosphine oxide (>30 examples, in yields of up to 97%).

References:

[1] See NASA website: https://climate.nasa.gov/causes/.
[2] IPCC, 2014: *Climate Change 2014*: *Synthesis Report*, available at: https://www.ipcc.ch/report/ar5/syr/.
[3] *Curr. Opin. Green Sustain. Chem.* **2017**, *7*, 31-38.

IRISH RESEARCH COUNCIL
An Chomhairle um Thaighde in Éirinn

Synthesis and Testing of Water-Soluble Near Infrared Azadipyrromethene (NIR-AZA) Fluorophores

Donal F. O' Shea and Cathal Caulfield

Cameron Chemistry Laboratory, Department of Chemistry, RCSI, Dublin 2

email: cathalcaulfield@rcsi.ie

Postoperative ureteral injuries can occur as a result of surgical operations in the abdominal region.[1] Fluorescence-guided surgery could be used to pre-empt such injury by identifying the ureter prior to surgery.

Water-soluble BF_2-azadipyrromethene (AZA) fluorophores **1** and **2** have been synthesised in 4[2] and 8 steps respectively for the purpose of real-time intraoperative ureteral imaging and identification. Emission maxima in aqueous solutions were recorded at 720 nm and 828 nm for **1** and **2** which are optimal for clinically used imaging instruments.[3] Successful *in vivo* ureter imaging studies have been carried out in rat and porcine models using **1**. The synthesis, photophysical properties, pharmacokinetics, and *in vitro* / *in vivo* imaging of **1** and **2** will be discussed.

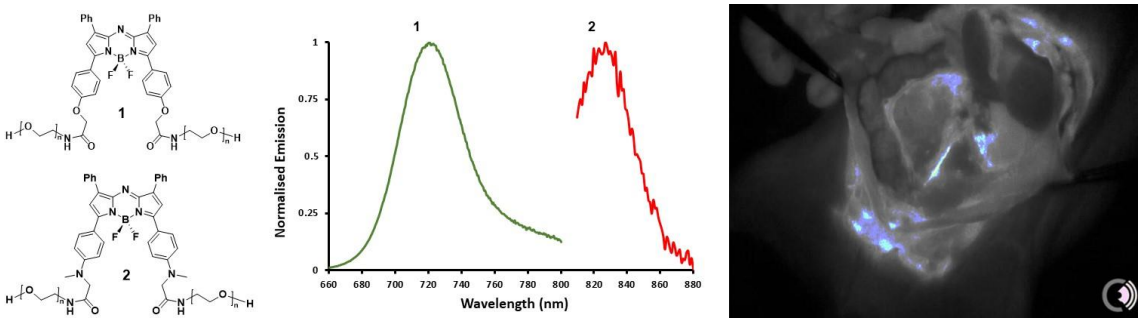


Figure 1. Structures of NIR-AZA fluorophores **1** and **2**; normalised fluorescence emission of **1** and **2** in water; *in vivo* ureter identification using **1** in rat model.

References:

(1) Daly, H. C.; Conroy, E.; Todor, M.; Wu, D.; Gallagher, W. M.; O'Shea, D. F. *Theranostics* **2020**, *10*, 3064.

(2) Wu, D.; Daly, H. C.; Conroy, E.; Li, B.; Gallagher, W. M.; Cahill, R. A.; O'Shea, D. F. *Eur J Med Chem* **2019**, *161*, 343.

(3) Achterberg, F. B.; Deken, M. M.; Meijer, R. P. J.; Mieog, J. S. D.; Burggraaf, J.; van de Velde, C. J. H.; Swijnenburg, R. J.; Vahrmeijer, A. L. *Eur J Nucl Med Mol Imaging* **2021**, *48*, 332.

