

3rd Graduate Student Symposium Program and Abstract Book

May 16-17, 2019

Saskatoon, Saskatchewan

Co-Chair: Doug Fansher

Co-Chair: Richard Pettipas

Sponsors

U of S Graduate Students Association (GSA), University of Saskatchewan Office of the Vice-Provost, Faculty Relations, University of Saskatchewan College of Graduate and Postdoctoral Studies, Chemistry Course Council (CCC), U of S Women in Chemistry (WIC), VWR, Agilent, Canadian Tire, Dairy Queen, Rexall and Peavy Mart.

Message from the organizers

We would like to thank everyone for attending the 3rd Graduate Student Symposium held May 16-17, 2019 at the University of Saskatchewan. This symposium serves to connect researchers within the U of S Department of Chemistry to speakers from academia and industry. This symposium also provides an excellent platform for students to practice and perfect their respective talks in preparation for national and international conferences.

The aim of this symposium is;

- To showcase student work taking place across the department,
- To provide students with the opportunity to present their research to the department
- To give students the chance to improve presentation and communication skills
- To allow students to network, engage in discussion and seek ideas from other members of the department and,
- To allow students to interact with speakers from both academia and industry

We would also like to thank the sponsors for recognizing and understanding the value of these workshops to graduate students of all different point of their graduate career. Finally, we hope everyone has a productive meeting and takes something away that will be beneficial to them in the future, whether than be in research or other aspects.

Sincerely,

Doug Fansher and Richard Pettipas

Schedule of events

Thursday, May 16, 2019-all presentations will take place in **THORV 105**

Time Event

9:00 Registration

Session 1 Chaired by Natasha Vetter

9:20 am Opening Remarks by Chairs Doug Fansher and Rick Pettipas

9:30 am **Tyler A. Morhart**
ATR-FTIR Chemical Imaging in Simple Microfluidic Systems

9:50 am **William Barrett**
Galvanic Synthesis and In Situ Speciation of Supported Palladium Nanoparticles in Methane Oxidation Environments

10:10 am **Jeveria Rehman**
Mixing Behavior in Anionic Gemini Surfactant-Perfluorinated Fatty acid Langmuir Monolayers

10:30 am **Coffee Break**

Session 2 chaired by William Barrett

11:00 am **Jeff Zimmer** (Saskatchewan Research Council Environmental Analytical Laboratories)

11:40 am **Dalia Ahmed**
ANS as a fluorescent probe for MtUGM, a potential antimicrobial drug target

12:00 am **Douglas Fansher**
Understanding the Substrate Scope of a Promiscuous Aldolase and its Application as a Biocatalyst for the Production of α,β -Unsaturated 2-Keto Acids

12:20pm **End of morning session**

Lunch Break (Lunch is not provided but we will be going to Marquis with the speakers and everyone is welcome to attend)

Session 3 Chaired by Moralba Dominguez-Garcia

1:50 pm **Florence Williams** (University of Alberta)
Taking Advantage of Strong Boron-Oxygen Associations for Chemoselective Reactions

- 2:50 pm **Karnjit Parmar**
The total synthesis of hyacinthacine A1
- 3:10 pm **Whitney Shannon**
[F-19/F-18] Isotopic Exchange of BODIPY Dyes Using Air-Stable Solutions of Lewis Acids
- 3:30 pm Attendee Picture and Door Prizes
- 3:40 pm **End of Afternoon Session. Coffee break**, poster viewing and judging
- Session 4**
- 3:40 pm Start of Poster Session
- 4:40 pm End of Poster Session
- 7:00 pm Mixer GSA Commons 1337 College Dr, Saskatoon on University Campus
- 9:00 pm End of Mixer

Friday, May 16, 2019- All presentations will take place in THORV 105

Session 5 Chaired by Jeveria Rehman

- 9:00 am **Murray Schultz** (Senior Manager of Applied Process Technology at The Mosaic Company)
The Future of One's Career
- 9:40am **Natasha Vetter**
Synthesis of carbocyclic analogues to probe enzymes involved in kanosamine biosynthesis
- 10:00 am **Josseline S. Ramos-Figueroa**
"F" in inhibitor design: fluorination of glucose 6-phosphate and its effect in enzyme-ligand interaction

