Late stage fluorination: lessons to be learned from the fluorinase enzyme

Véronique Gouverneur
University of Oxford, UK

The impact of fluorine chemistry in the life sciences is enormous. As many as 30–40% of agrochemicals and 20% of pharmaceuticals on the market are estimated to contain fluorine. $^{19}$F- and $^{18}$F-labelled compounds are also finding increasing applications in imaging such as Magnetic Resonance Imaging [MRI] or Positron Emission Tomography [PET]. As a result, there is an increasing demand for facile methods allowing for the fluorination using $^{19}$F and the radioisotope $^{18}$F of a large variety of structurally complex and functionalised small molecules as well as biologics. This lecture will discuss our recent contributions to the field of late stage fluorination with an emphasis on the challenges associated with the use of alkali metal fluoride, and how these can be overcome. The fluorinase enzyme will serve as a starting point for discussion.

Strained electrophiles: new tools for late-stage peptide modifications

Dr Lara Malins
Australian National University

Strained bonds\(^1\) provide unique opportunities for the construction of complex molecules, the design of new therapies and the preparation of high-value materials. Targeted release of the potential energy locked in high energy molecular constructs provides a particularly appealing approach to the chemoselective modification of complex biomolecules. This talk will focus on harnessing molecular strain for the direct modification of native amino acids and peptides.\(^2\) The synthesis of a valuable toolbox of highly-strained electrophiles, featuring the bicyclobutane motif, will be detailed together with the application of strain-enabled transformations for residue-specific bioconjugation and peptide modification.

References:

Noncanonical peptides as probes and inhibitors for flavivirus proteases

Crisoph Nitsche
Australian National University

Infections with flaviviruses, such as dengue, West Nile or the recently emerged Zika virus are serious global health threats. Currently, no effective treatments are known. Our research targets flavivirus proteases as the Achilles heel of viral replication. The talk presents three different strategies how peptides with noncanonical modifications can selectively target these viral enzymes.

In order to create covalent interactions with the active protease site, we developed small boronic acid-based peptides that not only showed pan-flaviviral protease inhibition in the nanomolar concentration range, but also served as valuable tools to structurally validate this important class of drug targets.

In an orthogonal strategy capitalising on an in vitro mRNA display screening of a genetically reprogrammed library, we de novo discovered macrocyclic peptides with allosteric inhibition modes. Remarkably, not all compounds with nanomolar protease affinity displayed inhibition of the protease activity.

Finally, we developed a method to spontaneously cyclise peptides under biocompatible conditions. Simple macrocyclization of the substrate sequence of flavivirus proteases generated high-affinity active-site inhibitors with remarkable proteolytic stability.

Nitsche, C., Proteases from dengue, West Nile and Zika viruses as drug targets. Biophys. Rev. 2019.


There is an urgent need to develop new antimicrobial agents to fight multidrug resistant (MDR) bacteria, which represent a public health threat in the hospital environment worldwide. My group focuses on Gram-negative MDR strains of *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Escherichia coli* and *Klebsiella pneumoniae*, which are particularly problematic. In this lecture, I will discuss the experiments that led us from our initial studies with antibiofilm dendrimer agents identified by combinatorial chemistry approaches,[1] to our latest antimicrobial peptide dendrimers[2] cyclic[3] and bicyclic peptides[4] identified using an innovative chemical space guided discovery strategy.[5] I will also discuss structure-function relationships in our peptide dendrimers and bicyclic peptides.


Conjugation strategies towards configurable enzyme cascades in flow bioreactors

Philip Robbins
CSIRO

A new approach to conjugation chemistry is required to better utilise the explosion in additive manufacturing and global ‘Maker Movement’ for flow biocatalysis. In this short talk I hope to demonstrate one possible strategy currently in development by CSIRO (Dr Philip Robbins) and ANU (Dr Lara Malins) that would establish a general platform for highly-modular enzyme cascades, and constitute a ‘frugal innovation’ directive in de-skilling biocatalysis.