RCSI Leading the world to better health
Apjohn Scholar

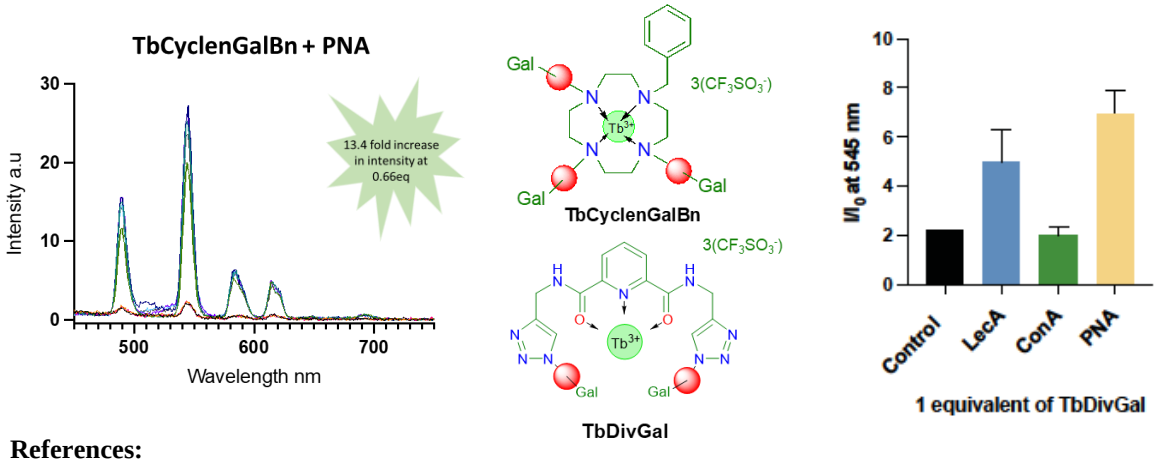
Shining A Light On Bacteria : Lanthanide-Based Glycoconjugate Molecular Sensors For Lectins

Karolina Wojtczak, Ian J. Murphy and Joseph P. Byrne

School of Chemical and Biological Sciences, NUI Galway, University Road, Galway, Ireland

email: k.wojtczak1@nuigalway.ie , joseph.byrne@nuigalway.ie

Lanthanide probes offer several advantages for sensing applications, including their characteristic and time-resolved emission spectra, which can be easily distinguished from background fluorescence of biological samples.[1] Many pathogenic bacteria such as *Pseudomonas aeruginosa* and *Escherichia coli* produce carbohydrate-binding proteins (lectins), which present viable targets for detection of these organisms, as well as for new therapies. Diagnostic methods for bacterial infections typically take several days, relying on cell culture, leading to delays in targeted treatment. New rapid detection methods would aid in the fight against antimicrobial resistance. The aim of this project is to use the selective nature of carbohydrate-lectin interactions to develop new visually responsive glycoconjugate probes, which would be suitable for diagnosis of infections, such as by *P. aeruginosa*, a bacterium classified as a Priority 1 pathogen by the WHO, with urgent need for new antibiotic treatments and diagnostics due to the ongoing problem of antimicrobial resistance.[2] LecA and LecB are lectins on the surface of P. aeruginosa with high affinity for galactoside and fucoside glycans respectively.[3] Many approaches have been developed to inhibit the binding of these lectins to human tissue cells by the development of inhibitory glycoconjugates with varying degrees of success.[4a-e] We report several multivalent glycoconjugate lanthanide complexes, based on different scaffolds and presentation modes, which demonstrate enhanced emission in the presence of relevant lectins. Integration of these probes into "smart" materials has potential for application in the medical devices industry. This strategy could be expanded to other bacteria in the future.



