RSC Organic Division - Ireland Regional Meeting

2nd May 2018

10:00 - 18:30

School of Chemistry and Chemical Engineering
Lecture Theatre 0G/012
David Keir Building
Queens University Belfast

ROYAL SOCIETY OF CHEMISTRY

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We wish to thank the following sponsors for their generous support of this meeting:

RSC Organic Division Ireland Regional Meeting

Wednesday 2nd May
Lecture Room 0G/012, David Keir Building
Queen's University Belfast

10:00 – 10:25	*Welcome tea and coffee*
Session 1. Chair: Dr Peter Knipe	
10:25 – 10:30	Opening remarks
10:30 – 11:00	**Dr Robert Elmes (Maynooth University)**
	Stimuli Activated Systems: Towards Responsive Receptors and Sensors
11:00 – 11:30	**Dr Paul Dingwall (QUB/University of Cambridge)**
	Construction of aldehydes and unsymmetrical ketones from non-stabilised diazo compounds in flow
11:30 – 12:00	**Professor Anita Maguire (UCC)**
	Synthetic and stereochemical aspect of C-H insertions with α-diazocarbonyl compounds
12:00 – 12:30	**Professor Patrick Guiry (DCU)**
	Recent Adventures in Ligand Design and Asymmetric Catalysis
12:30 – 13:30	*Break for lunch*
Session 2. Chair: Professor Paul Stevenson	
13:30 – 14:00	**Dr Miriam O'Duill (NUI Galway)**
	Rational Directing Group Design for the Stabilisation of Six-Membered Palladacycles
14:00 – 14:30	**Dr Matthew Helm (Almac Group)**
	Discovery and Characterization of Highly Potent and Selective Allosteric Inhibitors of USP7
14:30 – 15:00	**Professor Thorfinnur Gunnlaugsson (TCD)**
	Application of supramolecular recognition in synthesis and self-assembly formations
15:00 – 16:00	***Poster Session*** *and refreshment break*
Session 3. Chair: Professor Karl Hale	
16:00 – 16:30	**Dr Emma Coyle (DCU)**
	Catalysts for Organic Synthesis
16:30 – 17:30	**Professor Michael Greaney (University of Manchester)**
	RSC Bader Award Winner
	New Arylation Strategies for Synthesis
17:30 – 17:35	Closing remarks
17:35 – 18:30	*Wine reception and poster prizes (sponsored by* ***Almac Group****)*

Stimuli Activated Systems: Towards Responsive Receptors and Sensors

Robert B. P. Elmes

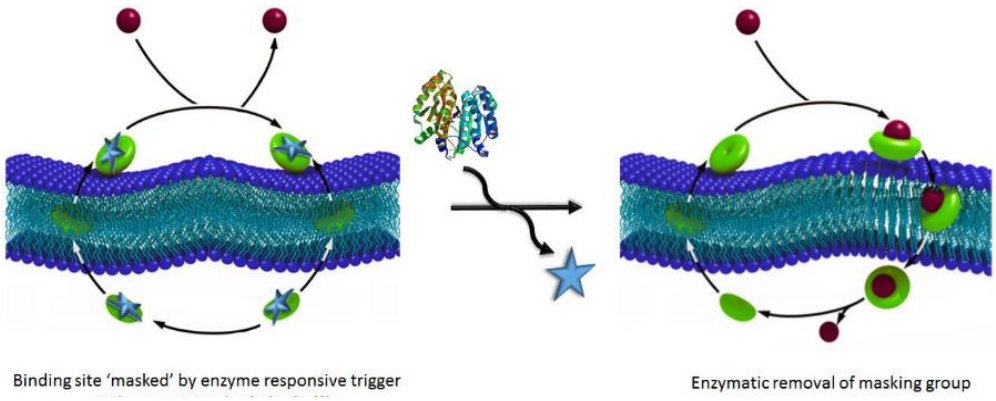
Department of Chemistry, Maynooth University, National University of Ireland, Maynooth, Co. Kildare, Ireland.

E-mail: robert.elmes@mu.ie

So-called 'smart' molecules are predicted to have an enormous impact on many aspects of society, including next generation healthcare, data storage and energy-related technologies to name just a few key areas. Much of the inspiration in this area often comes from the biological world where all living organisms take advantage of 'smart' biomolecules that dictate a myriad of biochemical reactions with astonishing selectivity, specificity and biocompatibility.

Synthetic stimuli activated systems that display the gating/switching behaviour observed in nature still remain relatively scarce in the literature. The ability of chemically triggered systems to operate under otherwise constant conditions should provide a precise level of control and offer the potential to 'switch on' recognition/sensing processes on demand.

This lecture will summarise some of our initial efforts to design easily accessible, sensitive and selective stimuli responsive compounds for use as receptors and sensors and their application towards solving problems of biological significance.



Construction of aldehydes and unsymmetrical ketones from non-stabilised diazo compounds in flow

Paul Dingwall

Department of Chemistry, University of Cambridge

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

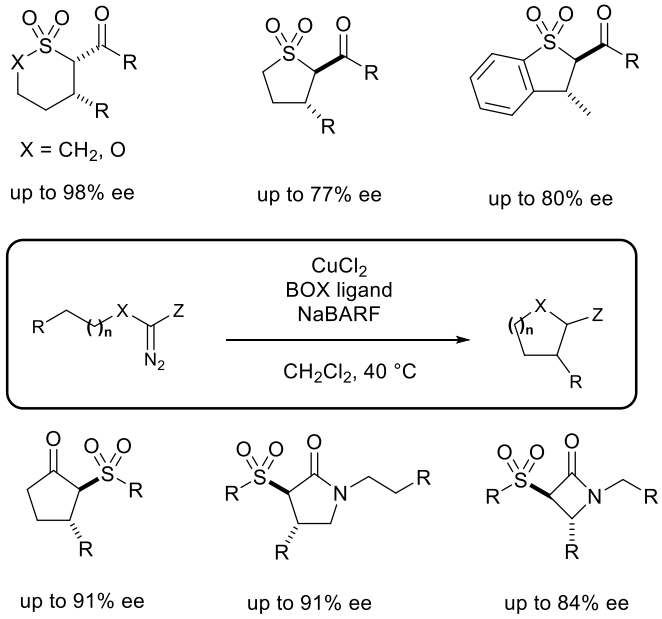
The difficulty in accessing and safely utilising non-stabilised diazo species has somewhat limited the application and utility of this class of compounds. Here we explore the use of oxadiazolines, non-stabilised diazo precursors which are bench stable, in direct, non-catalytic, aldehyde C-H functionalisation reactions under UV photolysis in flow. Commercially available aldehydes are coupled to afford unsymmetrical alkyl-alkyl and aryl-alkyl ketones in good to excellent yields while mild conditions and lack of transition metal catalysts allow for exceptional functional group tolerance. Examples are given on small scale and in larger continuous production. Furthermore, aldehydes can be synthesised through controlled coupling with formaldehyde.

Synthetic and stereochemical aspects of C–H insertions with α-diazocarbonyl compounds

Maguire, Anita R.

School of Chemistry and School of Pharmacy, Analytical and Biological Chemistry Research Facility, Synthesis and Solid State Pharmaceutical Centre, University College Cork, Cork, Ireland.

Transition metal catalysed reactions of α-diazocarbonyl compounds provide a wide range of transformations that can take place with a remarkable degree of selectivity and under very mild conditions.[1] Rhodium or copper catalysed intramolecular C–H insertion reactions of α-diazocarbonyl compounds allow the formation of carbocyclic and heterocyclic rings, often with high degrees of regio- and stereocontrol without requiring strongly basic reagents or acid catalysis.[2,3]
In particular, the use of a catalyst system prepared from copper(II) chloride, sodium tetrakis(3,5-bis(trifluoromethyl)phenyl)borate (NaBARF), and a bisoxazoline ligand is effective for enantioselective cyclisation of a range of α-diazocarbonyl substrates leading to cyclopentanones, sulfolanes, thiopyrans, sultones, and lactams.[4-6]



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3. A. Ring, A. Ford and A. R. Maguire, *Tetrahedron Lett.*, 2016, **57**, 5399–5406.
4. C. J. Flynn, C. J. Elcoate, S. E. Lawrence and A. R. Maguire, *J. Am. Chem. Soc.*, 2010, **132**, 1184–1185.
5. C. N. Slattery and A. R. Maguire, *Org. Biomol. Chem.*, 2011, **9**, 667–669.
6. L. A. Clarke, A. Ring, A. Ford, A. S. Sinha, S. E. Lawrence and A. R. Maguire, *Org. Biomol. Chem.*, 2014, **12**, 7612–7628.

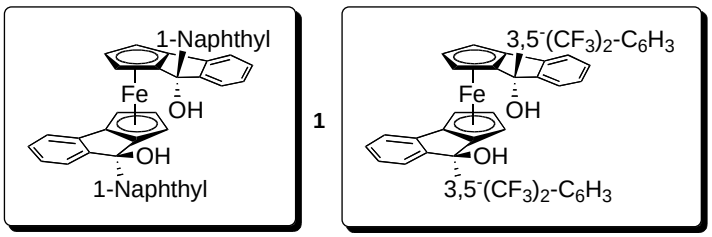
Recent Adventures in Ligand Design and Asymmetric Catalysis

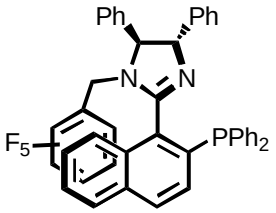
Professor Pat Guiry MRIA

Centre for Synthesis and Chemical Biology, School of Chemistry, University College Dublin, Belfield, Dublin 4, Ireland
http://www.guiryresearchgroup.com/
p.guiry@ucd.ie

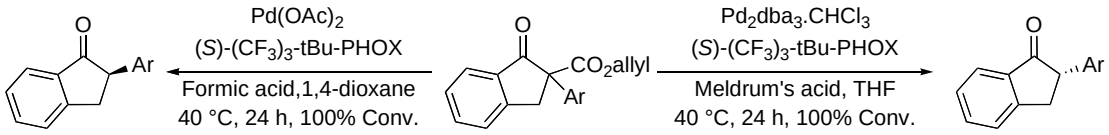
This presentation will describe the design and synthesis of novel ferrocene-containing diols **1** as a novel scaffold for asymmetric catalysis and the novel axially chiral P,N ligand, UCD-PHIM, and its applications in A3 coupling..

