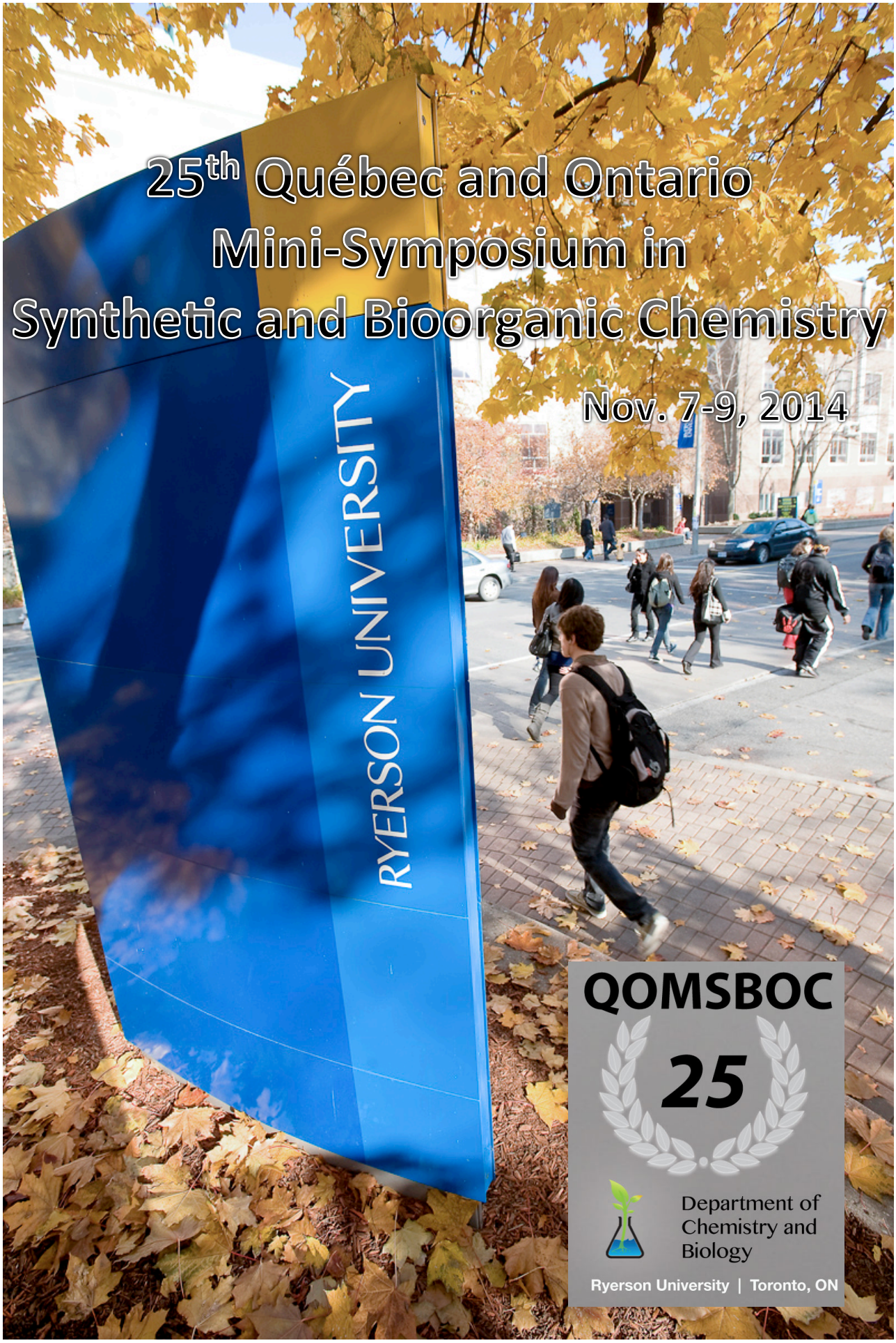


25th Québec and Ontario Mini-Symposium in Synthetic and Bioorganic Chemistry

Nov. 7-9, 2014

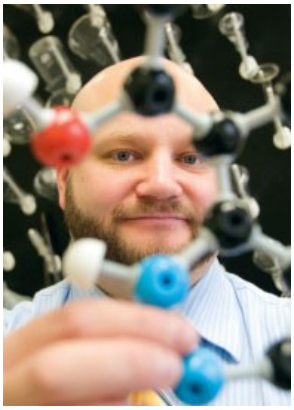
QOMSBOC

25

Department of Chemistry and Biology

Ryerson University | Toronto, ON

Welcome to QOMSBOC 25!