10:20 am **Coffee break**

Session 6 chaired by Tyler A. Morhart

- 10:40 am **Subha Chakraborty**
Raman microscopy of ice in the presence of salt and humic acid
- 11:00 am **Chase L. Radford**
Effect of Molecular Shape on the Properties of Non-Fullerene Acceptors: Contrasting Calamitic Versus 3D Design Principles
- 11:20 am **Erick Lins**
Commissioning of a Quantum Cascade Laser-based, Dual-Comb IR Spectrometer for Time Resolved Spectroscopy at the Canadian Light Source
- 11:40 pm **Rick Pettipas**
Synthesis of regioisomerically pure 1,7-dicyanoperylene diimide and its dimerization for photovoltaic applications
- 12:00 pm **End of morning session**
- 12:00 pm **Awards Presentation (Oral and Poster Awards Donated by VWR)**
- 12:10 pm **Closing Remarks**

Invited Speaker Abstracts

Chemistry Careers

Jeff Zimmer, Saskatchewan Research Council Environmental Analytical Laboratories

The SRC is one of Canada's leading providers of applied research, development and demonstration (RD&D) and technology commercialization. With more than 350 employees, \$75 million in annual revenue and over 71 years of RD&D experience, SRC provides products and services to more than 1,500 clients in a variety of different industries around the world.

Jeff Zimmer is the Manager of Saskatchewan Research Council (SRC) Environmental Analytical Laboratories (EAL). With over 60 staff and several million dollars' worth of state-of-the-art instrumentation, the EAL provides one of the widest arrays of testing services within a single facility in all of Canada. The laboratory has expertise in testing for chemical, radiochemical, organic, microbiological parameters in a wide variety of different sample matrices including water, soil, air, vegetation, cannabis, animal tissue and other biota. Services for aquatic toxicity testing are now also being offered.

Jeff has over 30 years of experience in analytical chemistry and testing laboratories. He has a wealth of knowledge regarding analytical methods and processes, instrumentation, quality control and quality assurance processes, laboratory accreditation, laboratory management and supervision as well as radiation safety. Jeff serves on a number of boards for various professional associations including the Saskatchewan Environment and Industry Managers Association (SEIMA); Association for the Chemical Profession in Saskatchewan (ACPS) and is chair of the board for the Canadian Association for Laboratory Accreditation (CALA).

In this presentation, Jeff will talk about the Saskatchewan Research Council including a brief overview of some of the types of projects conducted by the SRC. The discussion will focus on the Environmental Analytical Laboratories including some history of the laboratory's development and the impact the laboratory's services have had on various industries within the province. The growth of the laboratory over the years and changes within the analytical chemistry industry and industry in Saskatchewan will be discussed through the lens of Jeff's career at the SRC. Through his work with the ACPS (Association for the Chemical Profession of Saskatchewan), Jeff is committed to furthering recognition for chemistry as a profession with right to title as well as recognition for the important work conducted by chemists in a wide variety of different industries. Questions or lively discussion about various careers within the chemistry profession are strongly encouraged.

Taking Advantage of Strong Boron-Oxygen Associations for Chemoselective Reactions

Florence Williams, University of Alberta

The Williams lab has been investigating the utility of highly Lewis acidic boron centers for the activation and cleavage of alkyl ethers to generate alcohols. Such strategies have enabled the targeting of strong C–O bonds for cleavage in the presence of weaker and/or more polarized bonds. These methods have important applications for the sustainable degradation of lignocellulose – a biopolymer characterized by ether and acetal linkages – to provide renewable sources of aromatic chemicals such as vanillin. This talk will examine the development and applications of such boron-mediated methodologies, and will discuss the selectivity principles which arise from kinetic and thermodynamic considerations of boron-mediated alkyl ether cleavage. Finally, future work to expand boron-mediated ether cleavage to provide tandem processes for C–H amination will be outlined.

The Future of One's Career

Murray Schultz, Senior Manager of Applied Process Technology at The Mosaic Company

The future of one's career can take many turns as a person navigates the steps to professional success. You do have a choice on what to do but you can't always choose what you like to do. However, the Association of Chemical Professionals (ACPS) would like to offer up insights that can help match work with the passions that exist inside each and every one of us. As the ACPS continues to work on advancing the professional status within the province, a number of academic and industrial professionals are available to offer up their experience that has led them along their professional journey.

Student Abstracts

Oral Presentation/Session 1

ATR-FTIR Chemical Imaging in Simple Microfluidic Systems

Tyler A. Morhart, Stuart T. Read, Garth Wells, Michael Jacobs, Scott M. Rosendahl, Sven Achenbach, Ian J. Burgess

In this talk, I will describe our work constructing a horizontal ATR-FTIR microscope at the Mid-IR beamline of the Canadian Light Source and its application to chemical imaging of the hydrogen-deuterium exchange reaction in a simple microfluidic device.

Galvanic Synthesis and In Situ Speciation of Supported Palladium Nanoparticles in Methane Oxidation Environments

William Barrett and Robert W.J. Scott.