The development of the Pd-catalysed decarboxylative asymmetric protonation for the preparation of α-arylketones will be described, including recent advances in understanding the mechanisms involved in enantiodivergence and protonation with a chiral proton source.





(*S,S,R*$_a$)-**UCD-PHIM**



(*S*)- 92% *ee*

(*R*)- 93% *ee*

Rational Directing-Group Design for the Stabilisation of Six-Membered Palladacycles

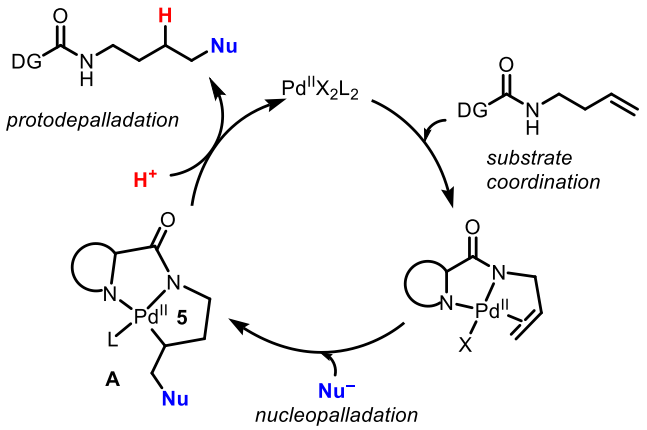
O'Duill, Miriam L.,[a,b] Matsuura, Rei,[b] Wang, Yanyan,[c] Turnbull, Joshua L.,[b] Gurak Jr., John A.,[b] Gao, De-Wei,[b] Lu, Gang,[c] Liu, Peng[c]* and Engle, Keary M.[b]*

a. School of Chemistry, NUI Galway, Galway, Ireland; b. Department of Chemistry, The Scripps Research Institute, La Jolla, USA; c. Department of Chemistry, University of Pittsburgh, Pittsburgh, USA

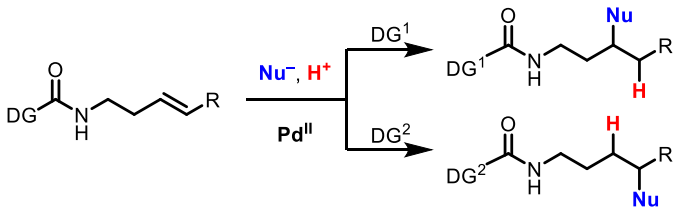
Olefin difunctionalisation reactions are an essential part of the modern synthetic organic chemist's toolkit and have been exploited for the synthesis of natural products and pharmaceutical compounds. The regiochemistry of the products is usually controlled by the steric and electronic properties of the substrate.

In the Engle group, a directing group approach is used for the regiocontrolled hydrofunctionalisation of alkenes and alkynes by intercepting Wacker-type intermediates with a protic acid.[1] Regiocontrol is achieved through formation of a stable, five-membered palladacyle **A**, which has been isolated and characterised by X-ray crystallography (Scheme 1a). 6-membered palladacycles are kinetically and thermodynamically disfavoured. By rational design of new directing groups, we now report the stabilisation of these elusive intermediates. Through systematic tuning of the directing group either the Markovnikov or the anti-Markovnikov product can thus be obtained under otherwise identical reaction condition (Scheme 1b). These results expand the synthetic toolkit to include directed alkene functionalisation reactions that have heretofore proven elusive and lays the groundwork for the development of ligand-controlled regioselective alkene functionalisation reactions.

(a) Wacker-type hydrofunctionalization: regiocontrol *via* directing group (DG) strategy



(b) This work: regiochemistry of products tuned by use of different directing groups (DG)



Scheme 1. Directing-group-controlled regioselectivity in transition-metal catalysed alkene hydrofunctionalisation.

References

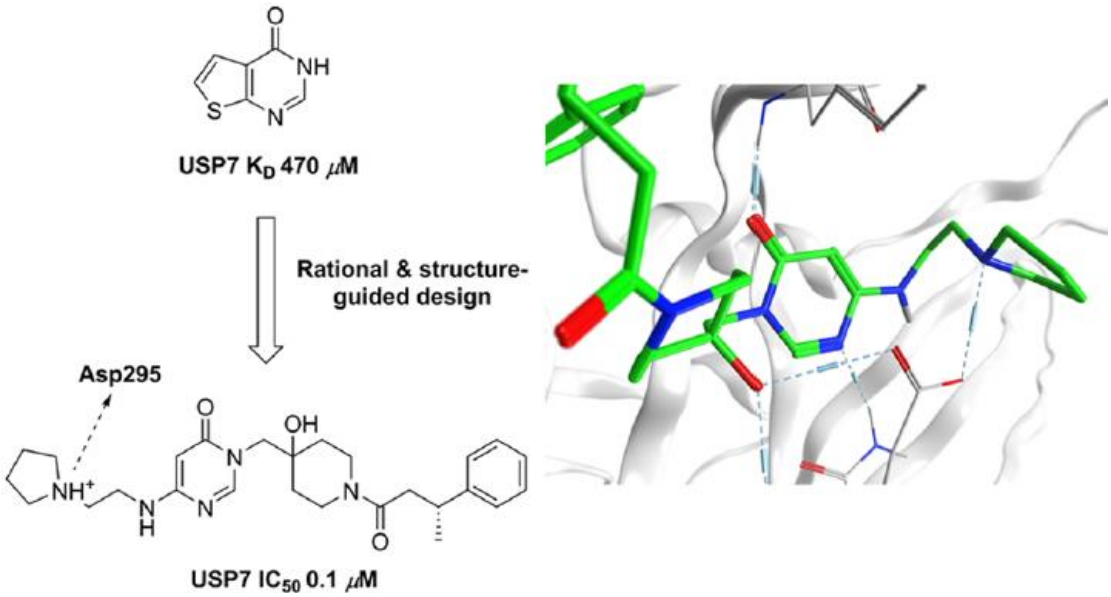
[1] (a) Gurak Jr., J. A.; Yang, K. S.; Liu, Z.; Engle, K. M. *J. Am. Chem. Soc.* **2015**, *138*, 5805; (b) Yang, K.; Gurak, J. A., Jr.; Liu, Z.; Engle, K. M. *J. Am. Chem. Soc.* **2016**, *138*, 14705; (c) Derosa, J.; Cantu, A. L.; Boulous, M. N.; O'Duill, M. L.; Turnbull, J. L.; Liu, Z.; De La Torre, D. M.; Engle, K. M. *J. Am. Chem. Soc.* **2017**, *139*, 5183.

Discovery and characterization of highly potent and selective allosteric USP7 inhibitors

O'Dowd, Colin R.[†], **Helm, Matthew D.**[†], Rountree, J. S. Shane[†], Flasz, Jakub T.[‡], Arkoudis, Elias[‡], Miel, Hugues[†], Hewitt, Peter R.[†], Jordan, Linda[†], Barker, Oliver[†], Hughes, Caroline[†], Rozycka, Ewelina[†], Cassidy, Eamon[†], McClelland, Keeva[†], Odrzywol, Ewa[†], Page, Natalie[†], Feutren-Burton, Stephanie[†], Dvorkin, Scarlett[‡], Gavory, Gerald[†], and Harrison, Timothy[†‡]

[†]*Almac Discovery*

[‡]*Centre for Cancer Research and Cell Biology, Queen's University Belfast*



Ubiquitin specific protease 7 (USP7, HAUSP) has become an attractive target in drug discovery due to the role it plays in modulating Mdm2 levels and consequently p53. Increasing interest in USP7 is emerging due to its potential involvement in oncogenic pathways as well as possible roles in both metabolic and immune disorders in addition to viral infections. Potent (IC50 < 10 nM), novel, and selective inhibitors of USP7 have been developed using both rational and structure-guided design enabled by high-resolution cocrystallography. Initial hits were identified via fragment-based screening, scaffold-hopping, and hybridization exercises. Two distinct subseries were discovered along with the associated structure−activity relationship trends. We have identified cancer cell lines hypersensitive to USP7 inhibition (EC50 < 30 nM) and demonstrate equal or superior activity in these cell models compared to clinically relevant MDM2 antagonists. Overall, these findings demonstrate the tractability and druggability of DUBs, and provide important tools for additional target validation studies. ***"Characterization of Highly Potent and Selective Allosteric Inhibitors of USP7"*** *Nat. Chem. Biol.* **2018**, *14*, 118−125. **"Identification and Structure-Guided Development of Pyrimidinone Based USP7 Inhibitors"** *ACS Med. Chem. Lett.* **2018**, *9*, 238−243.

Application of supramolecular recognition in synthesis and self-assembly formations

Thorri Gunnlaugsson

School of Chemistry and Trinity Biomedical Sciences Institute (TBSI), Trinity College Dublin, The University of Dublin, Dublin 2.

In this lecture, the development of various organic ligands based the 2,6-bis (1,2,3-triazol-4-y l) pyridine (**btp**) structure are presented, and their applications as building blocks for the formation of novel supramolecular self-assembly structures and materials is outlined.[1,2] The **btp** building block are privileged coordination ligands with similar coordination properties to that seen for terpyridine (**terpy**); but in contrast to **terpy**, they have been much less explored. At the same time the **btp** structure is highly modular, easily assessable from simple starting materials, and can often been formed through the use of one-pot synthesis.[3,4] Herein, our effort in exploring their use and applications as coordination ligands for various metal ions,[5,6] in the formation of mechanically interlocked molecules[7] and as building blocks for the formation of self-healing luminescent soft-materials[8] will be detailed.