References:

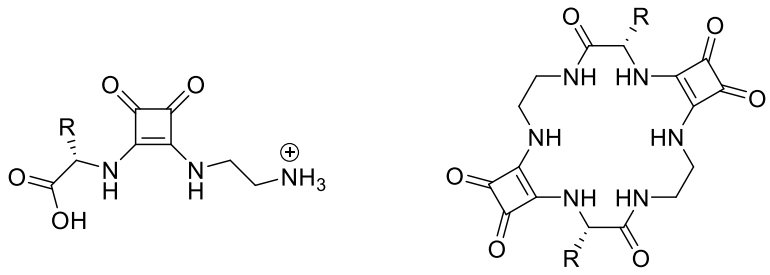
[1] D. Parker et al, Chem. Soc. Rev., 2021,50, 8193-8213
[2] Tillotson, G. Lancet Infect. Dis. 2018, 18 (3), 234–236
[3] Imberty, A. et al, Microbes and Infection, 2004, 6(2), 221-228
[4] a) Cecioni, S. et al, Eur. Chem. J., 2011, 17(7), 2146-2159 b) Kadam, R.U. et al, Eur. Chem. J., 2013, 19(50), 17054-17063 c) Reymond, J.-L. et al, Chem. Soc. Rev, 2013, 42(11), 4814. d) Wang, S. et al, Chem. Eur. J., 2016, 22, 1-11 e) Byrne, J.P. et al, RSC Adv., 2021, 11, 16318-16325

Squaratides: A New Family of Macrocyclic Peptidomimetics with Application as Anion Recognition Scaffolds

Hua Tong and Robert. B. P. Elmes
Chemistry Department, Maynooth University, Maynooth, Co. Kildare, Ireland

Email: hua.tong.2018@mumail.ie, robert.elmes@mu.ie

The ubiquitous role of anionic species in biology, medicine, catalysis and the environment has led to the establishment of anion binding, sensing and transport as a burgeoning area of research, particularly in the field of supramolecular chemistry.[1] Molecules with the ability to selectively bind to specific anionic targets have numerous potential applications in these areas.[2] Squaramides, a family of conformationally rigid cyclobutene ring derivatives, are rapidly gaining research interest towards this end.[3] Composed of two carbonyl hydrogen-bond acceptors in close proximity to two NH hydrogen-bond donors, this small molecular scaffold benefits from unique physical and chemical properties that render it extremely useful in the design of anion receptors, sensors and transporters. Moreover, their synthetic versatility renders squaramides practical for incorporation in a wide range of supramolecular scaffolds. Taking inspiration from nature, and through judicious molecular design we propose an entirely new peptidomimetic anion binding scaffold based on squaratides – a hybrid mix of squaramides and peptides (Figure 1).



Squaramino Acid monomer **1**

Cyclic dimer squaratide **2**

Figure 1: The proposed structures of monomer **1** and cyclic dimer **2**.

In this work we will describe our recent work towards the synthesis of a library of modified amino acid building blocks and their use in the construction of several cyclic peptidomimetic structures. To date, we have successfully synthesized several monomer building blocks based on **1** as well as optimizing their dimerization to form a family of cyclic dimers based on **2**.

Reference:

[1]: P. A. Gale, R. Perez-Tomas and R. Quesada, *Acc. Chem. Res*., **2013**, 46,2801–2813.

[2]: R. B. P. Elmes and K. A. Jolliffe, *Chem. Commun.*, **2015**,51, 4951-4968.

[3]: L.A. Marchetti, L.K. Kumawat, N. Mao, J.C. Stephens and R.B.P. Elmes, *Chem,* **2019**, 5, 1398-1485.

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

Liam S. Fitzgerald[1,2], Eimear Carroll[1], Paul V. Murphy[1,2]

[1] School of Biological and Chemical Sciences, National University of Ireland Galway, University Road, H91 TK33 Galway, Ireland; l.fitzgerald14@nuigalway.ie (L.S.F.)
[2] CÚRAM—Science Foundation Ireland Research Centre for Medical Devices, National University of Ireland Galway, H91 TK33 Galway, Ireland

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.

References

[1] Paget, J.; Spreeuwenberg, P.; Charu, V.; Taylor, R. J.; Iuliano, A. D.; Bresee, J.; Simonsen, L.; Viboud, C. Global Mortality Associated with Seasonal Influenza Epidemics: New Burden Estimates and Predictors from the GLaMOR Project. *J. Glob. Health* **2019**, *9* (2).