The presented research pursues the galvanic synthesis, speciation, and quantification of palladium nanoparticle catalysts in in situ environments. Palladium is an active catalyst for the oxidation of methane, a process required for the responsible use of natural gas in applications including natural gas power plants and natural gas vehicles. Synthetic methods for supported nanoparticle catalysts typically involve wetness impregnation techniques which have fundamental adversities due to the synthetic route; here we present galvanic deposition, a simple, clean and quick method for the production of Pd/SnO₂. Palladium catalytic activity is sensitive to the metal oxide support that the palladium particles are loaded onto, such that the support can influence the Pd-PdO-Pd(OH)₂ equilibrium that is seen in such catalysts. Quantification of this equilibrium in situ has been elusive, with it being particularly difficult to distinguish between PdO and Pd(OH)₂. PdO is catalytically active, however, is poisoned by water leading to a passivating layer of Pd(OH)₂, an inactive species. This research presents a method in which quantification and percent abundance of palladium species is collected via in situ X-Ray Absorption Spectroscopy analyzed with Linear Combination Fitting. The method has been shown to be able to distinguish between PdO and Pd(OH)₂ via correlations with other analytical techniques including XRD, XPS, and CO chemisorption. Applications of this work will assist in developing rationally designed palladium catalysts for methane oxidation.

Mixing Behavior in Anionic Gemini Surfactant-Perfluorinated Fatty acid Langmuir Monolayers

Jeveria Rehman, Matthew Paige, David Sowah-Kuma, Amy Stevens, Wei Bu

In this study, we explored the mixing behavior of a new class of anionic gemini surfactants based on N, N'-dialkyl-N,N'-diacetate ethylene diamine with perfluorocarbon at the air-water and air-solid interface. The miscibility and film structure of mixed Langmuir

monolayer films composed of anionic gemini surfactants, Ace(12)-2-Ace(12) and Ace(18)-2-Ace(18) with a monomeric perfluorinated surfactant, perfluorotetradecanoic acid (PF) have been investigated using a variety of thermodynamics and structural characterization methods. The effect of hydrocarbon tail length on the miscibility of films and film morphology was explored using compression isotherms, Brewster angle microscopy and atomic force microscopy. The two film components found to be miscible in Ace(12)-2-Ace(12)-PF mixed monolayers at lower surface pressures over a wide range of compositions and phase separated in Ace(18)-2-Ace(18)-PF mixed monolayers for different mixtures of two at all surface pressures. This indicated the attractive interactions between the two film components in Ace(12)-2-Ace(12)-PF mixed films and repulsive interactions between the film components in the Ace(18)-2-Ace(18)-PF mixed films. Brewster angle microscope measurements revealed structured, micron scale oval shaped domains in mixed films while atomic force microscopy indicated the multimolecular aggregate formation for all mixed films. The miscible behavior in Ace(12)-2-Ace(12)-PF mixed films was attributed to the short hydrocarbon chain length of Ace(12)-2-Ace(12) as compared to the Ace(18)-2-Ace(18).

Abstracts

Oral Presentation/Session 2

ANS as a fluorescent probe for MtUGM, a potential antimicrobial drug target

Dalia Ahmed, David Sanders

Mycobacterium tuberculosis (Mt), the causative agent of tuberculosis, has developed multiple antibiotic resistance mechanisms. Therefore, there is a need for novel therapeutic strategies. UDP-galactopyranose mutase (UGM) is an essential enzyme for M. tuberculosis, involved in bacterial cell wall synthesis. MtUGM represents an attractive potential drug target especially that it is not present in human. MS-208 was identified as an allosteric inhibitor of MtUGM with micromolar range inhibitory activity. There is a need for developing a fast direct method for screening the binding affinities of potential allosteric ligands. 8-Anilinonaphthalene-1-sulfonate (ANS) is a small molecule dye that is used as an external fluorescent probe to study the ligand binding interactions. Considering the location and the hydrophobic nature of the allosteric site, ANS is a good probe for this pocket. Fluorescence-based binding assay showed that ANS binds to MtUGM and the binding constant is not affected by the presence of the substrate. To exclude non-specific binding due to the aggregation, the assay in presence of 1% Triton showed similar binding constant. Thermal shift assay results showed that ANS is a stabilizer. In addition, the kinetic evaluation of the inhibitory activity of ANS against MtUGM showed competitive inhibition. Since not all competitive inhibitors are allosteric inhibitors, a future perspective of getting ANS co-crystallized with MtUGM will provide a proof whether it binds to the active site or the allosteric site.