[1] The btp [2,6-bis(1,2,3-triazol-4-yl)pyridine] binding motif: A new versatile terdentate ligand for applications in coordination, supramolecular and material chemistry", Joseph P. Byrne, Jonathan A. Kitchen and Thorfinnur Gunnlaugsson, *Chem. Soc. Rev*., 2014, **43**, 5302-5325.
[2] Lanthanide directed self-assembly of highly luminescent supramolecular 'peptide' bundles from α-amino-acid functionalized 2,6-bis(1,2,3-triazol-4-yl)pyridine (btp) ligands", Joseph P. Byrne, Jonathan A. Kitchen, John E. O'Brien, Robert D. Peacock and Thorfinnur Gunnlaugsson, *Inorg. Chem*. 2015, **54**, 1426−1439.
[3] "Lanthanide luminescent logic gate mimics in soft matter: [H+] and [F-] dual-input device in a polymer gel with potential for selective component release", Samuel J. Bradberry, Joseph P. Byrne, Colin P. McCoy and Thorfinnur Gunnlaugsson, *Chem. Commun*. 2015, **51**, 16565-16568.
[4] Chiroptical Probing of Lanthanide-Directed Self-Assembly Formation Using btp Ligands Formed in One-Pot Diazo-Transfer–Deprotection–'Click' Reaction from Chiral Amines", Joseph P. Byrne, Miguel Martínez-Calvo, Robert D. Peacock and Thorfinnur Gunnlaugsson, *Chem. Eur. J*. 2016, **22**, 486-490.
[5] A folded [2×2] metallo-supramolecular grid from a bis-tridentate (1,2,3-triazol-4-yl)-picolinamide (tzpa) ligand, Dawn E. Barry, Chris S. Hawes, Joseph P. Byrne, Bjørn la Cour Poulsen, Manuel Ruether, John E. O'Brien and Thorfinnur Gunnlaugsson, *Dalton Trans*., 2017, **46**, 6464-6472.
[6] A lanthanide luminescent cation-exchange material derived from a flexible tri-carboxylic acid 2,6-bis(1,2,3-triazol-4- yl)pyridine (btp) tecton, Eoin P. McCarney, Chris S. Hawes, Jonathan A. Kitchen, Kevin Byrne, Wolfgang Schmitt and Thorfinnur Gunnlaugsson, *Inorg. Chem.* 2018, **57**, 3920–3930.
[7] Self-templated btp [2]Catenanes Formed by Triazolyl Hydrogen Bonding; The Formation of Selective Anion Hosts for Phosphate", Joseph P. Byrne, Salvador Blasco, Anna B. Aletti, Gary Hessman and Thorfinnur Gunnlaugsson, *Angew. Chem. Int. Ed.* 2016, **55**, 8938-8943.
[8] Self-assembly formation of a healable lanthanide luminescent supramolecular metallogel from 2,6-bis(1,2,3-triazol-4-yl)pyridine (btp) ligands", Eoin P. McCarney, Joseph P. Byrne, Brendan Twamley, Miguel Martínez-Calvo, Gavin Ryan, Matthias E. Möbius and Thorfinnur Gunnlaugsson, *Chem. Commun*. 2015, **51**, 14123-14126 .

Catalysts for Organic Synthesis

Emma Coyle

School of Chemical Sciences, Dublin City University (DCU), Glasnevin, Dublin 9

To address a surge in identification of targets for drug activity, innovative synthetic routes are needed to access many more potential medicines. Adoption of new methodology is hindered by cost and environmental regulation, thus one that utilises low cost substrates, requires low energy and offers ease of validation presents an attractive option for the pharmaceutical and fine chemical industries.

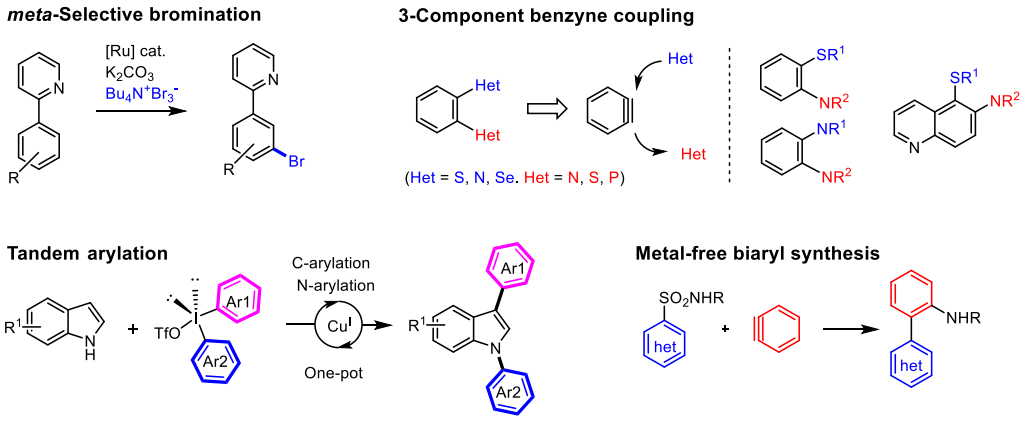
Dr Coyle's research focusses on translation of basic research in the catalytic Corey Chaykovsky reaction into a versatile and scalable methodology for use in process development.

New Arylation Strategies for Organic Synthesis

Michael Greaney

University of Manchester

Transition metal (TM) catalysts can control a vast range of chemical reactivity. At one extreme, they can harness and modulate the most energetic reactive intermediates, such as arynes and carbenes. Contrastingly, they can be used to activate inert, unreactive functional groups such as C-H bonds. Both of these areas offer tremendous potential for the discovery of new, catalytic reaction pathways for C-C and C-X bond construction. Focussing on the heterocyclic field, the talk will describe our progress in designing new TM-catalysed reaction systems and their application to modular heterocycle synthesis. [1,2]



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2. S. G. Modha, M. F. Greaney, *J. Am. Chem. Soc.* **2015**, *137*, 1416-1419. C. J. Teskey, A. J. W. Lui, M. F. Greaney, *Angew. Chem. Int. Ed.* **2015**, *54*, 11677-11680.

Bader Award 2017 Winner

Awarded for creative contributions to C-H activation, dynamic covalent chemistry, and reactive intermediates in organic synthesis

Michael Greaney was born in Liverpool and took his undergraduate degree at Oxford, completing his part II research project in the group of Sir Jack Baldwin. He then moved to London to carry out PhD work with William Motherwell at UCL, completing his thesis in the area of new fluorinating agents in 1999. He then left the UK on a GlaxoWellcome scholarship to take up a postdoctoral position with Jeffrey Winkler at the University of Pennsylvania, where he worked on the total synthesis of the tumour-promoting diterpene ingenol. He returned to the UK in early 2002, to a lectureship position at the University of Edinburgh. He was awarded an EPSRC Leadership Fellowship in 2008 for his work in organic synthesis, and in 2011 he moved to the University of Manchester to a personal chair in organic chemistry.

List of Posters

1 **Dáire Gibbons (TCD)**
Structure and Conformation of Photosynthetic Pigments and Related Compounds

2 **Ross Ballantine (QUB)**
Synthesis of Cyclic and Linear Analogues of Tridecaptin A1

3 **Elisabeth Sitte (TCD)**
Exploration of Novel Functionalization Reactions for Naturally Occurring Porphyrins

4 **Nicholas Mullins (Dundalk Institute of Technology)**
Synthesis and Structure-Activity Relationships of Novel Large-Conductance Ca^{2+}- Activated K^{+} (BK) Channel Modulators

5 **Andrew Cummings (QUB)**
Rapid Baeyer-Villiger oxidation of levoglucosenone analogues for the synthesis of nucleoside analogues

6 **Karolis Norvaiša (TCD)**
Nonplanar Porphyrins: New Concepts for Old Molecular Designs

7 **Ruairí O. McCourt (TCD)**
Rapid Access to Thiolactone Derivatives Through Acyl-Thiol-Ene (ATE) and Acyl-Thiol-Yne (ATY) Cyclisation

8 **Adam Myles (TCD)**
Aryldiazonium Based Multi-Surface Cyclodextrin Coating Technology

9 **Clare Brown (QUB)**
Development of aerobic Pd(II) catalyzed Wacker-type oxidation of styrenes

10 **Nan Mao (Maynooth University)**
A long wavelength colourimetric chemosensor for fluoride

11 **Gareth Brown (Almac Group)**
A green and highly stereoselective biocatalytic route to woody acetate

12 **Megan Smyth (Almac Group)**
Highly stereoselective biocatalytic synthesis of Ticagrelor key intermediate

13 **Lokesh Kumar Kumawat (Maynooth University)**
Squaramide Based Anion Receptors: Potential Chemosensors for Fluoride Ions

14 **Jamie Sweet (QUB)**
Preparation of Enantiopure "Axonium" Ions for Organocatalysis

15 **Matthew Blair (QUB)**
Design of Second Generation Pd(II) Catalysts for the Oxidation of Alkenes

16 **Eva-Maria Dürr (TCD)**
Synthesis and biological evaluation of 5'-phosphate mimics for oligonucleotides