[2] Kilbourne ED. Influenza Pandemics of the 20th Century. *Emerging Infectious Diseases*. **2006**;12 (1),9-14.

[3] Ji, Y.; White, Y. J.; Hadden, J. A.; Grant, O. C.; Woods, R. J. New Insights into Influenza A Specificity: An Evolution of Paradigms. *Curr. Opin. Struct. Biol.* **2017**, *44*, 219–231.

[4] Barik, S. New Treatments for Influenza. *BMC Med.* **2012**, *10* (1), 104.

[5] Friesner, R. A.; Banks, J. L.; Murphy, R. B.; Halgren, T. A.; Klicic, J. J.; Mainz, D. T.; Repasky, M. P.; Knoll, E. H.; Shelley, M.; Perry, J. K.; Shaw, D. E.; Francis, P.; Shenkin, P. S. Glide: A New Approach for Rapid, Accurate Docking and Scoring. 1. Method and Assessment of Docking Accuracy. *J. Med. Chem.* **2004**, *47* (7), 1739–1749.

[6] André, S.; O'Sullivan, S.; Koller, C.; Murphy, P. V.; Gabius, H.-J. Bi- to Tetravalent Glycoclusters Presenting GlcNAc/GalNAc as Inhibitors: From Plant Agglutinins to Human Macrophage Galactose-Type Lectin (CD301) and Galectins. *Org. Biomol. Chem.* **2015**, *13* (14), 4190–4203.

Metal-based Glycoconjugates for the Targeted Anticancer Chemotherapy

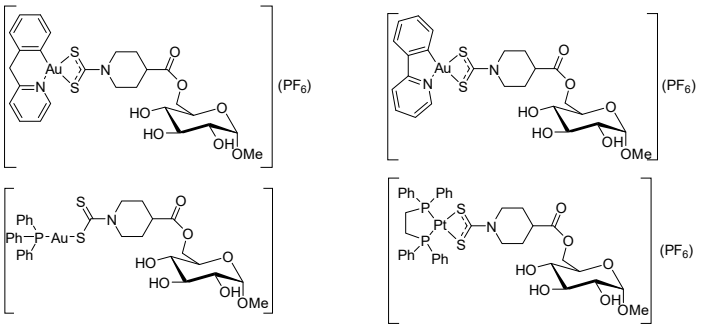
Ioannis Titilas,[a] Isolda Romero-Canelon[b] and Luca Ronconi[a,*]

[a]*National University of Ireland Galway, School of Biological and Chemical Sciences, Galway (Ireland)*
[b]*University of Birmingham, School of Pharmacy, Edgbaston (UK).*

email: I.TITILAS1@nuigalway.ie; luca.ronconi@nuigalway.ie

Glucose enters the cell by facilitated diffusion through the glucose transporters (GLUTs) and, subsequently, undergoes a series of biochemical steps to produce energy. In order to sustain their abnormal proliferation rates, cancer cells overexpress GLUTs to facilitate glucose internalization, thus satisfying their greater demand for energy. Remarkably, aerobic glycolysis was proved to be the major glucose metabolic pathway in tumor sites (the so-called "Warburg effect").[1] Therefore, conjugation of chemotherapeutic agents (including metallodrugs) to glucose-like substrates shows potential in a view to achieving tumor-specific intracellular drug transfer and delivery by taking advantage of the increased demand of glucose and the overexpression of GLUTs in cancer cells.[2]

In this context, we here report on the development of some platinum(II)- and gold(I/III)-dithiocarbamato glycoconjugates obtained by exploiting an elegant and efficient synthetic route recently developed by our group.[3,4] Such metal-glycoconjugates would combine the antitumor properties and the favorable toxicological profile of the metal-dithiocarbamato non-glycosylated analogues,[5] along with improved tumor selectivity and cellular uptake provided by the glucose-containing ligand coordinated to the metal center, through the exploitation of the glucose-mediated cellular internalization facilitated by overexpressed GLUTs.