It gives me great pleasure to welcome everybody to the 25th Québec and Ontario Mini-Symposium in Synthetic and Bioorganic Chemistry! For a quarter century now, this meeting has been the premier regional conference for students from our two provinces who conduct research in synthetic organic or bioorganic chemistry to present their work. This year, we can look forward to 18 oral and 53 poster presentations, representing contributions from 33 research groups across 17 universities. We also have three very exciting keynote speakers in professor Ramanarayanan Krishnamurthy from the Scripps Research Institute, Dr. Zhongxin Zhou from Gilead Alberta, and professor Alison J. Frontier from the University of Rochester.

I am very grateful to professor Bryan Koivisto and the many Ryerson graduate and undergraduate students who have provided tireless help in the organization and execution of this conference. Also, QOMSBOC would not have been possible without the support of the generous sponsors listed below.

Enjoy the weekend!
Russ Viirre
Chair, QOMSBOC 25

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Keynote Lecture #1 – Saturday 11:10 am

RNA: Towards an Understanding of its Emergence

Ramanarayanan Krishnamurthy
rkrishna@scripps.edu
Department of Chemistry, The Scripps Research Institute
10550 North Torrey Pines Road, La Jolla, CA 92037, U.S.A

Abstract: RNA is arguably the most central of the class of biomolecules in extant biochemistry on earth. The focus on RNA as a key player in origins of life research is exemplified by the RNA-world hypothesis where RNA functioned both as the carrier of information and as a catalyst of many reactions. With new functions of RNA being discovered almost daily, there is much to learn about the operational versatility of this biopolymer. The past-present-future omnipresence of RNA has made it a molecule of intense appeal from a structural, functional and application perspective.

RNA's chemistry and biology, which are intertwined with the physicochemical properties of its chemical components in a neutral aqueous environment, are incompatible with plausible prebiotic environments. The question arises whether RNA could have appeared later, at a stage where both the chemical processes and the environment would have been more conducive for RNA's sustained origination and function.

The presentation will focus on our search for alternatives to RNA, and the insights gained by comparing them to RNA. The results from these studies not only allow for a greater understanding of the structure-function relationship of RNA, but also have implications for the consideration of RNA as a product of chemical evolution.

Biography: Ramanarayanan Krishnamurthy is an Associate Professor of Chemistry at the Scripps Research Institute in La Jolla, a member of the NSF-NASA sponsored Center for Chemical Evolution, and a member of the Simons foundation sponsored Simons Collaboration on the Origins of Life. He received his B.S. from University of Madras in 1984, M.S. from the Indian Institute of Technology, Bombay in 1986 working with Professor K. D. Deodhar, and Ph.D. from the Ohio State University in 1992 under Professor David Hart. After graduate work at Ohio State University, he was a postdoctoral fellow at the Swiss Federal Institute of Technology (ETH) with Professor Albert Eschenmoser, where he remained until 1994. He then moved to La Jolla for a second postdoctoral experience at the Scripps Institution of Oceanography working with Professor Gustaf Arrhenius. He became a Senior Research Associate of the Skaggs Institute for Chemical Biology (1996-1997) and an Investigator (2005-2009). He joined the chemistry faculty of the Scripps Research Institute in 1998 as an Assistant Professor. His research is focused on the use of synthetic organic chemistry and methodology to experimentally address questions concerning the origins of life, as well as to develop tools for molecular bio-mimicry and chemical therapeutics. He has received the ISSOL Fellow Award (2011) and is a member of the NASA Astrobiology Science and Technology Instrument Development Review Panel since 2006, and the NASA Exobiology and Planetary Protection Research Review Panel since 2002.

Keynote Lecture #2 – Saturday 3:20 pm

A Race for Cure: Development of Medicines That Transform the Landscape of HCV Therapy.