Understanding the Substrate Scope of a Promiscuous Aldolase and its Application as a Biocatalyst for the Production of α,β -Unsaturated 2-Keto Acids

Douglas Fansher, Richard Granger & David R. J. Palmer

Aldolases are wide spread in nature and are able to catalyze aldol reactions with a high degree of stereoselectivity and enantioselectivity that is often difficult to achieve with traditional synthesis. However, many unaltered aldolases are only able to accept substrates closely related to the natural substrate. Previously, trans-o-hydroxybenzylidene pyruvate hydratase-aldolase (tHBPHA) was shown to catalyze the aldol reaction of pyruvate with several aromatic aldehydes.¹ The reaction results in the generation of α,β -unsaturated 2-keto acids, but when using β -fluoropyruvate, the fluorinated aldol product is observed.² To date, there has not been a comprehensive study looking at which aromatic aldehydes are accepted when pyruvate is used as a nucleophile. We have tested >40 aromatic and aliphatic aldehydes and determined that in nearly every case the enzyme is able to couple them to pyruvate efficiently to generate α,β -unsaturated 2-keto acids in high yields. These products have the benefit of being substrates for aminotransferases, ammonia lyases and aminomutases for the generation of amino acids.³ To improve scalability, reactions can be carried out in the presence of whole cells harboring tHBPHA gene on a multi-gram scale. This work sets the stage for the preparation of a diverse array of products under mild conditions.

Abstracts

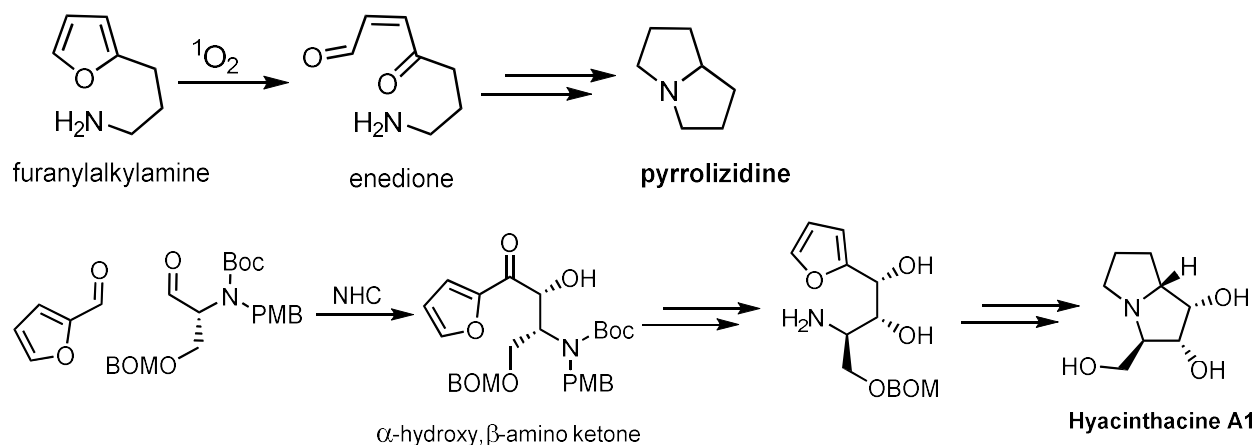
Oral Presentation/Session 3

The total synthesis of hyacinthacine A1

Karnjit Parmar, Pouyan Haghshenas, and Michel Gravel

Furans have long been exploited in total synthesis due to their stability as well as latent functionality. The ability to selectively unmask a furan to a more reactive intermediate is a valuable strategy for quickly building complexity at a late stage. An often-used transformation is the conversion of a furan derivative to an enedione via a singlet oxygen mediated photooxidation. This intermediate can further react with pendant functionalities such as amines to form pyrrolizidine derivatives.

It was envisioned that this photooxygenation-amine cyclization (PAC) strategy could be utilized in tandem with a N-heterocyclic carbene catalyzed cross-benzoin methodology in the synthesis of the glycosidase inhibitor Hyacinthacine A1. The route towards the crucial amino diol precursor, the optimization of the photooxygenation as well as the final few steps towards Hyacinthacine A1 will be discussed.