Acknowledgements. Financial support by NUI Galway (*Millennium Fund Minor Project 2013* to LR) and the Irish Research Council (*Postgraduate Scholarship GOIPG/2018/38* to IT) is gratefully acknowledged.

References:

[1] van der Heiden, M. G.; Cantley, L. C.; Thompson, C. B. *Science* **2009**, *324*, 1029.
[2] Pettenuzzo, A.; Pigot, R.; Ronconi, L. *Metallodrugs* **2015**, *1*, 36.
[3] Pettenuzzo, A.; Montagner, D.; McArdle, P.; Ronconi, L. *Dalton Trans.* **2018**, *47*, 10721.
[4] Pettenuzzo, A.; Vezzù, K.; Di Paolo, M.L. *et al. Dalton Trans.* **2021**, *50*, 8963.
[5] Marzano, C.; Ronconi, L.; Chiara, F. *et al. Int. J. Cancer* **2011**, *129*, 487.

Metallacarboranes: a versatile new player in biomedicine

N. Murphy,[a,b] Dr. A. Saini, [b] Dr. R. Dwyer,[a,c] Dr. Pau Farràs,[a,b]

[a]NUI Galway, Centre for Research in Medical Devices, Galway (Ireland); [b]NUI Galway, School of Chemistry, Galway, (Ireland)[3]; [c]NUI Galway, Lambe Institute for Translational Research, Galway (Ireland);

email: n.murphy30@nuigalway.ie

Abstract

Metallacarboranes are boron cluster's answer to 'sandwich complex' metallocenes, a group of polyhedral cluster compounds comprising of carbon, boron, hydrogen and a metal centre. Properties such as high stability in biological systems, amphiphilicity and tuneability has seen interest in these molecules surge in recent times.[1-6] The focus of this project is on triple-negative breast cancer, which accounts for 20-25% of all breast cancers and has a generally poor prognosis.[7] Four metal centres have been investigated regarding toxicity, with their individual strengths evaluated vs TNBC cell lines, as well as investigations into their mechanism of action. A second target of the project is incorporation of metallacarboranes into ion pair complexes with common biomarkers of breast cancer such as glutamine. This is with a view to detect levels of these compounds in saliva as a form of diagnostics, having already seen success in wastewater analysis.[8]

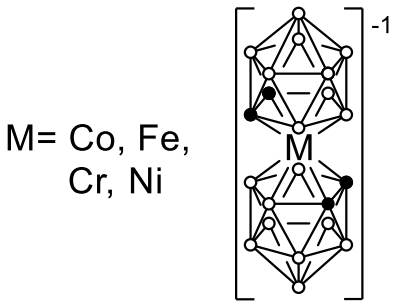


Figure 1: Metallacarboranes at the focus of the study

References

[1] R. N. Grimes, Coord. Chem. Rev., **2000**, *200–202*, 773–811.

[2] P. Farràs, E. J. Juárez-Pérez, M. Lepšík, R. Luque, R. Núñez and F. Teixidor, *Chem. Soc. Rev.*, **2012**, *41*, 3445–3463.

[3] T. Popova, A. Zaulet, F. Teixidor, R. Alexandrova and C. Viñas, *J. Organomet. Chem.*, **2013**, *747*, 229–234.

[4] E. Kvasničková, J. Masák, J. Čejka, O. Maťátková and V. Šícha, *J. Organomet. Chem*., **2017**, *827*, 23–31.

[5] M. Gozzi, B. Schwarze and E. Hey-Hawkins, *Pure Appl. Chem*., **2019**, *91*, 563–573.

[6] P. Stockmann, M. Gozzi, R. Kuhnert, M. B. Sárosi and E. Hey-Hawkins, *Chem. Soc. Rev.*, **2019**, *48*, 3497–3512.