Zhongxin Zhou, Ph.D., MBA
Zhongxin.Zhou@gilead.com
Sr. Director
Gilead Alberta ULC
Process Research and Development
1021 Hayter Road
Edmonton, Alberta, T6S 1A1, Canada

Abstract: The search for successful therapeutic drugs for the treatment of life-threatening diseases and improvement of the quality of life is known to be a very complex, costly and time-consuming process. Like any therapeutic area, the development of hepatitis C virus (HCV) therapy has reached to its critical stage with medicines that could revolutionize the therapeutic treatment: the cure of HCV, being launched. This talk will provide: 1) an overview of pharmaceutical development and the status of the industry; 2) the current landscape of hepatitis C Virus therapeutic development and the role Gilead plays; 3) the chemistry of HCV therapy; and 4) for the benefit of prospective employees, a brief description of process chemistry.

Biography: After receiving his B.Sc. in chemistry and M.Sc. in catalysis, Dr. Zhou had worked for 5 years at Hubei Research Institute of Chemistry, China, focusing on organic process research and development for the fine chemical industry. He then moved to Canada and received his Ph.D. from Memorial University of Newfoundland in 1994, working with Dr. Chat Jablonski. After close to two-year stay at Dr. Howard Alper's group at the University of Ottawa as a postdoctoral fellow, he took a position at Raylo Chemicals as a Senior Research Chemist in 1996, became the Research Manager in 1998 and then the R&D Manager in 2003, heading the efforts of process research and development, process safety, kilo-lab manufacturing and process transfer to manufacturing plants. He has moved on to be part of Gilead Sciences since 2006 and is now the Senior Director of Process Research and Development at Gilead Alberta, looking after the department that designs and develops chemical processes suitable for the manufacture of active pharmaceutical ingredients at different stages of the drug development, from preclinical studies through commercialization. His department has contributed significantly to most of Gilead's drugs on the market and in the development pipeline covering HIV, liver diseases, oncology and cardiovascular therapeutic areas. He also holds an MBA degree from the University of Alberta.

Keynote Lecture #3 – Sunday 10:30 am

Stereocontrolled Cyclizations

Alison J. Frontier
Frontier@chem.rochester.edu
Professor of Chemistry
University of Rochester, Department of Chemistry
RC Box 270216, Rochester, NY 14627, U.S.A.

Abstract: The development of novel, synthetically useful cyclization strategies will be described. The strategies capitalize upon electrocyclic reactions, cationic rearrangements, and multistep cascades that occur with high levels of stereochemical control. Examples of the application of these cyclization methods to the synthesis of polycyclic natural product targets will also be presented.

Biography: Dr. Alison J. Frontier was born and raised in suburban Detroit, Michigan. She attended Harvard University, where she worked in the laboratory of Professor Yoshito Kishi. In June 1992 she graduated with an AB in chemistry and became a research scientist at Merck Research Laboratories in Rahway, New Jersey, in the Basic Medicinal Chemistry division. She enrolled in the doctoral program at Columbia University in September 1994, conducted graduate work under the direction of Professor Samuel Danishefsky, and received her Ph.D. in June 1999. She was an NIH postdoctoral fellow in the laboratory of Professor Barry Trost at Stanford University from 1999-2001, and began her independent career at the University of Rochester in January 2002. Dr. Frontier was promoted to associate professor in 2008 and professor in 2013. In 2004, she launched "not voodoo" a website dedicated to students who are beginning independent experimentation for organic chemistry research projects. This site attracts hundreds of visitors daily from research laboratories around the world.