Using computer simulations to clarify the mechanism of action of bioactive lipid inhibitors on the Glycine Transporter, GlyT2

Katie Wilson
Australian National University

Chronic pain is a significant global health, economic and social problem, in part due to the low effectiveness of currently used analgesics. This indicates the need to discover new classes of pain-relieving drugs. The glycine transporter, GlyT2 is interest for the therapeutic treatment of chronic pain. Previous work by our experimental collaborators has developed a series of bioactive lipids that are able to provide pain relief through their action on GlyT2. These bioactive lipids are believed to bind to an allosteric pocket of GlyT2 based on a combined mutagenesis and molecular docking investigation. Nevertheless, it is unknown if this is the only site the bioactive lipids bind to on GlyT2 and the pathway for bioactive lipid binding to GlyT2, whether directly from solution or membrane mediated, is unknown. The current work uses computer modelling to provide insight into the pathway of binding to the allosteric site and identifies additional possible mechanisms of action of this new class of bioactive lipid analgesics.
Small Molecule Agonists of the Oxytocin Receptor for Treatment of Social Dysfunction

Tristan Reekie  
Australian National University  
Co-Authors: Prof. Michael Kassiou, Dr Eryn Werry, Dr William Jorgensen (University of Sydney)  
With approval from Kinoxis Therapeutics (USyd Spin-off) that owns the IP

Oxytocin is a cyclic neuropeptide that has well known neuromodulatory roles in social behaviour. Deficiencies in the oxytocin signalling pathways are implicated in social dysfunction, a pathophysiology concomitant with psychiatric disorders such as depression and anxiety. Developing stabilised analogues of the oxytocin ligand has shown some benefit for peripheral administration, but poses significant challenges for crossing the blood-brain barrier for neurological effects. Therefore, we have developed small molecule agonists of the oxytocin receptor designed to be active in the central nervous system.

A clear structure-activity relationship amongst compounds has shown we can target the oxytocin receptor over other related receptors with varied pharmacological profiles. Furthermore, in vitro studies have shown positive results in a social preference paradigm illustrating the potential therapeutic effects of these compounds. These compounds are now being investigated as treatments for autism and addiction.

Materials Chemistry for Water and Energy Challenges

Rachel A. Caruso  
Applied Chemistry and Environmental Science, RMIT University, Melbourne, Australia  
Rachel.caruso@rmit.edu.au

The United Nations Development Programme has established 17 Sustainable Development Goals, which include goals on Clean Water and Sanitation and Affordable and Clean Energy. In materials chemistry we can use targeted approaches to enhance material properties to improve the performance of the materials when applied in a range of water purification and energy conversion or storage applications. Key material properties, such as structure and composition, can be controlled during the synthesis process. We have applied hydrothermal/solvothermal, self-assembly, preformed templates and electrospinning approaches to vary the morphological features of inorganic materials. This results in variation of crystal size, pore size and overall structure as observed using X-ray diffraction, electron microscopy and gas sorption techniques.

For the application of such porous structures and films we have looked at energy conversion, energy storage, photocatalytic degradation of aqueous pollutants and the adsorption of heavy metal ions. When considering these applications, the characteristics for enhancing the performance of the material specific to that application become important. For example, the total surface area of the materials and the pore size are significant if reactions are taking place at the surface and efficient diffusion of reactants and products to and from the active sites is vital. In this presentation the synthesis, characteristics and application of porous materials for water purification and energy applications will be discussed.
**Poster snapshot presentations**

### De novo engineering of solid-state metalloproteins

Rapson, T.D., Church, J.S., Warden, A.C., Liu, J.W., Dunn, C.J., Musameh, M.M., Blanford, C.F., Nakamura, N., Jackson, C.J., Sutherland, T.D.

*CSIRO, Black Mountain, Canberra, Australia*

Despite its common use in organic synthesis, tributyltin hydride is a toxic and hard to remove radical mediator, with trace amounts often remaining after purification. Although there have been recent efforts to find a suitable alternative, this has proven difficult to find. This work investigates the potential of an atom transfer radical polymerization (ATRP) inspired radical mediation process utilizing the reducing agent 1,3-dimethyl-2-phenylbenzimidazoline (DMPBI). As a proof of concept, the efficiency of this novel method was tested by performing dehalogenation reactions on 1-(allyloxy)-2-iodobenzene and phenyl 2-bromo-2-methylpropanoate.

### Investigating a Novel ATRP Inspired Carbon-Based Radical Mediator

Isabella Russell, Phil Norcott, Benjamin Noble, Michelle Coote

*Research School of Chemistry, the Australian National University.*

Despite its common use in organic synthesis, tributyltin hydride is a toxic and hard to remove radical mediator, with trace amounts often remaining after purification. Although there have been recent efforts to find a suitable alternative, this has proven difficult to find. This work investigates the potential of an atom transfer radical polymerization (ATRP) inspired radical mediation process utilizing the reducing agent 1,3-dimethyl-2-phenylbenzimidazoline (DMPBI). As a proof of concept, the efficiency of this novel method was tested by performing dehalogenation reactions on 1-(allyloxy)-2-iodobenzene and phenyl 2-bromo-2-methylpropanoate.
A revised biosynthetic pathway for cofactor F$_{420}$ in bacteria