[7] C. Liedtke, C. Mazouni, K. R. Hess, F. André, A. Tordai, J. A. Mejia, W. F. Symmans, A. M. Gonzalez-Angulo, B.Hennessy, M. Green, M. Cristofanilli, G. N. Hortobagyi and L. Pusztai, *J. Clin. Oncol*., **2008**, *26*, 1275–1281.

[8] A. Saini, J. Gallardo-Gonzalez, A. Baraket, I. Fuentes, C. Viñas, N. Zine, J. Bausells, F. Teixidor and A. Errachid, *Sensors Actuators B Chem.*, **2018**, *268*, 164–169.

Novel Process Strategies for the Stabilization of Biopharmaceuticals for Parenteral Use

Ashutosh Sharma[1], Pierre-Andre Cazade[3], Dikshitkumar Khamar[2], Jason Beirne[2], Ambrose Hayden[1], Damien Thompson[3] and Helen Hughes[1]

[1]*Pharmaceutical and Molecular Biotechnology Research Centre (PMBRC), South East Technological University (SETU), Cork Road, Waterford, X91K0EK, Ireland.*

[2]*Sanofi, Manufacturing Science, Analytics and Technology (MSAT), IDA Industrial Park, Waterford, X91TP27, Ireland.*

[3]*Department of Physics, Bernal Institute, University of Limerick, Limerick, V94 T9PX, Ireland.*

e-mail: ashutosh.sharma@postgrad.wit.ie

In the past two decades, biopharmaceuticals have been a breakthrough in improving the quality of lives of patients with various cancers, autoimmune and genetic disorders. With the growing demand of biopharmaceuticals, the need for reducing manufacturing costs is essential without compromising on the safety, quality, and efficacy of the product. Freeze-drying is the primary commercial means of manufacturing solid biopharmaceuticals[1]. However, Freeze-drying is an economically unfriendly means of production with long production cycles[2] and heavy capital investment[3], resulting in high overall costs. Spray-drying is a continuous process with only 20 % of the manufacturing cost involved during Freeze-drying[4]. This research focuses on assessing novel processing technologies such as Active-freeze-drying, Spray-drying, Spray-freeze-drying etc. and their relevance to the commercial biopharmaceutical manufacturing area[5]. Existing literature available on these methods to produce biopharmaceuticals is very limited. The potential impact of these novel technologies will significantly reduce time, energy and costs associated with the manufacturing of biopharmaceuticals. Studying the product through orthogonal techniques such as UV-vis spectroscopy, MADLS, SEC, DSC etc. provides enormous information on the critical quality attributes (CQAs) of the products that have not been studied before[5]. Moreover, molecular modelling will predict the effect of such processes on the product. This research will develop new methods that underpin any future change in the manufacturing strategy with the potential of manufacturing safe drug products at reduced costs.

Figure: Innovative Drying Technologies for Biopharmaceuticals

In vitro and In vivo Biological Evaluation of Functionalized Ultrasmall Gold Nanoparticles for Targeted Drug

Avelino Ferreira, Jennifer Fernández Alarcón, Martina B Violatto, Sergio E Moya, Paolo Bigini and Marco P Monopoli

RCSI – Royal College of Surgeons in Ireland, Department of Chemistry, Dublin 2, Ireland

email: avelinoferreira@rcsi.com

Ultrasmall gold nanoparticles (NPs) (diameter < 10nm) have been increasingly explored as a novel approach for theranostic applications. Their attractiveness comes from the synergy between well known gold properties, such as ease of surface modifications, biocompatibility and fluorescence quenching[1,2] and the specific advantages of nanoparticles in this size range, like increased surface area and higher tissue penetration capability[3,4]. Combined with the increase of circulation time and specific targeting, these systems have can expand the range of biomedical applications, both therapeutical and diagnostics.

In this project, PEGylated ultrasmall gold NPs were functionalized with either a targeting or a control targeting molecule, and a fluorophore. Their interaction with biological entities of interest were assessed. Here is presented the scope of the entire process, from the synthesis, functionalization and characterization to in vitro and in vivo studies, such as safety profile, uptake pathways or biodistribution. The results obtained to date highlight the robustness and promise of these constructs for the development of novel solutions for theranostic approaches.