Poster session and banquet will be held on the 4th floor of the Mattamy Athletic Centre (formerly Maple Leaf Gardens)

QOMSBOC 25

Department of Chemistry and Biology

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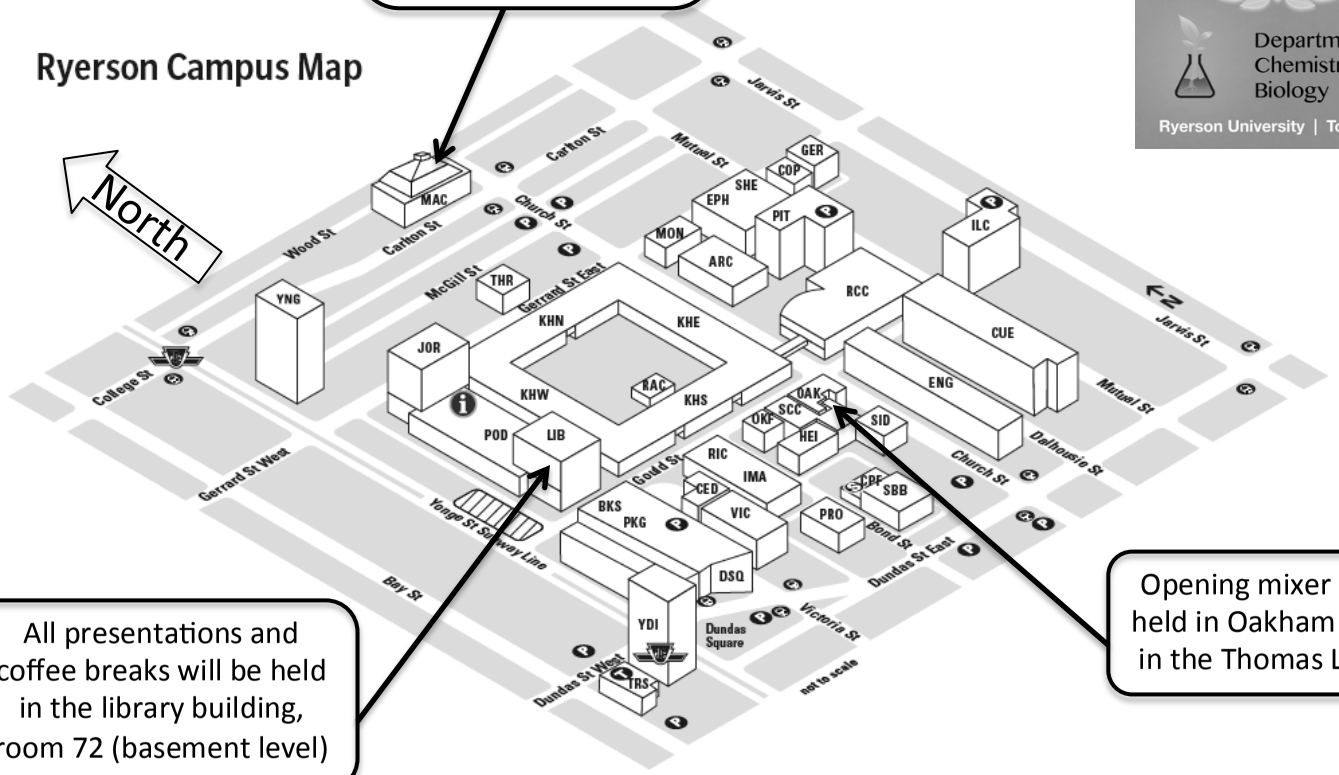
Ryerson Campus Map



All presentations and coffee breaks will be held in the library building, room 72 (basement level)

Opening mixer will be held in Oakham House, in the Thomas Lounge

Conference Schedule

Friday November 7

7:00 – 10:00 pm **Mixer and Registration:** Thomas Lounge, ground floor of Oakham House, SW corner of Church and Gould streets

Saturday November 8 - Morning

8:00 am **Registration opens:** Room 72 (basement level) of the Library Building, NW corner of Victoria and Gould streets)

8:40 am **Welcome/Opening Remarks – Professor Russ Viirre,** Chair of QOMSBOC25.

8:50 am **OR1:** Synthesis of heterocyclic hubs and oligoheterocycles using novel boron-containing building blocks. **C. Frank Lee**, Jeffrey D. St. Denis, Shinya Adachi, Andrei K. Yudin*, University of Toronto.

9:10 am **OR2:** The thermodynamics of chalcogen bonding in solution. **Graham E. Garrett**, Gregory L. Gibson, Rita. N. Straus, Dwight S. Seferos, Mark S. Taylor*, University of Toronto.