James Antony$^{1,2}$, Ghader Bashiri$^3$, Ehab N. M. Jirgis$^3$, Mihir V. Shah$^3$, Blair Ney$^{1,2}$, Janine N. Copp$^4$, Stephanie M. Stuteley$^3$, Sreevalasan Sreebhavan$^5$, Brian Palmer$^6$, Martin Middleditch$^3$, Nobuhiko Tokuriki$^4$, Chris Greening$^{2,6}$, Colin Scott$^2$, Edward N. Baker$^3$, Colin J. Jackson$^{1,2}$

$^1$Research School of Chemistry, Australian National University. $^2$Synthetic Biology Future Science Platform, CSIRO Land & Water, Canberra. $^3$School of Biological Sciences and Maurice Wilkins Centre for Molecular Biodiscovery, The University of Auckland. $^4$Michael Smith Laboratories, University of British Columbia. $^5$Auckland Cancer Society Research Centre, Faculty of Medical and Health Sciences, The University of Auckland. $^6$School of Biological Sciences, Monash University.

Cofactor F$_{420}$ plays critical roles in primary and secondary metabolism in a range of prokaryotes; however, its biosynthetic pathway has not been fully elucidated. Here we present a revised biosynthetic pathway incorporating two previously unreported enzymatic activities and two novel intermediates, allowing us to produce F$_{420}$ in a non-native organism.

A Radical Approach to Unnatural Amino Acids

Joshua M. Hammond$^a$ and Lara R. Malins$^{a,*}$

"Research School of Chemistry, Australian National University, Acton 2601 Australia"

In this work, we have developed an innovative approach to unnatural amino acid synthesis using sulfinates as a source of alkyl radicals that are amenable to functionalisation. The synthesis of amino acid sulfinates from native amino acids is explored and their reactivity with various thiol-based and heteroaromatic radical traps probed. As unnatural amino acids feature heavily in peptide-based therapeutics, this chemistry could provide solutions to problems like antibiotic resistance by allowing easy access to novel peptide-based antibiotics.
Practical artificial photosynthesis for solar fuel production

Professor Can Li
Chinese Academy of Sciences

This lecture presents the research progress made on CO$_2$ hydrogenation which could be considered as a dark reaction for artificial photosynthesis as long as the hydrogen is produced from solar energy. A thermal catalytic hydrogenation of CO$_2$ utilizing the hydrogen from photocatalysis essentially coincides with the photosynthesis where the photoreaction and dark reaction take place sep. in order. A solid soln. metal oxide catalyst ZnO-ZrO$_2$ was found to be highly active and selective for CO$_2$ hydrogenation to methanol, and that the Zn site is more active for hydrogen activation and the Zr site is responsible for CO$_2$ adsorption and activation. A synergetic effect between the two sites makes the selectivity high (CH$_3$OH selectivity >90%) even at temps. over 300°C. Furthermore, we demonstrated that a tandem catalyst based on the ZnO-ZrO$_2$ catalyst combined with SAPO zeolite can selectively produce low olefins (selectivity >80%). It was revealed that a kinetic and thermodynamic coupling between the methanol synthesis and olefin formation greatly enhances the conversion and selectivity in low olefins prodn. The hydrogen can be produced from water splitting by photocatalysis, photoelectrocatalysis and electrolysis with solar energy. The great challenge of solar energy conversion photocatalysis lies in its complicated processes including light absorption (harvesting), charge sepn. and transfer, and catalytic reactions. In order to achieve high solar energy conversion efficiency, the photocatalytic system must harmonically guarantee high efficiencies of all these three processes instead of only one of them. Among the three aspects, the photogenerated charge sepn. could be regarded as a central issue of photocatalysis. A brief discussion focuses on the photogenerated charge sepn. driven by phase junction, cocatalysts and different facets.

The formation of plant-based antimony nanoparticles by inorganic Sb species

Dr Sánchez-Palacios
Institute for Applied Ecology, Faculty of Science and Technology, University of Canberra