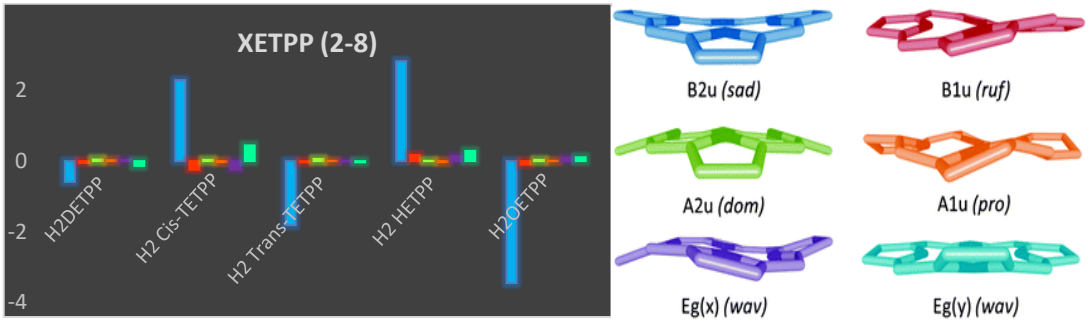
17 **Peter McNeice (QUB)**
Ionic Liquids for Base-Catalysed Reactions

18 **Adam Henwood (TCD)**
TBA

Poster 1: Structure and Conformation of Photosynthetic Pigments and Related Compounds

Gibbons, Dáire, Flanagan, Keith J. and Senge, Mathias O.
School of Chemistry, SFI Tetrapyrrole Laboratory, Trinity Biomedical Science Institute, 150-160 Pearse St., Trinity College Dublin, the University of Dublin, Dublin 2, Ireland
Email: gibbondi@tcd.ie, *sengem@tcd.ie*

Normal-coordinate Structural Decomposition (NSD) has been used to study the role of distortions of tetrapyrroles in biochemical mechanisms.[1] In the Senge group, NSD has been used to determine the extent that different modes of distortions contribute similar but distinct porphyrinoid macrocycles.[2] In this project we are intending to conduct a detailed comparative analysis of chlorophyll related molecules at an atomic level. Additionally, we will also establish how effective the NSD is by determining specific 3D features of porphyrins, chlorins, and their metal derivatives. With this in mind we used the Cambridge Structural Database[3] to obtain the X-ray crystal structures of free base 5,10,15,20-tetraphenylporphyrins (**TPP**); free base 2,3,7,8,12,13,17,18-octaethylporphyrins (**OEP**); free base porphyrins with increasing β-substituted ethyl groups (**XETPP**) (X = 0–8); free base chlorins with increasing β-substituted ethyl groups (**XETPC**) (X = 0–8) and the Zn(II) derivatives of the four groups mentioned above. The NSD of these compounds were then obtained using the NSDGUI developed by Shelnutt and co-workers.[4]



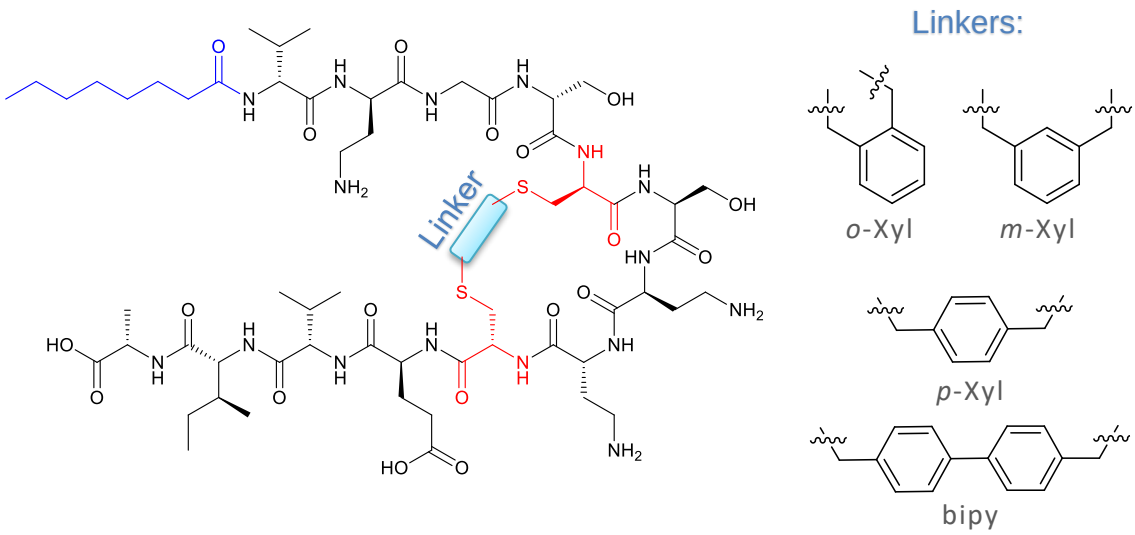
Chlorophylls and porphyrins have been shown to exhibit a wide range of different macrocycle conformations. These can occur by metalation, steric effects of peripheral or axial ligands, N-substitution, protonation, and π-aggregation in the environment. The compounds listed above were discussed in terms of their out-of-plane (oop) and in-plane (ip) distortion modes. In the TPPs, the main oop distortion mode is *wav*(x). In OEPs, the main oop mode is *wav*(y). Increasing the number of ethyl chains on the β carbons in the XETPPs increases the oop distortion, which is clearly seen in the *sad* distortion. In the XETPCs (X = 2), increases of roughly 1.0 Å exist in the *sad* mode compared to corresponding porphyrins. When X = 4(cis), distortion decreases occur when ethyl chains are on the reduced pyrrole and increases when ethyl chains are on the non-reduced pyrrole. The insertion of a Zn(II) results in a *wav*(x) decrease in TPP of 0.1 Å. This can be rationalized by the N-Zn(II) bond contracting the porphyrin core. Additionally, peripheral substitutions have a larger impact on 3D structure than Zn(II) metal insertions. This is mainly seen in the difference between *sad*, *ruf* and *dom* distortions in XETPPs and XETPCs. From these results, we can now go on and use these observations to discuss the macrocycle conformations in chlorophyll.

References:

[1] Jentzen, W.; Simpson, M. C.; Hobbs, J. D.; Song, X.; Ema, T.; Nelson, N. Y.; Medforth, C. J.; Smith, K. M.; Veyrat, M.; Mazzanti, M.; Ramasseul, R.; Marchon, J. C.; Takeuchi, T.; Goddard, W A.; Shelnutt, J. A. *J. Am. Chem. Soc*. **1995**, *117*, 11085–11097.
[2] Senge, M. O.; MacGowan, S. A.; O'Brien, J. M. *Chem. Comm.* **2015**, ***51***, 17031–17063.
[3] Groom, C. R. Bruno, I. J.; Lightfoot, M. P.; Ward, S. C. *Acta Cryst*. **2016**, *B72*, 171–179.
[4] Jentzen, W.; Song, X. Z.; Shelnutt, J. A. *J. Phys. Chem. B*. **1997**, *101*, 1684–169.

Poster 2: Synthesis of Cyclic and Linear Analogues of Tridecaptin A1

Ballantine, Ross, McCallion, Conor and Cochrane, Stephen
Queen's University Belfast, University Rd, Belfast BT7 1NN.



Tridecaptin A1, an antimicrobial lipopeptide that has strong activity against multi-drug resistant strains of Gram negative bacteria, operates by a membrane disruption pathway.[1] Previously, the active conformation of this peptide in dodecylphosphocoline (DPC) micelles when bound to Lipid II was found to a looped structure, stabilised by a π-stacking interaction of D-Trp-5 and Phe-9.[1] In this project, we synthesised Oct-Tridecaptin A1 analogues by Fmoc solid-phase peptide synthesis before carrying out various cross-linking reactions to create thioether and alkyl linkages. Tridecaptin A1 also contains expensive, nonproteinogenic amino acids. Here, we replaced these amino acids (L-Dab, D-Dab and D-aIle) with cheaper alternatives such as lysine and ornithine. MIC values were then obtained for theses analogues against Gram negative *Escherichia coli* and *Staphylococcus aureus*. Oct-TriA1 (5-D-Cys, 9-Cys) crosslinked with *meta*- and *ortho*-xylene showed activity against *E. coli* while the cheaper analogues retained complete activity of Oct-Tridecaptin A1.

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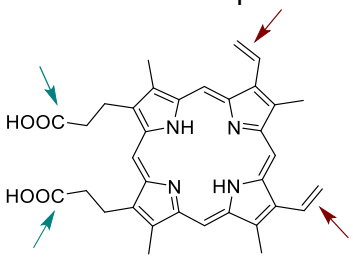
Poster 3: Exploration of Novel Functionalization Reactions for Naturally Occurring Porphyrins

Hallen, Lukas, Sitte, Elisabeth and Senge, Mathias
School of Chemistry, SFI Tetrapyrrole Laboratory Trinity Biomedical Sciences Institute, 152-160 Pearse Street, Trinity College Dublin, the University of Dublin, Dublin 2, Ireland
Medicinal Chemistry, Trinity Translational Medicine Institute, Trinity Centre for Health Sciences, Trinity College Dublin, the University of Dublin, St. James's Hospital, Dublin 8, Ireland
email: esitte@tcd.ie

Heme is a complex of protoporphyrin IX with iron and acts as the prosthetic group of hemoproteins. These proteins have a wide range of essential functions in nature, such as oxygen storage and transport, as well as electron transport and catalysis.[1] Due to their multiple cellular functions hemoproteins are potential drug targets. Recent studies report on the modification of natural porphyrins and porphyrin derivatives to alter their catalytic activity.[2, 3] These findings suggest that if the cellular uptake of natural porphyrin analogues can be achieved it offers the possibility to administer porphyrins that have been chemically modified to perform a specific function in cells. Such abiotic porphyrins can act as potential intracellular bio-probes and therapeutic catalysts.



Protoporphyrin IX

The present work focuses on synthetic modifications of protoporphyrin IX. The objective is to establish new viable routes for the facile functionalization of protoporphyrin IX by modern organometallic chemistry. We investigate halogenations of the protoporphyrin vinyl groups and subsequent functionalization by palladium-catalyzed cross-coupling reactions. Furthermore, modification reactions at the carboxylic acid groups are explored to provide a tool for selective double functionalization.