9:30 am **OR3:** The use of (dichloro)iodobenzene for the gem-dichlorination reactions of diazo- and hydrazone-containing compounds. **Keith E. Coffey**, Farhana Z. Abbas, Ryan E. Moreira, Graham K. Murphy*, University of Waterloo.

9:50 am **OR4:** Adapting a catalytic aerobic dearomatization of phenols to the synthesis of oxindoles. **Zheng Huang**, Mohammad S. Askari, Kenneth V. N. Esguerra, Xavier Ottenwaelder, Jean-Philip Lumb*, McGill University.

10:10 am **COFFEE BREAK**

10:30 am **OR5:** Synthesis and properties of monofluorinated dimyristoylphosphatidylcholine derivatives: potential fluorinated probes for the study of membrane topology**. Marie-Claude Gagnon,** Michèle Auger* and Jean-François Paquin*, Université Laval.

10:50 am **OR6:** Synthesis and in vitro assessment of chemically modified siRNAs containing 2'-ribose modifications and triazole linked backbone modifications. **Gordon Hagen**, and Jean-Paul Desaulniers*, University of Ontario Institute of Technology.

11:10 am **Keynote 1:** RNA: Towards an Understanding of its Emergence. **Professor Ramanarayanan Krishnamurthy**, The Scripps Research Institute, La Jolla, CA.

12:00 noon Adjourn for lunch (not provided)

Saturday November 8 – Afternoon

1:10 pm **OR7:** Stereodivergent synthesis of vinyl halides via palladium-catalyzed carbohalogenation of hindered alkynes. **Christine M. Le**, Perry J. C. Menzies, David A. Petrone, Mark Lautens*, University of Toronto.

1:30 pm **OR8:** Palladium-catalyzed carbonylative C-H functionalization of heterocycles. **Jevgenijs Tjutrins**, Bruce Arndtsen*, McGill University.

1:50 pm **OR9:** Palladium-catalyzed decarboxylative allylation of sulfones: method development and mechanistic insight. **Monica A. Gill** and Jeffrey M. Manthorpe*, Carleton University.

2:10 pm **OR10:** Palladium-catalyzed carbonylation of halo arene-cis-dihydrodiols to the corresponding carboxylates. Access to compounds unavailable by toluene dioxygenase-mediated dihydroxylation of benzoates. **Jordan Froese**, Jason Reed Hudlicky and Tomas Hudlicky*, Brock University.

2:30 pm **SHORT BREAK**

2:40 pm **OR11:** Development of a direct macrolactonization protocol via hafnium (IV) catalysis. **Mylène de Léséleuc** and Shawn K. Collins*, Université de Montréal.

3:00 pm **OR12:** New agonists of the Keap1 – Nrf2 pathway, a potential solution for oxidative stress related diseases. **Ludovic Deny**, Hussein Traboulsi, Martin V. Richter, Eric Marsault, Guillaume Bélanger*, Université de Sherbrook.

3:20 pm **Keynote 2:** A Race for Cure: Development of Medicines That Transform the Landscape of HCV Therapy. **Dr. Zhongxin Zhou**, Sr. Director, Gilead Alberta ULC Process Research and Development.

4:10 pm Adjourn to move to the poster venue, 4th floor of the Mattamy Athletic Centre

4:30 – 6:30 pm **Poster Session**, 4th floor of the Mattamy Athletic Centre. A cash bar will be available.

7:00 – 10:00 pm **Banquet**, Alumni Lounge, 4th floor of the Mattamy Athletic Centre

Sunday November 9

9:50 am **OR13:** Synthesis of new rigidified merocyanine dyes: A Knoevenagel condensation as the key step. **Katharina Christina Kreß**, Sabine Laschat and Holger S. Eichhorn*, University of Windsor.

10:10 am **OR14:** Brønsted acid catalyzed synthesis of propargylic ethers from acetals using potassium alkynyl trifluoroborate salts. Matthew Baxter, Yuri Bolshan*, University of Ontario Institute of Technology.

10:30 am **Keynote 3:** Stereocontrolled Cyclizations. **Professor Alison J. Frontier**, University of Rochester.