This study aims to determine the plant-based formation of Sb-nanoparticles in vitro and in situ by single particle ICP-MS analysis. In vitro experiments showed that leaves of terrestrial yellow box Eucalyptus sp. and semi aquatic Typha sp. produced Sb-nanoparticles, with great variation in particle size ranging from 30 to 100 nm and 30 to 90 nm, respectively. A linear relationship between Sb concentration and particle size was detected for both terrestrial and semi-aquatic plants. Terrestrial plants showed a good linear model when using the inorganic oxidised form Sb(V) (antimonate) to form Sb-nanoparticles. By contrast, semi-aquatic plants showed a good linear model when using the inorganic reduced form Sb(III) (antimonite). This suggests a preferential formation of plant-based Sb-nanoparticles based on plant type and Sb forms. Preliminary in situ experiments showed that weed Urtica dioica (Stinging nettle) and native grass Austrostipa sp., growing on Sb-rich mineral waste, accumulated higher levels of Sb in various tissues parts. For instance, Stinging nettle accumulated nearly four times as much Sb in their root tissue compared to Austrostipa sp. with 3720 ug/kg and 1000 ug/kg, respectively. By contrast, above ground parts accumulated similar concentrations of Sb between plants species, 130 ug/kg and 100ug/kg, respectively. As for Sb nanoparticle formation, Austrostipa sp. produced bigger particle size in roots (118 nm) relative to shoots (83 nm); while Stinging nettle produce similar particle size between shoots and roots with 162 nm and 163 nm, respectively. Overall, the variation in particle size between in vitro and in situ methods suggests that mechanism of Sb-detoxification may play an important role in the variation of Sb-nanoparticles formation in plants. More detail testing of in situ Sb accumulation in U. dioica and Austrostipa sp. is required to determine the plant molecules and Sb forms involved in the Sb-nanoparticles formation.
Electrochemical Alkoxyamine Cleavage; an ‘on-demand’ source of radicals and cations for synthesis

B.B Noble, a C. Hammill, P. Norcott, S. Ciampi b, M. L. Coote a, *

a ARC Centre of Excellence for Electromaterials Science, Research School of Chemistry, Australian National University, Canberra ACT 2601, Australia, b Nanochemistry Research Institute, Department of Chemistry, Curtin University, Bentley, Western Australia 6102, Australia.

Alkoxyamines have been widely used as initiators and mediators for Nitroxide Mediated Polymerization (NMP). Unfortunately, relatively high temperatures (ca. 80–120 °C) are needed to maintain sufficient levels of alkoxyamine homolysis, and at those temperatures unwanted side reactions limit the scope and utility of the process. We recently demonstrated that alkoxyamines can be cleaved electrochemically (via a 1-electron oxidation) under much more mild conditions. 1 This cleavage occurs via a radical-cation intermediate that fragments at room temperature to release a nitroxide and alkyl cation. In the present work, we use a combination of high-level quantum chemistry and experimental techniques to explore the electrochemical cleavage of a wide array of different alkoxyamines. 2 The influence of different alkyl and nitroxide functionality on this oxidative cleavage and the use of the resulting species as initiators/mediators for polymer synthesis is also investigated. 2 Finally, the scope and utility of alkoxyamines as energy storage materials 3 and for electrochemical organic synthesis is explored.

References:
Stimulus-responsive Shape-Changing Polymeric Materials

Dr Zhen Jiang
Australian National University

Nature is a common source for the inspiration to develop artificial intelligent materials that can adapt and actuate in response to external stimuli. The ability to actively change shape is essential to many living organisms. For example, the Venus flytrap closes its leaves in less than seconds to efficiently catch flies, and pine cones open their scales when the environment is dry to release their seeds. Inspired by such phenomena, scientists are aiming to develop artificial smart materials which undergo shape transformations under the action of an external stimulus. Among the various classes of shape-changing materials so far proposed, hydrogels and liquid crystalline elastomers represent the most studied polymer systems. Moreover, such shape changing polymers have also attracted significant interest for a wide range of applications in soft robotics, artificial muscles, three-dimensional (3D) cell culture and drug or cell delivery devices.

In last decade I have been dedicated to developing new type of shape changing polymers with unprecedented material functionalities: (1) Utilizing the upconversion luminescence technology, I have conceived and developed long wavelength light-responsive polymer actuators.\(^1\) The use of the long wavelength light which has deeper penetration depth into the tissue is much more desirable for various applications, especially biological applications. The advantages of using this novel red-light-controllable soft actuator in potential biological applications have also been demonstrated as negligible thermal effect and its excellent penetration ability into tissues. (2) I have also proposed a new type of multi-responsive poly(ethylene oxide) based hydrogel actuators, prepared just through one-pot polymerization using commercially-available monomers.\(^2\) Such soft actuators exhibited controllable, reversible and repeatable 3D deformations driven by changes in light, temperature or ionic strength. (3) Most recently, I have been focusing on the development of multifunctional hydrogel actuators with high toughness, self-healing, fast actuation and shape memory, through the use of numerous dynamic bonds.