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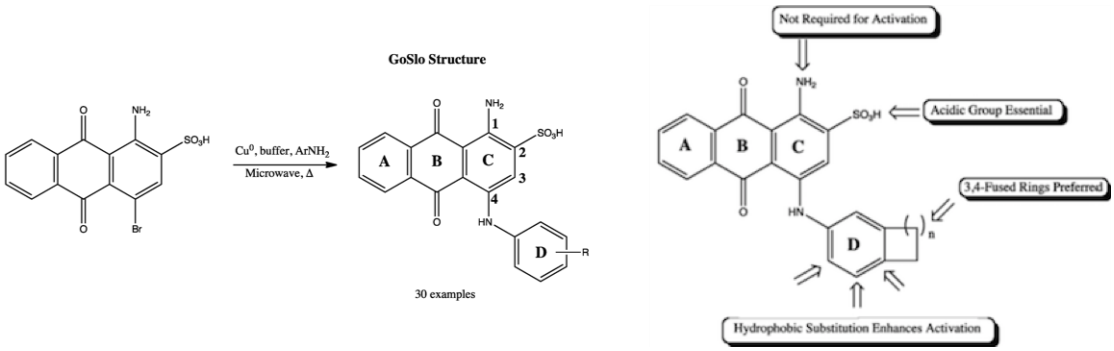
Poster 4: Synthesis and Structure-Activity Relationships of Novel Large-Conductance Ca^{2+}- Activated K^+ (BK) Channel Modulators

Mullins, Nicholas, Dudem, Srikanth, Sergeant, Gerard, Thornbury, Keith, Roy, Subhrangsu, Large, Roddy, Bradley, Eamonn and Hollywood, Mark.

The Smooth Muscle Research Centre, Dundalk Institute of Technology, Dublin Road, Dundalk, County Louth, Ireland; Email: nicholas.mullins@dkit.ie

Chronic Obstructive Pulmonary Disease (COPD) is a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation.[1] COPD is the fourth largest cause of death worldwide (3 million people in 2012).[1] In Ireland, approximately 400,000 people suffer from COPD,[2] while it is estimated that 384 million people are afflicted globally.[3] Ion channels are near-ubiquitous membrane spanning proteins which regulate the transport of ions across the cell membrane. Abnormally functioning ion channels have been implicated in diseases such as COPD, cystic fibrosis and asthma.[4-6] We have developed a novel family of efficacious and potent modulators of large conductance calcium-activated potassium (BK) ion channels, namely the GoSlo series of molecules.[7-9]

A library of GoSlo compounds was prepared from commercially available bromaminic acid.[10] The role played by three structural features of these compounds in activating ion channels was investigated: (1) the influence of both the size and substitution pattern of the D-ring attached to the anthraquinone core upon ion channel activation; (2) the importance of the acidic nature of C-2 substituent of the C-ring in increasing the potency and hydrophilicity of the compounds and (3) the effect of the amino moiety on C-1 of the C-ring in causing activation.



This work is funded by the INTERREG VA Health and Life Sciences Programme.

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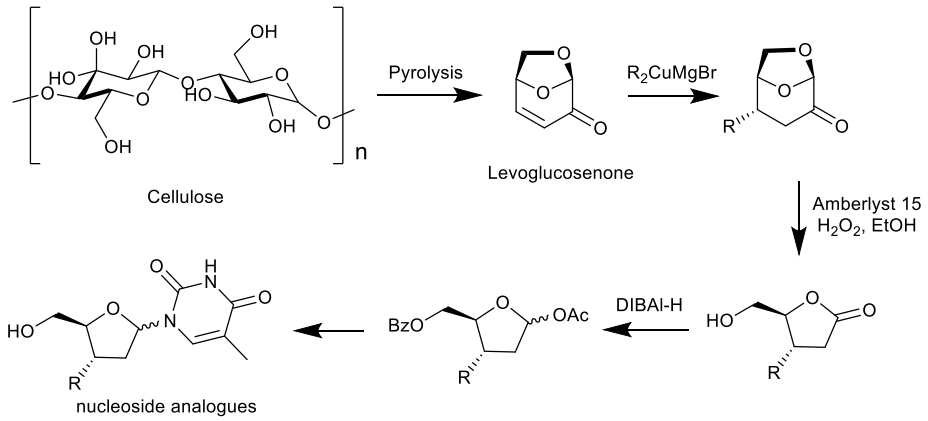
Poster 5: Rapid Baeyer-Villiger oxidation of levoglucosenone analogues for the synthesis of nucleoside analogues

Cummings Andrew J., Rice Clare, Murnaghan Christopher and Sheldrake Gary, N
School of Chemistry and Chemical Engineering, Queen's University Belfast

Levoglucosenone, a pyrolytic product of cellulose, has great potential as a chiral synthon for synthesis,[1] it has been used in the synthesis of drugs[2], rare sugars,[3] macrocycles[4] as well as chiral auxiliaries.[5] Within our research group the focus is on the synthesis of novel sugar analogues with an emphasis on amino-sugars and nucleoside analogues.

We have developed a new rapid microwave assisted catalytic method for the Baeyer-Villiger oxidation of levoglucosenone derivatives to their corresponding lactones. The method employs cheap and green Amberlyst 15 resin and hydrogen peroxide in ethanol. This is a 2-step 1-pot synthesis that reduces the reaction time from > 8 hours to < 1 hour affords high yields and very clean reaction products. We have demonstrated the potential of this reaction by generating a small library of lactones some of which have been reduced to their corresponding lactols with the long term aim of synthesising nucleoside analogues.



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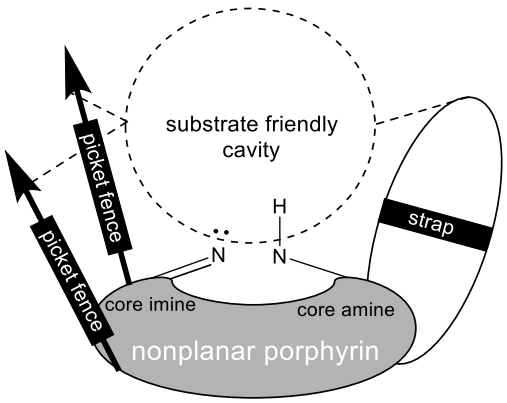
Poster 6: Nonplanar Porphyrins: New Concepts for Old Molecular Designs

Norvaiša, Karolis, Gibbons, Dáire and Senge, Mathias O.
School of Chemistry, SFI Tetrapyrrole Laboratory, Trinity Biomedical Science Institute, 152-160 Pearse St., Trinity College Dublin, the University of Dublin, Dublin 2, Ireland
Email: norvaiak@tcd.ie

Some previous studies have shown that highly distorted porphyrins are able to bind small molecules[1] but no studies have been done so far on small molecule activation capabilities. Porphyrin N-H units of planar analogues are usually not involved in intermolecular interactions due to the 'shielding' properties of the macrocycle system. Nevertheless, distortion causes degree of outwards orientation of inner pyrrolic hydrogens that makes these protons the "active center" and thus more accessible to substrates. Most recent studies have shown that highly distorted metal-free ('free base') porphyrins can be utilized as bifunctional organocatalysts.[2] The only aspect of bifunctionality in these catalysts is the fact that nonplanar porphyrins with deactivated acidic pyrrole N-H units are incapable of organocatalysis. There has been little quantitative analysis of nucleophilic and electrophilic substrate interaction with the free base porphyrin itself. Therefore, it is still unknown whether these bifunctional systems participate in general or specific catalysis-like mechanisms. Thus, the key aspect of this research is to imply old molecular designs, such as "picket fence" and "strapped" porphyrins on the nonplanar porphyrin scaffold. That leads to a decreased cavity radius, but tighter fitting surroundings that can potentially facilitate nucleophilic and electrophilic substrates for more in-depth binding studies as well as help to discriminate between different sized substrates. One of the means to achieve nonplanar porphyrins is steric overcrowding in highly substituted porphyrins.[1] A series of porphyrins with high degrees of distortion were synthesized using an Alder-Longo condensation reaction. Problems included difficult isolation of particular atropisomer of an intermediate that yielded multiple crystalline compounds. Structures were analyzed using single crystal X-ray diffraction showing a high degree of hydrogen bonding.



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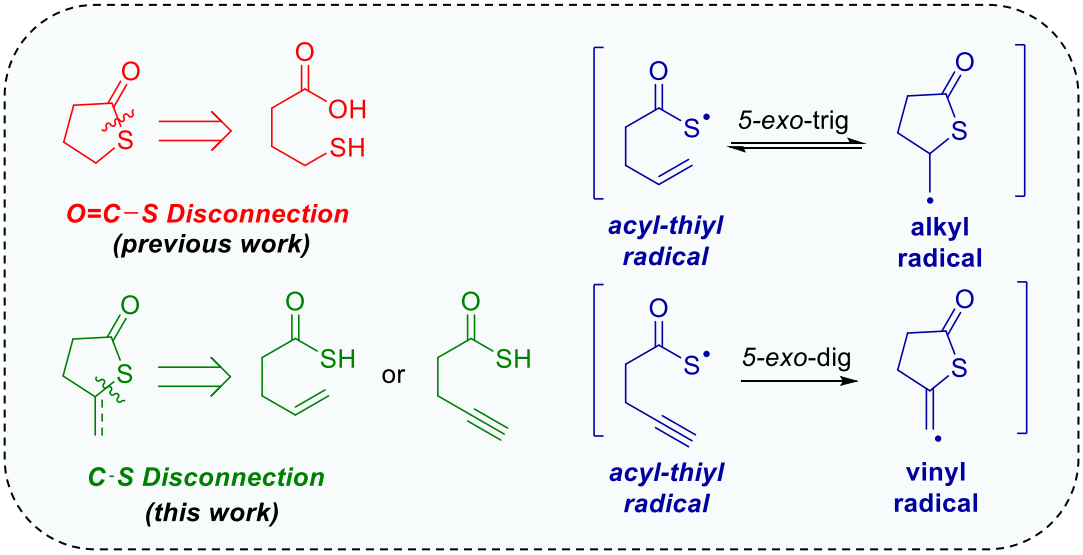
Poster 7: Rapid Access to Thiolactone Derivatives Through Acyl-Thiol-Ene (ATE) and Acyl-Thiol-Yne (ATY) Cyclisation