[F-19/F-18] Isotopic Exchange of BODIPY Dyes Using Air-Stable Solutions of Lewis Acids

Whitney Shannon and Eric Price

Bimodal imaging agents allow for the assessment of biological activity via synergistic exploitation of the orthogonal attributes associated with differing imaging modalities such as positron emission tomography (PET) and optical imaging (OI). Despite the superior thermal- and photo-stability of 4,4-difluoro-4-bora-3a,4a-diaza-s-indacenes (BODIPY) fluorophores compared to commonly used fluorescent molecules, the field of molecular imaging has only recently begun exploring their application. BODIPY dyes possess several

unique spectroscopic properties such as high fluorescence quantum yields, relatively short Stokes Shifts, and sharp emission peaks, which make them good candidates for OI. Furthermore, the BF₂-moiety of the BODIPY core affords a site of [18F/19F]-radioisotopic exchange to produce a bimodal PET imaging agent. These characteristics together make the BODIPY dyes suitable candidates for the design of PET/OI-bimodal imaging agents. The Lewis acid-assisted [18F/19F]-isotopic exchange method previously reported by Li et al. (2013), has become the dominant method for promoting trans-fluorination of BODIPY molecules. Of the Lewis acids assessed, SnCl₄ and TiCl₄ had shown the greatest success and has become the primary catalyst of choice, despite their sensitivity to air exposure. However, only a small number of Lewis acids were assessed at the time, and due to lack of consistency in the literature we believe there is a need for re-optimized methodology. This project seeks to investigate the effects of differing air-stable solutions of Lewis acids with comparable bond dissociation energies to that of SnCl₄ on the radiofluorination of a commercially available BODIPY dye. The efficacy of the [18F]-fluorination reaction using different Lewis Acids is currently being evaluated, along with optimization of reaction parameters such as temperature, time, heat, and applied phase transfer catalysts.

Abstracts

Poster Presentation/Session 4

Spectroscopic and Thermodynamic Study of Biopolymer Adsorption Phenomena in Heterogeneous Solid-Liquid Systems

Leila Dehabadi, Abdalla Karoyo and Lee Wilson

Hydration phenomena at biopolymer-solution interfaces play a key role in physical and biophysical processes in aqueous solutions. Based on the previous isotherm studies for binary (water+ethanol; W-E) solvent systems, the molecular level details related to the solvent uptake process is poorly understood. This paper reports on the solid-solution phase fractionation of water from ethanol in binary solutions using polysaccharide sorbent materials. Several polysaccharide sorbents (starches with different percentages of amylose/ amylopectin and cellulose) were studied by complementary methods (gravimetry, thermal analysis, and spectroscopy) to assess solvent swelling, hydration, and selective solvent uptake properties in binary W-E mixtures. The surface accessibility of the hydroxyl (-OH) groups of the biopolymers was estimated using a dye decolorization method. This study contributes to a greater understanding of the role of structure and functional group accessibility that govern hydration properties, biopolymer-solvent interactions, and the molecular level process of biopolymer sorptive fractionation in W-E mixtures.

Performance of Single Atom Catalysts in Selective Catalytic Reactions

Brandon Chivers and Robert W.J. Scott

Nanoparticle (NP) catalysis continues to be a prominent field of research, owing to the numerous types of catalysts that can be synthesized and utilized in catalytic reactions. The trend associated with nanoparticle catalysis is the ever-decreasing size of the catalyst. As a catalyst is made smaller, the surface free energy available for catalysis increases, improving the catalytic performance of the material. As we move into the single-atom limit of nanomaterials, the number of active centers that are being targeted increases, increasing the specific activity per metal atom. There are various types of supports for isolated atom dispersion; they could be alloyed with another metal, dispersed on metal oxide or graphene, or on graphitic carbon nitride (g-C₃N₄), to name the most common types in literature. The interaction between these supports and isolated metal atoms on its surface are crucial to the catalytic success of the material and enhances the field of study by creating a multitude of different isolated metal atom-support combinations that can be evaluated. Our work involves the synthesis and subsequent catalytic testing of Pd-based single atom materials in selective oxidation and hydrogenation reactions. The discussion will include two types of catalysts; a quasi-homogeneous AuPd bimetallic single atom alloy catalyst and heterogeneous g-C₃N₄ supported Pd single atom catalyst. The poster will also include initial results and future work to be completed in 2019.