Reference:

Solar Quantum Cutting and Spectral Downconversion using Ytterbium-Doped Metal-Halide Perovskites

Daniel R. Gamelin
Department of Chemistry, University of Washington, Seattle, WA, USA
gamelin@uw.edu

Yb$^{3+}$-doped lead-halide perovskites ($\text{Yb}^{3+} : \text{CsPb(Cl}_{1-x}\text{Br}_x)_3$) have emerged as unique materials combining strong, tunable broadband absorption with near-infrared photoluminescence quantum yields (PLQYs) approaching 200% at ambient temperature. These remarkable properties make $\text{Yb}^{3+}:\text{CsPb(Cl}_{1-x}\text{Br}_x)_3$ an extremely promising candidate for spectral shaping in solar energy conversion devices. This talk will describe some of our group’s recent research into controlling, understanding, and exploiting the physical properties of these doped metal-halide perovskites for photon management and solar applications. Materials development and fundamental spectroscopic/electronic-structure properties will be described as they pertain to understanding some of the unusual photophysics observed in these highly luminescent materials. Modeling and application of these materials for solar photon management will also be discussed.


2D Materials Science and Applications for Electrocatalysis and Electronics

Dr Zongyou Yin
Australian National University

Nano science and technology offer a vast and fascinating playground to explore the novel physiochemical properties of nanomaterials with the development for various applications including electronic and energy-conversion devices. In this talk, I will present the recent investigation on two-dimensional (2D) materials surfaces/interfaces and their effects on the WS$_2$ based nano electrocatalysis and the diamond-based surface charge doping, such as surface molecular tunable crystal phase engineering with 2D WS$_2$ towards stable electrocatalytic hydrogen evolution reaction and 2D hydrogenated MoO$_3$ layer as a novel efficient sustainable surface charge acceptor to improve the transferrability from Hall structure to diamond transistors. These 2D interface science and engineering enable the enhancement of functional efficiency and the extension of performance stability in electrocatalytic and electronic devices. This talk highlights the synergistic interface science and engineering can provide the opportunities to customize nanomaterials for advanced applications development.
Transition-metal carbynes bridged by main-group heteroatoms

Benjamin J. Frogley, Anthony F. Hill
Research School of Chemistry, Australian National University, Canberra, ACT 2601, Australia

Transition-metal carbyne complexes, LₙM≡CR, have historically been limited to examples bearing hydrocarbyl (R = alkyl, aryl, etc.), amino or silyl substituents. The comparative scarcity of carbynes bearing other heteroatoms arises primarily because the classical synthetic pathways generally cannot be extended to rest of the p-block.¹ Synthetic challenges notwithstanding, there is a strong incentive to investigate such compounds due to their potentially useful synthetic, electronic and physical properties which may be modified significantly by the choice of p-block substituents.

Lalor’s halocarbynes [M(≡CX)(CO)₂(Tp*)] (M = Mo, W; X = Cl, Br; Tp* = hydrotris(3,5-dimethylpyrazolyl)borato)² have proven to be useful precursors to such species. Derivatives can be prepared not only by simple nucleophilic halide substitution, but also by an “umpolung” approach whereby treatment with lithium reagents generates lithiocarbyne intermediates, [M(≡CLi)(CO)₂(Tp*)], which can subsequently react with suitable electrophiles. The versatility of this latter procedure has allowed the first examples of carbynes with ‘heavy-metalloid’ lead,³ antimony and bismuth substituents⁴ to be prepared. Extension of this chemistry allows polymetallic derivatives to be prepared⁵ which may serve as useful building blocks to extended frameworks or interrupted molecular wires. This has particularly interesting consequences for intermetallic electronic communication where the heteroatoms may serve as modulators or ‘switches’ in such structures.

References:

Supramolecular frameworks prepared in water

Nicholas White
Australian National University

We have used charge-assisted hydrogen bonds to prepare a range of supramolecular organic frameworks by simply mixing amidinium and carboxylate tectons. The resulting open crystalline frameworks show good stability, including to boiling water and hot DMSO. Our use of a modular “node-and-linker” approach allows the synthesis of materials containing a range of functionalities in a somewhat predictable manner.
Poster Presentations

**An Allelopathic Compound from Festuca spp. as a Lead Molecule for Development of Pre-emergent Herbicides for Weed Management**
Craig D. Stewart*, Russell A. Barrowb, Sajid Latifb, Leslie A. Westonb, Tristan A. Reekiea*  
a*Research School of Chemistry, Australian National University. bGraham Centre for Agricultural Innovation, Charles Sturt University (Wagga Wagga).
There is a great need for the development of herbicides with novel modes of action, due to increasing evolution of herbicide resistance in common weed species and the lack of new modes of action in commercial herbicides introduced in recent years. We have synthesised several analogues based on the bioactive architecture of the phytotoxic natural product m-tyrosine, with improved herbicidal activity and will evaluate extended environmental half-life, and investigate potential mode(s) of action.