These nanoparticles were shown to selectively bind to the receptor of interest, with the interaction being modulated by active targeting in dose-dependent fashion. Moreover, cellular uptake, determined by flow cytometry and ICP-MS, was also completely dependent on the nanoparticles surface functionalization, and, importantly, independent on the presence of serum in the uptake media. This suggests that these constructs are able to reduce the impact that indiscriminate protein adsorption has on their properties. This increased uptake prompted us to assess the potential difference in uptake pathways taken by these constructs, using known pharmacological inhibitors to that end. A clear distinction between targeted and control NPs was observed, which can be exploited for drug delivery, by modulating intracellular trafficking. Finally, in vivo studies confirm the differential behaviour and biodistribution of targeted NPs, as they arrive earlier, and penetrate deeper into liver tissue than control NPs.

These results illustrate how promising these constructs are concerning future biomedical applications.

References

1. Elahi, N., Kamali, M. & Baghersad, M. H. Recent biomedical applications of gold nanoparticles: A review. *Talanta* **184**, 537–556 (2018).

Synthetic Strategies Towards Improving the Solubility Profile of Novel Antimicrobial Coumarin Derivatives

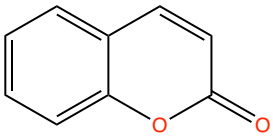
Erika Mooney[1], Bernadette Creaven[2], Fintan Kelleher[1], and Matthias Tacke[3]

1. *School of Science and Computing, TU Dublin Tallaght.*
2. *School of Chemical and Pharmaceutical Sciences, TU Dublin City Campus.*
3. *UCD Centre for Synthesis and Chemical Biology, School of Chemistry, University College Dublin, Belfield, Dublin 4, Ireland*

email: bernie.creaven@tudublin.ie, X00117667@mytudublin.ie

Antimicrobial resistance (AMR), one of the top-ten global human health threats,[1] was attributed as the cause of 1.2 million global deaths in 2019.[2] It is now widely considered the 'overlooked pandemic',[2] and there is an urgent need for the development of novel antimicrobial therapies to combat this ever-growing threat to global human health. Our group has focused on coumarin compounds as target molecules to fight the growing threat from AMR. First discovered in 1820, coumarin (**1**), a naturally occurring heterocyclic compound has solidified itself as a privileged chemical scaffold for the design and synthesis of pharmacologically active compounds.[3] Due to its ease in synthesis and ability to be altered, it is an ideal candidate for the development of novel antimicrobial therapies.[4]

We have previously reported the excellent antimicrobial activity of a series of silver(I) coumarin complexes, but the solubility of these complexes was limited, and they were prone to degradation in solution,[5][6] limiting the clinical usefulness of the complexes. To overcome these limitations, novel coumarin silver(I) complexes with improved solubility profiles have been synthesised. Presented here is a summary of the synthetic strategies used so far towards the isolation of coumarin silver(I) complexes with better solubility profiles than those previously reported. In addition, the preliminary antimicrobial data of some of the coumarin silver(I) complexes synthesised to date will be discussed.



(1): Structure of Coumarin Scaffold

References:

(1) EClinicalMedicine.;. *eClinicalMedicine* **2021**, *41*.

(2) Laxminarayan, R.; *Lancet* **2022**, *399* (10325), 606–607.

(3) Jameel, E. et al.; *Chem. Biol. Drug Des.* **2016**, *87* (1), 21–38.

(4) Annunziata, F. et al.; *Int. J. Mol. Sci.* **2020**, *21* (13), 4618.

(5) Creaven, B. S. et al.; *Inorganica Chim. Acta* **2006**, *359* (12), 3976–3984.

(6) Creaven, B. S. et al.; *J. Inorg. Biochem.* **2016**, *163*, 53–67.

Grant Code: PHEA1705