Cu(II) Uptake by Tweezers-like Biopolymers

Bahareh Vafakish, Lee D. Wilson

A modified chitosan structure was synthesized by grafting aniline rings to chitosan backbone and characterized by FT-IR and ¹H-NMR spectroscopy to provide supportive evidence of grafting. The prepared adsorbent shows high uptake properties in batch experiments toward Cu(II) in aqueous solutions at ambient pH and temperature. Equilibrium sorption studies show the adsorption capacity (Q_m) of 103.8 mg/g according to Sips isotherm. Kinetic studies revealed that time depended adsorption behavior adopted pseudo-first order model. Time dependent adsorption was as well studied by intra-particle diffusion model. Adsorption mechanism was suggested by evaluation of FT-IR, X-ray photoelectron spectroscopy (XPS), scanning electron microscopy (SEM) and ¹H-NMR spectra before and after adsorption and revealed that the adsorption occurred through synergism between electron rich aromatic rings to make strong cation- π interactions besides nitrogen of amine groups to make N-Cu(II) complexes. Thermodynamic parameters represent an endothermic and spontaneous adsorption process. The reuse of adsorbent was tested in five consecutive adsorption-desorption cycles. The modified chitosan aqueous solution shows a strong fluorescence emission at 420 nm which quenched prominently in the presence of even very low copper concentrations at ppb level due to complex formation. The quenching process represents a linear response in the range of 0.05-5 mM. This feature can make it very interesting for rapid detection of low level of copper in aqueous solutions. This research reveals a new insight to detect and remove Cu(II) as a pollutant heavy metal from water resources.

A structural study of self-assembled chitosan-based sponge materials

Chen Xue and Lee D. Wilson

Uncontrolled dissolution in solvent media is a key challenge related to the utility of chitosan composite materials. Thermal annealing offers a solution to address this problem. However, conventional characterization methods pose limitations regarding key structural features, especially for carbohydrate materials that possess similar biopolymer components. Herein, self-assembled chitosan-based sponges were prepared with and without annealing to compare their structural and physicochemical properties. The utility of Raman micro-imaging is reported with dye probe etching as an effective and facile method to reveal structural features for chitosan-based composite materials, before and after thermal annealing. We proposed that such composites undergo a structural change from a loosely packed to a more densely packed structure. As well, the multi-functional role of polyethylene oxide in the composites and the potential role of solvent etching was evaluated. The improved stability of the treated composites reveals their potential utility for applications in aqueous media.

Graphene Oxide-Chitosan Cross-Linked Composites for Wastewater Treatment

Mina Sabzevari , Duncan Cree and Lee Wilson

Graphene oxide (GO)-chitosan materials have been reported as potential adsorbents for applications in wastewater treatment. In this study, the removal of organic water contaminants was studied using MB as a model compound of pesticides or other personal care products such as antimicrobials. Experimental results revealed that GO chemical structure has the potential to be modified by the cross-linking method to produce a composite framework material. Therefore, in this study, cross-linking of GO structure using chitosan biopolymer as a cross-linker agent was investigated. GO composites were prepared by cross-linking GO with chitosan using a green solution-based chemistry approach. Chemical structural, morphological and thermal stability in the cross-linked GO composites were investigated using Fourier transform infrared (FT-IR) spectroscopy, scanning electron microscopy (SEM), and thermal gravimetric analysis (TGA). Also, adsorption properties of samples were obtained using methylene blue (MB) as a cationic probe, in solution phase. According to the spectroscopy results, cross-linked composites suggested interaction between the GO sheets with chitosan through electrostatic attraction and covalent bonding. SEM results showed irregular layer shapes of GO sheets connected to each other with higher surface roughness in cross-linked samples. Changes in the thermal stability of cross-linked samples can be ascribed to the cross-linking effect. Equilibrium and kinetic adsorption studies indicated higher sorption capacity of cross-linked samples toward MB in aqueous phase compare to pure GO and chitosan. This work contributes to the development of composite materials with tunable adsorption properties for remediation of waterborne organic contaminants.

High-resolution X-ray Structures of an Allosteric Site Mutant of *Campylobacter jejuni* Dihydrodipicolinate Synthase in Complex with Natural and Synthetic Allosteric Inhibitors

Sagar Saran, Yulia Skovpen, David R. J. Palmer, and David A. R. Sanders

Campylobacter jejuni (*C. jejuni*) is a gram-negative bacterium that is responsible for many of the gastroenteritis related human deaths each year. Potential antibiotics can be developed against this bacterium by targeting the cell wall. In *C. jejuni*, the dihydrodipicolinate synthase (DHDPS) tetrameric enzyme is the first committed step for the biosynthesis of lysine in the diaminopimelate pathway and is an antibiotic target. Biophysical studies have shown that C.jDHDPS is allosterically inhibited by lysine, and the synthetic inhibitor bislysine, but the structural determinants responsible for transmission of such allosteric inhibition signals are poorly understood. The crystal structures of C.jDHDPS bound with the inhibitors have revealed key residues required for binding of the inhibitor to the allosteric site, including a histidine residue that forms a direct hydrogen bonds to the inhibitor. Mutation of this residue to asparagine resulted in minimal inhibition by lysine but stronger inhibition by bislysine, despite these inhibitors binding in near-identical fashion. The research presented in my study shows the first high-resolution crystal structures of this mutant in the presence and absence of lysine and bislysine, revealing the precise effects of inhibitor binding on the protein structure.