**Zinc biochemistry in industrial hemp (Cannabis sativa. L)**
Carly Beggs, Tona Sánchez-Palacios*, Simon Foster*.
Institute for Applied Ecology, University of Canberra.
Industrial hemp is a sustainable material that can be used to produce plant-based building materials, biodegradable plastics and renewable biofuels. Yet, little is known about hemp metal-biochemistry. Using ICP-MS technology we determined hemp can be grown under Zn-rich conditions, providing the opportunity to repurpose land with moderate heavy metal contamination.
Synthesis of Stable Isotope Labelled Steroids

Christopher C. Fitzgerald* and Malcolm D. McLeod **
*Research School of Chemistry, The Australian National University

Stable Isotope Labelled (SIL) reference materials have many applications in medicinal, anti-doping and analytical sciences. New methods of synthesis have been developed to prepare SIL steroid conjugates, including selectively labelled bisconjugates, which provide powerful tools for analytical chemistry and fundamental science.

Exploring artificial enzymes: Inspired by nature

Ayana Bhaskaran,a Zeyun Xiao,b Mitchell Blyth,a Mitchell Nothling,b Megan O’Mara,a Michelle Coote,a Luke Connal*aa
aResearch School of Chemistry, Australian National University. bDepartment of Chemical Engineering, University of Melbourne.

Enzymes are nature’s exquisitely efficient catalysts. Here, we mimic their chemistry to create artificial bio-catalysts. The positioning of the catalytic residues in the microenvironment of the enzyme mimic delivers hydrolysis reminiscing the action of the natural catalytic triad. These recyclable polymer supported catalysts could be tailor-made for applications such as low-temperature detergents, bio-diesel production paving way for economical industrial processes with reduced carbon footprint.
A pH-Switchable Electrostatic Catalyst for the Diels-Alder Reaction

Mitchell T. Blyth, Michelle L. Coote*

ARC Centre of Excellence for Electromaterials Science, Research School of Chemistry, ANU, Canberra, ACT, Australia

Electrostatic catalysis is the as-yet under-explored ability of oriented electrostatic fields to stabilise polar transition states in non-redox chemical reactions. We use quantum chemistry to design a pH-switchable molecular framework capable of catalysing the Diels-Alder reaction using electrostatic catalysis in a variety of synthetically-relevant conditions.

Chemoenzymatic Total Syntheses of Platencin and Certain Derivatives

Rehmani M. N and Martin G. Banwell*

Research School of Chemistry, The Australian National University, Canberra ACT 2601, Australia

The emergence of severe resistance to existing antibiotics has become a global health issue. In the search for new-generation anti-bacterial agents, Merck-based researchers recently discovered the natural product platencin (1) using advanced screening technologies. This structurally novel compound was isolated from Streptomyces platensis (MA7339) and shown to exhibit broad-spectrum antibacterial activity against MRSA by blocking both FabF (KAS II) and FabH (KAS III) enzymes. This presentation will describe a total synthesis of platencin (1) and efforts to exploit the associated methodologies for the purposes of generating biologically active platencin analogues/various structural variants of the platencin core (2). A key feature of such efforts involves exploiting the enantiomerically pure cis-1,2-dihydrocatechol (3) as the starting material. Compound (3) is obtained through the whole-cell biotransformation of iodobenzene using a genetically engineered form of E.coli.
Alkynylselenolatoalkylidyne complexes as a potential building block for mixed metal/main-group extended frameworks

Chee S. Onn, Benjamin J. Frogley, and Anthony F. Hill*

*Research School of Chemistry, Australian National University, Canberra, Australian Capital Territory, ACT 2601, Australia.

The reactions of [W≡CBr(CO)₂(Tp*)] (Tp* = hydrotris(dimethylpyrazolyl)borate) with lithium alkynylselenolates LiSeC≡CR (R = SiMe₃, Si′Pr₃, ′Bu, ′Bu, Ph, p-tolyl) furnishes the alkynylselenolatoalkylidyne complexes [W≡CSeC≡CR(CO)₂(Tp*)]. Desilylation of the SiMe₃ complex furnishes the parent [W≡CSeC≡CH(CO)₂(Tp*)], which can be further derivatised by deprotonation and treatment with various electrophiles. This procedure extends to dichlorosilanes and trichlorosilanes, giving the unusual bimetallic and trimetallic complexes respectively.