Ruairí O. McCourt [1], Fabrice Dénès [2], Goar Sanchez-Sanz [3], and Eoin M. Scanlan[1]*

[1]*School of Chemistry, Trinity Biomedical Sciences Institute (TBSI), Trinity College Dublin, The University of Dublin, Ireland,* [2]*UFR des Sciences et des Techniques, Nantes, France,* [3]*Irish Centre for High-End Computing, Dublin, Ireland,*
*scanlae@tcd.ie

Thiolactones have attracted considerable attention in recent years as bioactive natural products, lead compounds for drug discovery,[1] molecular probes[2], and reagents for polymerisation[3]. Hindering the wider application of this relatively simple structural motif has been the often harsh conditions required and the absence of a general strategy for their synthesis. Previous retrosynthetic analyses have focused on the disconnection of the O=C-S linkage (thioesterification). Our identification of an unusual C-S disconnection (thiol-ene) highlighted a novel route to this family of compound. We have recently developed a new synthetic approach to γ-thiolactones that employs an efficient radical acyl-thiol-ene (ATE) or acyl-thiol-yne (ATY) cyclisation to convert unsaturated thiocarboxylic acid derivatives into thiolactones under very mild conditions using UV light. These two aforementioned processes occur with high overall yields, fast kinetics, high diastereoselectivity, excellent regiocontrol, and broad substrate scope. These attributes render these reactions as a useful approach for diversity-oriented synthesis, and drug discovery efforts, with further application in the field of materials chemistry. Computational studies of the cyclisation process has provided an insight and justification for the observed regio- and diastereocontrol.



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Poster 8: Aryldiazonium Based Multi-Surface Cyclodextrin Coating Technology.

Myles, Adam, Behan, James, Twamley, Brendan, Colavita, Paula and Scanlan, Eoin.
School of Chemistry, Trinity College Dublin, College Green, Dublin 2, Ireland.
Centre for Research on Adaptive Nanostructures and Nanodevices (CRANN), Trinity College Dublin.
Advanced Materials and BioEngineering Research (AMBER), Trinity College Dublin.

Cyclodextrins are glycosidic oligosaccharides possessing a torus structure with a hydrophilic exterior and a hydrophobic cavity. They are capable of forming host-guest complexes with a wide range of hydrophobic compounds. Surface bound cyclodextrins have found a multitude of uses in environmental monitoring, drug delivery, and separation technologies. Though widely used, current methods of surface modification are limited to specific surfaces or require extensive surface pre-treatment.[1-4]
Herein we report on the synthesis and characterisation of an aryldiazonium based β-cyclodextrin coating. We have developed a robust scalable grafting protocol applicable to a range of carbon, metal and polymeric surfaces. This coating produces a hydrophilic, protein resistant coating with retained host-guest activity probed by cyclic voltammetry.

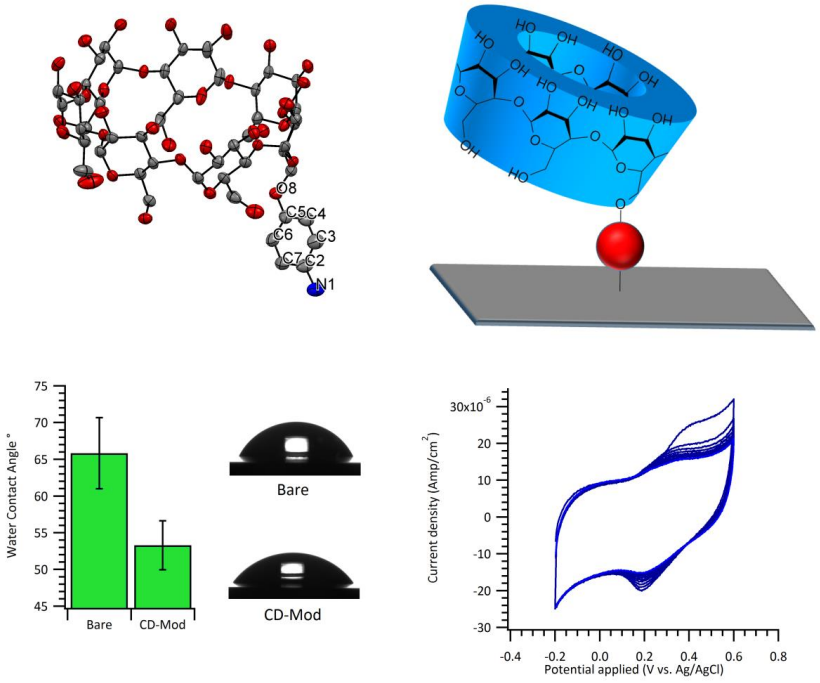

Figure 1 Shown above are; The x-ray crystal structure of the aryldiazonium β-cyclodextrin precursor molecule **(top left)**; A graphical illustration of the covalently bound surface cyclodextrin unit **(top right)**; The water contact angle of a surface before (Bare) and after cyclodextrin modification (CD-Mod) **(bottom left)**; The cyclic voltommogram of cavity bound ferrocene. Peaks display oxidative reductive behaviour of ferrocene captured within the cyclodextrin coating, no peaks are observed for unmodified surfaces **(bottom right)**.

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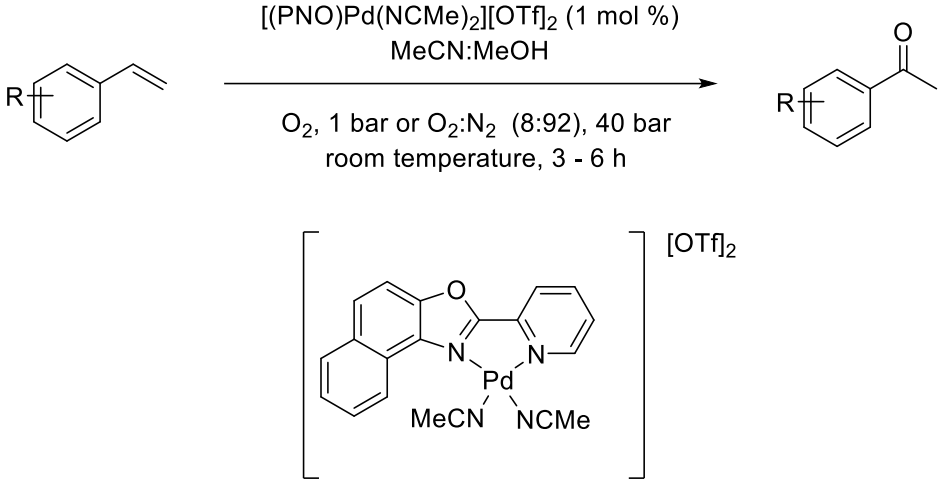
Poster 9: Development of aerobic Pd(II) catalysed Wacker-type oxidation of styrenes

Brown, Clare[a], Murray-Williams, Meadhbh[a], Chai, Hongxin[b], Cao, Qun[a], Dornan, Laura[a], Hughes Louise[a], Nockemann, Peter[a], Li, Jiarong[b] and Muldoon, Mark[a].
[a] *School of Chemistry and Chemical Engineering, Queen's University of Belfast.*
[b] *School of Chemical Engineering and Environment, Beijing Institute of Technology.*



Ligand = 2-(pyridin-2-yl)naptho[1,2-*d*]oxazole (PNO)

Oxidations reactions are less frequently performed in industry than other catalytic transformations, as such, there is a need to develop sustainable and scalable reactions. The Wacker Process is a notable exception, where the Pd(II) catalysed oxidation of ethylene to acetaldehyde is performed on a large scale. The substrate scope was broadened by the introduction of the Wacker-Tsuji conditions, which by introducing an organic co-solvent allowed for the oxidation of longer chain olefins. Despite the prevalence of the Wacker Oxidation in the literature there is still limited mechanistic data on the reaction pathway. This is further complicated by the use of redox active co-catalysts such as copper salts,[1] benzoquinones,[2] and polyoxometalates.[3] We are interested in developing reactions using no co-catalyst and preferably using simple terminal oxidants, namely peroxides or oxygen. The use of single molecular catalysts is beneficial for mechanistic elucidation. Better understanding of these reactions will enable new catalysts to be designed in the future and improve the potential scalability of such reactions. The work presented here describes the development of a previously published system, employing cationic Pd(II) catalysts and dioxygen as terminal oxidant.[4] The catalyst performance has been improved by changing the solvent composition, and the system can now utilise oxygen at atmospheric pressure (balloon) or reduced oxygen concentrations at elevated pressures. Reaction times are now greatly reduced and it is also possible to go to lower catalyst loadings at moderate temperatures (40 – 60 ◦C). Mechanistic studies, involving kinetics, spectroscopy and isotopic labelling are currently underway.