Modification of enzyme-cleavable linkers to guide the design of Antibody Drug Conjugates

Moralba Dominguez-Garcia, Brady Vigliarolo, Eric W. Price / Christopher Phenix

Antibody drug conjugates (ADCs) have emerged as an effective cancer treatment due to their high specificity and affinity to recognize cancer-associated receptors, delivering the drug into the tumour microenvironment. Often, ADC linkers are cleaved by Cathepsin B (CTB) – an overexpressed protease in metastatic cancers – and upon cleavage releases the drug inside or adjacent to cancer cells. However, the effects of linker structure on cellular uptake and CTB hydrolytic rates are usually not evaluated, which could lead to side effects and inefficacy. Four probes that mimic ADC behavior have been synthesized using a CTB sensitive fluorescent reporter instead of a drug to evaluate how linker length, attachment group, and substrate recognition elements affects CTB hydrolysis and protease selectivity. Based on previous developed prodrug- fluorogenic peptides in Phenix lab, as selective substrates for CTB, its expected new probes will be more selective for CTB since they contain same peptide substrate. Following enzymatic assays, the probes will be conjugated via thiol conjugation to Nimotuzumab, an epidermal growth factor receptor antibody, to test cellular uptake, hydrolysis rates in vitro and structural linker effect. The most selective and stable probes will be radiolabeled and evaluated in vivo in murine models of aggressive cancers for biodistribution, PET imaging, and optical imaging studies.

Abstracts

Oral Presentation/Session 5

Synthesis of carbocyclic analogues to probe enzymes involved in kanosamine biosynthesis

Natasha D. Vetter and David R.J. Palmer*

Carbocyclic sugar analogues are useful synthetic compounds for interrogating the mechanism of many enzyme-catalyzed transformations; particularly those for which conformation, configuration, and open/closed chain form of the substrate is not known. We have previously generated carbocyclic analogues of glucose 6-phosphate on small scales using the Ferrier-II carbocyclization approach to probe the reaction catalyzed by NtdC, a glucose 6-phosphate 3-dehydrogenase that is required for kanosamine biosynthesis in *B. subtilis*. Using these analogues, we have determined the form and configuration of the substrates recognized by this enzyme. The synthesis of carbocyclic sugars is well known in the literature and many examples use a Ferrier-II carbocyclization reaction to install the carbocyclic methylene. This approach, however has been limited to the generation of small quantities of final product due to the number of steps involved, and several low-yielding key steps in the synthesis. Current approaches to improve the synthesis of these carbocyclic analogues will be discussed.

“F” in inhibitor design: fluorination of glucose 6-phosphate and its effect in enzyme-ligand interaction

Josseline S. Ramos-Figueroa, David R. J. Palmer

“F” substitution is widely used in medicinal chemistry to enhance metabolic stability, bioavailability and protein-ligand interactions. Moreover, the introduction of fluorine as a part of the scaffold in phosphonate analogs of phosphate-containing molecules have long been used to probe enzyme active sites. alpha-Fluorine substitution modulates phosphonates pKa's and ultimately influences their binding modes. Glucose 6-phosphate (G6P) is an important cell metabolite and participates in several metabolic pathways, behaving as substrate for many enzymes. myo-Inositol phosphate synthase (mIPS) uses G6P as a substrate during the catalysis the first committed step in the biosynthesis of myo-inositol. In humans, high levels of myo-inositol have been related to bipolar disorder. In disease-causing organisms such as *Mycobacterium tuberculosis* and *Trypanosoma brucei*, mIPS has been shown to be essential for the organism survival. mIPS is therefore a potential therapeutic target and as such, we have synthesized fluorinated analogues of G6P to evaluate the effect of the F-substitution in their interaction with mIPS using inhibition studies.

Abstracts

Oral Presentation/Session 6

Raman microscopy of ice in the presence of salt and humic acid

Subha Chakraborty and Tara F. Kahan

Seawater and sea ice are important environmental reaction media. Seawater can contain high concentrations of inorganic salts and organic matter (OM). In frozen systems, the distribution of solutes between the ice bulk and surface, as well as their lateral distribution across the ice surface, can affect physical uptake and reaction rates. We used Raman microscopy to investigate the distribution of organic and ionic solutes in frozen aqueous solutions as well as the solutes' effects on liquid water content. We show that frozen aqueous sodium chloride (NaCl) solutions contain deep channels of liquid brine, and that the surface consists of both liquid brine and bare ice, whereas surface-active OM such as humic acid is excluded to the ice surface where it forms a film that nearly completely coats the surface. In frozen solutions containing both NaCl and humic acid, the fractional liquid content is much greater than that in NaCl-only solutions. Further, liquid brines are observed at temperatures well below the eutectic point of NaCl-water binary mixtures, with the temperature at which the phase change occurs depending on the humic acid concentration. These results have implications for gas-ice partitioning and heterogeneous reactions in solute-containing snow and ice, such as sea ice.