Copper versus Rhodium in enantioselective metal-catalyzed [3+3]-cycloaddition reactions of enoldiazosulfones with nitrones

Frady G Adly and Michael P Doyle

Department of Chemistry, The University of Texas at San Antonio, San Antonio, Texas, 78249, United States.

Chiral copper(I) catalysts carrying chiral bisoxazoline ligands have recently emerged as an alternative to expensive chiral dirhodium(II) catalysts for asymmetric [3+3]-cycloadditions involving enoldiazo compounds. The effectiveness of these catalysts has previously been extended to enoldiazo-amides, -esters and -ketones with which high yields and enantioselectivity have been obtained. We have now extended their utility to enoldiazosulfones that with nitrones form 1,2-oxazines in high yields and excellent enantiocontrol (up to >99% ee). After dinitrogen extrusion, the metal-bound enol-carbene rearranges to a donor-acceptor cyclopropene that is normally the resting state for the carbene. With enoldiazosulfones, however, the sulfone group stabilizes the generated cyclopropene so that dirhodium(II) catalysts are ineffective in reforming the metal-carbene. However, chiral bisoxazoline-ligated copper(I) catalysts are able to overcome this limitation to effect the desired [3+3]-cycloaddition.
Synthesis and Reactivity of the Bridging C1 Ligand

Harrison J. Barnett, Anthony F. Hill
Research School of Chemistry. Australian National University, Building 137, Sullivans Creek Road, Acton, ACT, 2601

Monoatomic carbon bridges (μ-carbido) are notably rare in transition metal chemistry. When considering μ-carbido complexes, two formal bonding modes are reported; the symmetric cumulenic (M=C=M), and the asymmetric metallacarbyne (M≡C-M).

This work focussed on the synthesis of a simple novel rhodium cumulenic μ-carbido species, [Rh₂(μ-C)Cl₂(PPh₃)₄], which was formed via activation of a thiocarbonyl ligand with catecholborane. Reactivity studies have been carried out targeting the phosphine, chloride and carbido ligand.

Novel Platinum(II) Complexes: Applications in Photoredox Catalysis

Liam K. Burt, Anna M. Ranieri, Alex C. Bissember and Massimiliano Massi
School of Natural Sciences – Chemistry, University of Tasmania. School of Molecular and Life Sciences – Chemistry, Curtin University.

Traditionally the development of metal-based photoredox catalysts has centred on ruthenium and iridium complexes featuring octahedral metal coordination geometries. However, platinum(II) complexes are readily accessible synthetically and possess interesting photophysical properties with tuneable absorption/emission wavelengths. We prepared a number of novel platinum(II) complexes that were evaluated for their ability to facilitate a selection of representative photoredox-catalysed processes.
The Synthesis of Potential Host-targeted Anti-malarial Inhibitors of Human Ferrochelatase

Patrick A. Yates, Anna Ehmann, Brendan J. McMorran, Malcolm D. McLeod

Research School of Chemistry, The Australian National University. The John Curtin School of Medical Research, The Australian National University.

The arrival of new multi-drug resistant Plasmodium strains calls for new ways of thinking about malaria drug development. Strategies developed for analogue generation around the lead compound ‘D75’, an inhibitor of the enzyme human ferrochelatase, and their subsequent potencies will be shown.

The odd nature of tungsten C₃ and C₅ complexes

Richard A. Manzano, Anthony F. Hill

Research School of Chemistry, Australian National University.

A simple, yet elegant method has been developed towards the synthesis of tungsten propargylidyne \([W(\equiv CC\equiv CR)(CO)₂(Tp*)]\) and pentadiynylidyne \([W(\equiv CC\equiv CC\equiv CR)(CO)₂(Tp*)]\) complexes, by palladium-mediated cross-coupling of the tungsten bromocarbyne \([W(\equiv CBr)(CO)₂(Tp*)]\) and various terminal alkynes. Further reactivity of the trimethylsilylpentadiynylidyne \([W(\equiv CC\equiv CC\equiv CSiMe₃)(CO)₂(Tp*)]\) demonstrates its utility as a C₅ scaffold.
Tuning the Redox Properties of 1,2,4-Triazinyl Radicals

Fergus J. M. Rogers, Alfred K. K. Fung and Michelle L. Coote

Research School of Chemistry, The Australian National University

1,2,4-Benzotriazinyls (Triazinyls) are heterocyclic persistent radicals of growing interest to synthetic and materials chemistry. Their reactivity can be effectively tuned through modest structural adaptations, which modify the environment of the unpaired electron. In an effort to explore these substituent effects, adiabatic electron affinities and ionisation potentials for a variety of simple Triazinyl derivatives have been modelled in silico, using conventional computational techniques.