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Poster 10: A long wavelength colourimetric chemosensor for fluoride

Luke A. Marchetti[a], Nan Mao[a], Tobias Krämer[a], Jonathan A. Kitchen[b,c] and Robert B. P. Elmes[a]

[a]*Department of chemistry, Maynooth University, National University of Ireland, Maynooth, Ireland;* [b]*Chemistry, University of Southampton, Southampton, UK;* [c]*Chemistry, Institute of Natural and Mathematical Sciences, Massey University, Auckland, New Zealand*

e-mail: Nan.Mao.2016@mumail.ie; Robert.Elmes@mu.ie

Squaramides with their inherent rigidity and strong hydrogen bond donor ability have proven themselves to be useful building blocks in supramolecular chemistry, particularly in the design of anion receptors.[1-4] Herein, we report a new family of chemosensors based on the squaramidoquinoxaline (SQX) moiety (cyclobuta[b]quinoxaline1,2(3H, 8H)-dione) that have been assembled by a simple room temperature one step synthesis.[5] X-ray crystallographic analysis of the nitro-substituted compound **SQX1** demonstrated both strong hydrogen bond donor ability and tendency to π stack in the solid state. Moreover, **SQX1**, with its strongly electron withdrawing nitro-substituent, showed an obvious F^- selective colour change (when measured against other halides) clearly visible to the naked eye from pink to green in DMSO solution. Further addition of F^- led to a second colour change from green to yellow. Using TD-DFT, UV/Vis and NMR analysis we conclude that the observed colour changes are likely to be due to a two-step process involving two NH deprotonation steps. Colour changes of other SQX compounds were not as apparent in the presence of F^- owing to the reduced acidity of the NH functionality of the squaramidoquinoxaline. The study demonstrates the use of squaramide derivatives as valuable building blocks in the field of anion recognition and demonstrates that the electron withdrawing aryl substituent is directly related to the sensing ability/acidity of the squaramide protons and can be used to tune their anion recognition behaviour.

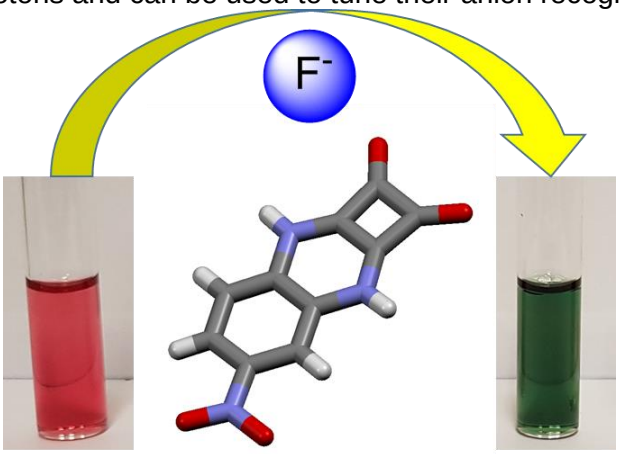

Figure 1: A long wavelength colourimetric chemosensor for fluoride

References:

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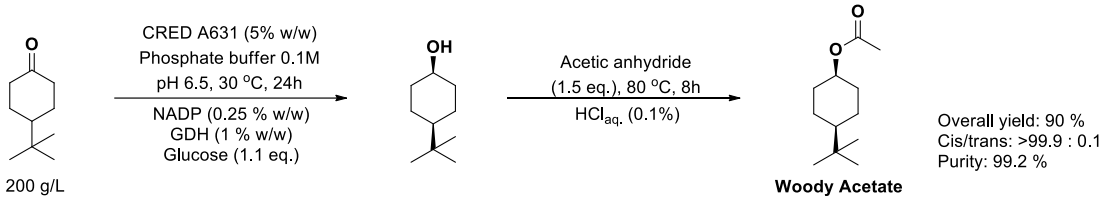
Poster 11: A green and highly stereoselective biocatalytic route to woody acetate.

Brown, Gareth[1], Miskelly, Iain[1], Mix, Stefan[1] and Moody, Tom[1]

[1] *Department of Biocatalysis and Isotope Chemistry, Almac Sciences, 20 Seagoe Industrial Estate, Craigavon BT63 5QD, Northern Ireland, United Kingdom.*

Carbonyl Reductase (CRED) technology has enabled the rapid and efficient preparation of both *cis*- and *trans*-4-*tert*-butylcyclohexanol, the *cis*-isomer being the precursor to bulk fragrance compound Woody Acetate. This work has resulted in a cost-effective, easy scalable and volume efficient process. The mild reaction conditions, ease of work-up and relatively benign waste streams make this a more attractive process than asymmetric catalysis reactions involving high temperatures/pressures, corrosive reagents and expensive metal catalysts.



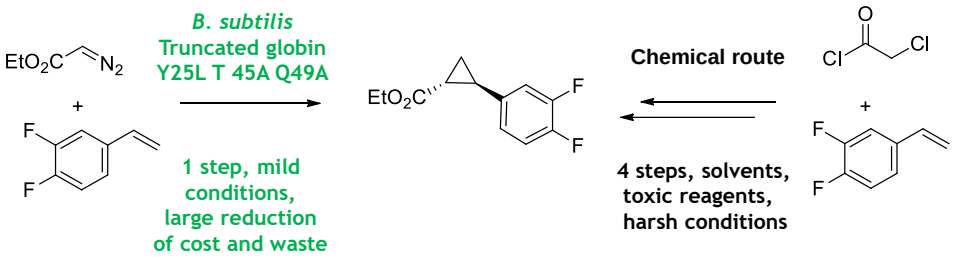
Scheme 2: Synthesis of Woody Acetate using CRED technology,

Poster 12: Highly stereoselective biocatalytic synthesis of Ticagrelor key intermediate.

Smyth, Megan[1], Brown, Gareth[1], Wharry, Scott[1], Assaf, Camille[1], Miskelly, Iain[1], Quinn, Derek[1], Mix, Stefan[1], Moody, Tom[1]
Zhang, Chen[2], Botejue, Ajit[2], Forte, Jared[2], Rozzell, David[2]

[1] Department of Biocatalysis and Isotope Chemistry, Almac Sciences, 20 Seagoe Industrial Estate, Craigavon BT63 5QD, Northern Ireland, United Kingdom. [2] Provivi Inc., Santa Monica, California, 90404, United States.

Pharmaceutical synthesis can benefit greatly from the selectivity gains associated with enzyme catalysis. Here, we report an efficient biocatalytic process to replace a multistep chemical synthesis for the large-scale manufacture of the cyclopropane precursor of the antithrombotic agent Ticagrelor.[1] An engineered heme enzyme obtained from the truncated globin of *Bacillus subtilis via* directed evolution, was found to catalyze the cyclopropanation of 3,4-difluorostyrene with ethyl diazoacetate as carbene precursor. This was performed on a preparative scale to afford ethyl-(1*R*,2*R*)-2-(3,4-difluorophenyl)-cyclopropanecarboxylate with high diastereoselectivity (> 99% *de*) and enantio-selectivity (> 99% *ee*) in preparation of subsequent multi-kg scale up.[2] This work adds one more enzyme and reaction class to the ever expanding biocatalalysis tool box of the modern manufacturing chemist, gradually replacing less efficient and less environmentally friendly methods.



Scheme 3: Synthesis of Ticagrelor key intermediate.

Poster 13: Squaramide Based Anion Receptors: Potential Chemosensors for Fluoride Ions

Kumawat. Lokesh Kumar, Abogunrin, Anthony and Elmes, Robert B. P.,
Department of Chemistry, Maynooth University, Maynooth, Co. Kildare, Ireland
Lokesh.Kumawat@mu.ie, Robert.Elmes@mu.ie

Abstract:
In recent years, the squaramide moiety has emerged as a useful scaffold in supramolecular chemistry.[1] The advantageous features exhibited by squaramides such strong H-bond donor ability, supramolecular recognition properties and efficient self-assembly behaviour[2] make it potentially applicable for a variety of applications such as bio-conjugation,[3] asymmetric catalysis,[4] anion transport and sensing,[5,6] and drug delivery.[7] In this poster, we describe two new anion receptors based upon a squaramide functionalised scaffold with a fluorescent naphthalimide reporter unit. We also evaluate the self-assembly of the squaramide receptors with through SEM analysis of 3-D networks and spectroscopic dilution studies. Furthermore, UV-vis and fluorescence spectra of compound **SQNp-1** and **SQNp-2** were recorded in the presence of a diverse set of anions, at various host:guest ratios and different solvent mixtures to evaluate the selectivity and sensitivity of the anion recognition process. Interestingly, both receptors showed a selective red shift in their absorption spectra in the presence of fluoride in aqueous solution and exhibit a naked eye colour change. Emission studies of SQNp-1 also showed a “turn–on-off” fluorescence response in the presence of fluoride.

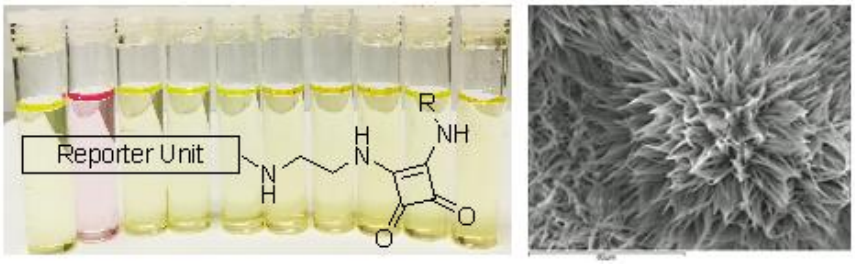


Figure 1: Squaramide motif with 3-D network and naked eye anion sensing.

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Poster 14: Preparation of Enantiopure "Axonium" Ions for Organocatalysis

Sweet, Jamie and Knipe, Peter.
Queen's University Belfast, Chemistry and Chemical Engineering, David Keir Building, Stranmillis Road, Belfast, BT9 5AG.