Effect of Molecular Shape on the Properties of Non-Fullerene Acceptors: Contrasting Calamitic Versus 3D Design Principles

Chase L. Radford, Arthur D. Hendsbee, Maged Abdelsamie, Nicholas M. Randell, Yuning Li, Michael F. Toney, and Timothy L. Kelly

Organic solar cells have recently seen a renaissance due to advances in the design of nonfullerene acceptor semiconductors. Modern high-performance nonfullerene acceptors rely on two main design principles: the calamitic design, with side chains arranged orthogonally to a planar chromophore, and the 3D design, where the chromophore is forced to adopt a nonplanar structure. Until now, there has been no direct comparison of these designs. This presentation will compare small molecule nonfullerene acceptors with both the calamitic design (FBRCN) and the 3D design (XFBRCN), bearing the same chromophore unit with similar solubilities. The 3D semiconductor has a higher extinction coefficient, broader absorbance bands, and a higher permittivity than the calamitic semiconductor. Meanwhile, the calamitic semiconductor has a higher electron mobility, is more miscible with polymeric OPV donors, and is more crystalline than the 3D XFBRCN. This is attributed to the long alkyl chains of FBRCN encouraging efficient solid-state packing. This work highlights the differences between the two material design principles, and helps to elucidate the role of side chains in controlling film morphology and the performance of solid-state electronic devices. In this presentation, the relative

optoelectronic and solid state device characteristics of the two chromophores will be presented.

Commissioning of a Quantum Cascade Laser-based, Dual-Comb IR Spectrometer for Time Resolved Spectroscopy at the Canadian Light Source

Erick Lins, Stuart Read, Scott Rosendahl, Ian Burgess

Quantum cascade lasers (QCLs) represent a paradigm change in mid-IR spectroscopy due to their high brilliance. As QCL-based instruments begin to proliferate, innovative applications are emerging including the use of dual frequency comb, multi-heterodyne spectroscopy for time-resolved IR spectroscopy. Conventional IR spectrometers using rapid-scan mirror interferometers require tens of milliseconds to collect a single interferogram. Typically, hundreds of interferograms must be co-added to afford a single spectrum with adequate signal to noise ratios. Faster time windows can be achieved using step-scan approaches but many repeat measurements are required at every mirror retardation position meaning that the overall experiment time is on the order of hours to days. Dual comb spectroscopy removes the necessity of a moving mirror by using two infrared laser combs with slightly different free spectral ranges (the spacing between successive lasing lines). Each frequency pair in the comb produces a heterodyne beat at a radio frequency corresponding to the difference of the optical frequencies. By downshifting the optical interference pattern to radio frequencies, the multi-heterodyne beat pattern produced on a standard MCT photodetector can be digitized without the need of a moving mirror. A single QCL pairing can be tuned to produce ca. 100 cm^{-1} bandwidth combs with 0.25 cm^{-1} resolution. Recently, the mid-IR beamline at the Canadian Light Source procured a turn-key multi-heterodyne spectrometer. Our efforts to commission the instrument will be discussed. This will include a comparison of electrochemical ATR and ATR-SEIRAS data obtained with conventional and multi-heterodyne spectrometers for both static and time-resolved applications.

Synthesis of regioisomerically pure 1,7-dicyanoperylene diimide and its dimerization for photovoltaic applications

Rick Pettipas, Chase Radford, and Tim Kelly

Perylene diimide has proven itself to be an ideal building block for the design of new electron acceptors for organic solar cells due to its high extinction coefficient and electron deficient nature. Current efforts to modify perylene diimide to improve solar cell efficiency have been focused on functionalization of the bay region to tune the domain size, solubility, and energy of frontier orbitals. This strategy has made it difficult to tune these properties simultaneously, owing to the limited number of positions where functional groups can be introduced. I will discuss the benefits and synthetic challenges of an alternative approach which makes use of the electronically isolated Imide region to disrupt the intermolecular π - π interactions, while using the bay positions to modify the energies of frontier orbitals. I will show how this strategy affects the performance of organic solar cells.