Computational Design of Phosphorus-based Ligands for Atom Transfer Radical Polymerisation

Vincent Doan, Benjamin B. Noble, Alfred K.K. Fung, Michelle Coote

ARC Centre of Excellence for Electromaterials Science, Research School of Chemistry, Australian National University, ACT 2601, Australia

Atom Transfer Radical Polymerisation (ATRP) has revolutionised polymer synthesis; enabling the precise construction of sophisticated macromolecules under mild conditions. In ATRP, a redox active metal mediator (usually Cu) activates a ‘dormant’ organohalide initiator, generating carbon-based radicals that can be harnessed for polymer chain growth. Crucially, this reaction is reversible and so ‘living’ polymerisations can be achieved by carefully balancing this activation/deactivation equilibrium (KATRP). While current ATRP methodology can polymerise a wide-array of monomers, activation of less-stabilised alkenes remains problematic. Indeed, for monomers such as vinyl chloride and vinyl acetate, the N-based ligands usually employed in Cu-based ATRP are not sufficiently activating. In this work, we use high-level computational theory to assess the performance of P-based ligands in Cu-based ATRP. First, we examine how structural features of a diverse set of ligands affect KATRP. Next, we establish rational design criteria based on electrostatic arguments and ligand-field theory. Finally, using these design criteria, we propose a range of ‘next-generation’ ATRP ligands that are predicted to have unprecedented activity.
**Electrostatic Switching between Sn1 and Sn2 Pathways**

Li-Juan Yu, Michelle L. Coote*

ARC Centre of Excellence for Electromaterials Science, Research School of Chemistry, Australian National University, Canberra, ACT 2601, Australia.

A test set of 264 nucleophilic substitution reactions was computationally studied to establish the relative preferences for SN1 versus SN2 mechanisms. Reactions involving anionic nucleophiles and leaving groups favored SN2 pathways in low polar solvents, while SN1 is preferred for those involving neutral nucleophiles and leaving groups. For neutral nucleophiles and anionic leaving groups, SN2 is generally preferred over SN1. SN1 or SN2 preferences could be switched by both charged functional groups and point charges (i.e., electric fields) along the reaction axis.

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**Tuning triazine stabilities via substituent effects**

Alfred. Fung,* Fergus. Rogers* and Michelle L. Coote*

*Research School of Chemistry, The Australian National University.

Persistent free radicals offers an effective pathway by which to control the effects of radicals in solution. Substituent effects allows us to effectively control triazine reactivity, thus increasing the utility of persistent free radicals.
The Mechanism of Oxidative Alkoxyamine Cleavage: The Surprising Role of Solvent and Supporting Electrolyte

Chelsey Hammill¹, Benjamin Noble¹, Philip Norcott¹, Simone Ciampi², Michelle Coote¹
¹ARC Centre of Excellence for Electromaterials Science, Research School of Chemistry, Australian National University, Canberra ACT2601, Australia.
²Nanochemistry Research Institute, Department of Chemistry, Curtin University, Bentley, Western Australia 6102, Australia.

Alkoxyamines are well-known thermal initiators and crucial intermediates in Nitroxide Mediated Polymerisation (NMP). However, recent work has revealed that electrochemical oxidation of alkoxyamines (to produce a radical-cation intermediate) can produce ‘on-demand’ in situ radicals and cations. This work explores the influence of different alkyl functionality on oxidative cleavage and examines exciting applications for electrochemically-mediated synthesis of small organic molecules.

Synthesis of (S)-2',3'-di-O-benzylpropyl 2,3,5-tri-O-acetyl-β-D-riboside: A precursor for accessing naturally occurring arsenosugars

Eman Alkasasbeh, Simon Foster, Frady G. Adly and William A. Maher
Faculty of Science and Technology, University of Canberra, Canberra, ACT, 2601

Arsenic containing carbohydrates constitutes an important class of natural products found in marine macroalgae. Their importance emerges from being part of the transformation and cycling of arsenic species in the marine environment. In this work, the first total synthesis of (S)-2',3'-di-O-benzylpropyl 2,3,5-tri-O-acetyl-β-D-riboside, a key precursor for accessing several naturally occurring optically active arsenic containing carbohydrates, is described starting from (R)-2,3-di-O-benzylglycerol. Key steps in the synthesis are glycosidation and selective protection/deprotection of hydroxy groups to obtain the desired product in 74% yield.