The design and synthesis of enantiopure quinolinium salts (axonium ions) will be described and prepared through the uses of different synthetic techniques including diastereoisomer formation and axially chiral N-C formation *via* chiral phosphine ligands.[1] A library of axially chiral catalysts will be compiled with their resulting physical properties and intermolecular interactions analysed. Furthermore, the application of these enantiopure quinolinium salts as asymmetric organocatalysts with contributing axial chirality and anion-π interactions will be investigated when used in simple alkylation reactions.[2,3]

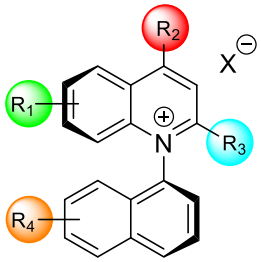

Figure 2**. *An enantiopure axonium salt.***

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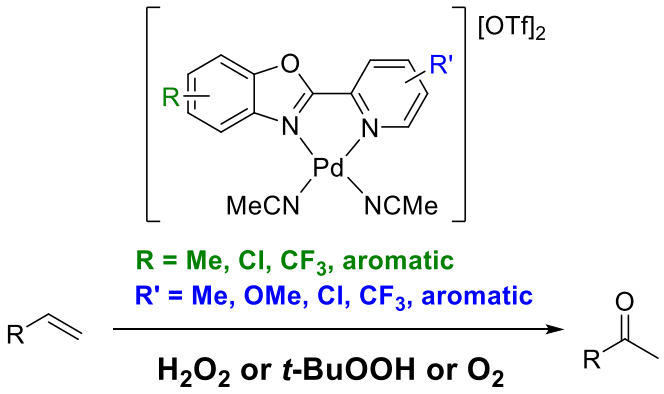
Poster 15: Design of Second Generation Pd(II) Catalysts for the Oxidation of Alkenes

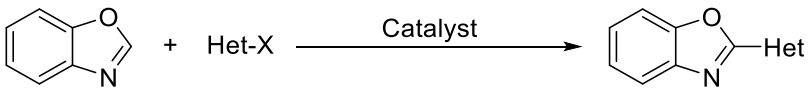
Blair, Matthew,[1] Chai, Hongxin,[1] O'Hagan, Roisin,[1] Li, Yitong,[1] and Muldoon, Mark J.[1]

[1] *Queen's University Belfast, mblair09@qub.ac.uk*

The transformation of an alkene into a ketone is one that is potentially valuable for the synthesis of many fine chemicals, agrichemicals and pharmaceuticals. The Wacker process, which produces acetaldehyde from ethene, is a classic example of industrial homogeneous oxidation catalysis, however is not suitable for longer chain olefins. On the laboratory scale, "Wacker-Tsuji" conditions have been used to oxidize these higher alkene substrates, however the efficiency of these reactions is not up to the standard required for industrial scale-up. We are interested in the development of new catalysts which use sustainable oxidants, such as peroxides or O_2 to carry out these reactions without the need for redox-active co-catalysts to be used. Recent work from within our group has led to the discovery of new catalysts[1] and subsequent mechanistic investigations on this[2] and complimentary catalyst systems[3] have already given insights into the complex nature of these reactions.



Knowledge of the underlying mechanism of the *tert*-butyl hydroperoxide (TBHP) mediated oxidation reaction[2,3] is now being exploited to design a range of substituted second generation catalysts that will have improved performance for this oxidant. The convenient, one-step synthesis route to these new catalysts through metal catalysed benzoxazole coupling will be highlighted and the results obtained to date using these catalysts in the TBHP mediated Wacker-type oxidation will be presented.



1 (a) Q. Cao, D. S. Bailie, R. Fu and M. J. Muldoon, *Green Chem.*, 2015, **17**, 2750–2757. (b) H. Chai, Q. Cao, L. M. Dornan, N. Louise Hughes, C. L. Brown, P. Nockemannm J. Li, M. J. Muldoon, Eur. J. Inorg. Chem., 2017, 5604-5608

2 K. L. Walker, L. M. Dornan, R. N. Zare, R. M. Waymouth and M. J. Muldoon, *J. Am. Chem. Soc.*, 2017, **139**, 12495–12503.

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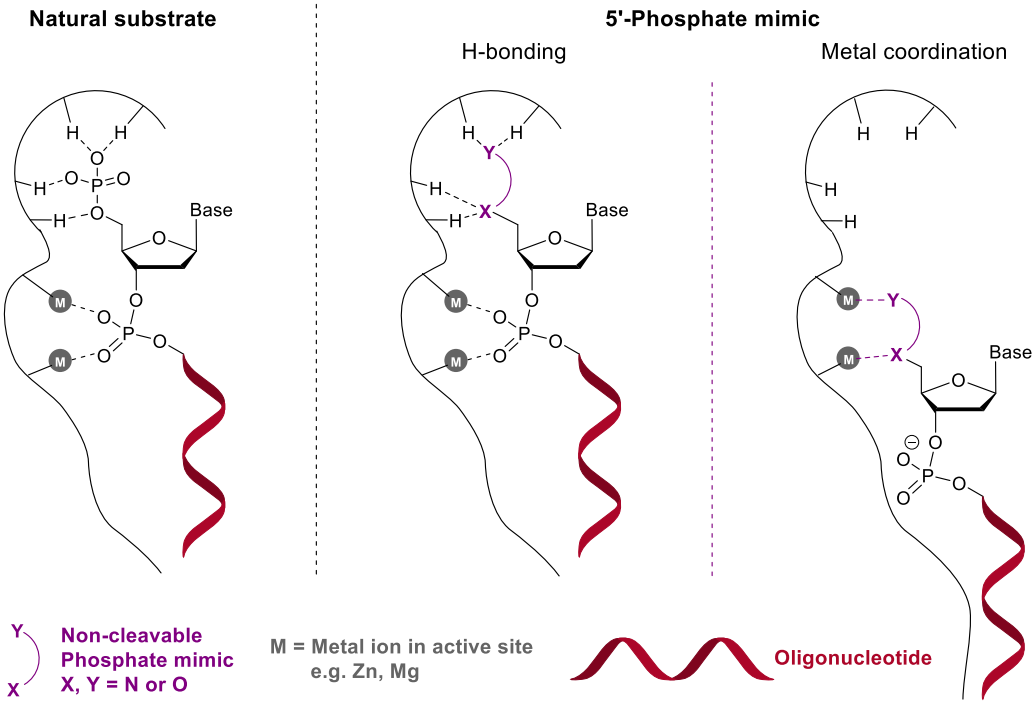
Poster 16: Synthesis and biological evaluation of 5’-phosphate mimics for oligonucleotides

Dürr, Eva-Maria,[a] Doherty, William,[a] El-Sagheer, Afaf H.,[b] Brown, Tom,[b] McHugh, Peter J.,[c] Gileadi, Opher[d] and McGouran, Joanna F.[a,*]

a: School of Chemistry, Trinity College Dublin, Ireland. b: Department of Chemistry, University of Oxford, UK. c: Department of Oncology, University of Oxford, UK. d: Structural Genomics Consortium, University of Oxford, UK.

Oligonucleotides have found application in a range of areas such as sensing,[1] as therapeutics or as diagnostics where they interact with nucleic acids or enzymes.[2] The 5’-phosphate group is an important recognition element for many enzymes and affects the activity of nucleic acids.[3,4] However, it is easily removed in a cellular context by non-specific phosphatases.[5] Modified oligonucleotides containing a non-cleavable phosphate mimic at the 5’-end are expected to be recognised by enzymes, unlike oligonucleotides containing a 5’-OH group as a result of hydrolysis. This strategy has been successfully applied for specific short ss siRNAs,[5,6] and holds promise for other types of oligonucleotides. We present the synthesis and biological evaluation of a range of heteroatom-containing groups as phosphate mimics at the 5’-end of oligonucleotides. The interaction of the modified oligonucleotides with the exonuclease SNM1A gives insight into their recognition as phosphate mimics and their binding mode in the active site of SNM1A.



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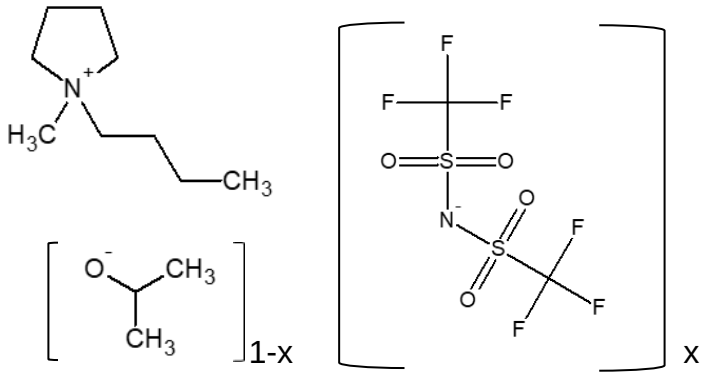
Poster 17: Ionic Liquids for Base Catalysed Reactions

McNeice, Peter,[1] Marr, Andrew C, Marr, Patricia C, and Seddon, Kenneth R

[1] *Queen's University Belfast*

We address here the dual problems of ionic liquid instability under basic conditions, and the lack of versatile basic ionic liquids. Ionic liquids are materials which are composed entirely of ions, and are often hailed as "Green Solvents".[1] They are effectively non-volatile and non-flammable, which can make them safer than organic solvents.[2] Exchanging one ion for another allows the properties of ionic liquids to be tuned, which has led to the concept of "functionalised ionic liquids" (previously known as task-specific ionic liquids).[3] However, there are relatively few examples of base-catalysed reactions being performed in ionic liquids, probably because of the lacuna of basic ionic liquids, resulting from the instability of many ionic liquids under basic conditions.

We have prepared binary mixtures of ionic liquids containing alkoxide anions to produce highly basic ionic liquids (see figure). The basicity of these materials is higher than many traditional bases such as Et_3N, pyridine and even KOH. These ionic liquids use cheap, sustainable alcohol starting materials such as ethanol and *iso*-propanol. These novel materials have been proven to be homogeneous basic catalysts for the Knoevenagel condensation of propanedinitrile [$CH_2(CN)_2$; malononitrile] and benzaldehyde. Flammable and harmful bases are traditionally used for this reaction and the synthesised ionic liquids could replace these in a greener synthesis.



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