11:20 am **COFFEE BREAK**

11:40 am **OR15:** Brønsted acid catalyzed kinetic resolution enables access to enantioenriched β-aminocarbonyl compounds from alkenes. **Amanda Bongers**, P. Moon and A. Beauchemin*, University of Ottawa.

12:00 noon **OR16:** Development of diazepane carboxylate organocatalysts for asymmetric Cope rearrangement. **Dainis Kaldre**, James L. Gleason*, McGill University.

12:20 pm **OR17**: An enantioselective formal synthesis of 'iso' NSC 51046 allocolchicine and related analogues via catalytic conjugate addition reactions. **Mariam Mehdi**, Sinisa Djurdjevic and James R. Green*, University of Windsor.

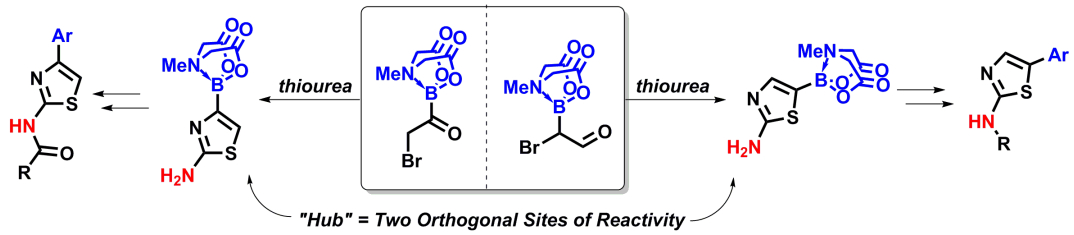
12:40 am **OR18:** Racemic and enantioselective total syntheses of mosquito oviposition pheromone from a naturally available unsaturated fatty acid. **David Hurem** and Travis Dudding*, Brock University.

1:00 pm **Closing Remarks – Professor Russ Viirre,** Chair of QOMSBOC25.

OR1 Synthesis of heterocyclic hubs and oligoheterocycles using novel boron-containing building blocks

C. Frank Lee, Jeffrey D. St. Denis, Shinya Adachi, Andrei K. Yudin*, Department of Chemistry, University of Toronto, Toronto, ON, M5S 3H6, ayudin@chem.utoronto.ca

Amphoteric molecules and their utility in macrocycilzation and heterocyclic synthesis have recently been developed; in particular, α-bromo acyl boronates and 2,4-/2,5-substituted thiazole 'hubs' for the synthesis of oligoheterocycles are described. Depending on the building block used, 2,4-/2,5- substituted aminothiazoles can be regioselectively accessed.[1,2] We also demonstrate the utility of these 'hubs' through careful optimization of modified boron functionalization followed by $-NH_2$ functionalization to afford oligoheterocycles. With increased interests in the 2-aminothiazole scaffold for biological applications, our borylated heterocycles allow facile chemoselective functionalization which would otherwise be difficult to access, generating compounds useful for chemical probe design in medicinal chemistry.



1. He, Z.; Trinchera, P.; Adachi, S.; St. Denis, J. D.; Yudin, A. K. *Angew. Chem. Int. Ed*. **2012**, *51*, 11092-11096.
2. St. Denis, J. D.; Zajdlik, A.; Tan, J.; Trinchera, P.; Lee, C. F.; He, Z.; Adachi, S.; Yudin, A. K. **2014**. *Submitted.*

OR2 The thermodynamics of chalcogen bonding in solution

Graham E. Garrett, Gregory L. Gibson, Rita. N. Straus, Dwight S. Seferos, Mark S. Taylor* Department of Chemistry, University of Toronto, Toronto, ON, M5S3H6,

Electron poor chalcogen atoms (Group VI: S, Se, Te) are known to engage in secondary bonding interactions, or chalcogen bonds, in the solid and gas phases.[1] We synthesized a series of electron deficient chalcogen containing compounds, and using them, obtained accurate measurements of the thermodynamics of chalcogen bonding in solution. Association constants were determined using UV-vis and NMR. Chalcogen bonded complexes were also observed by nanospray-MS techniques. The interactions were then modeled computationally to support the experimental findings.

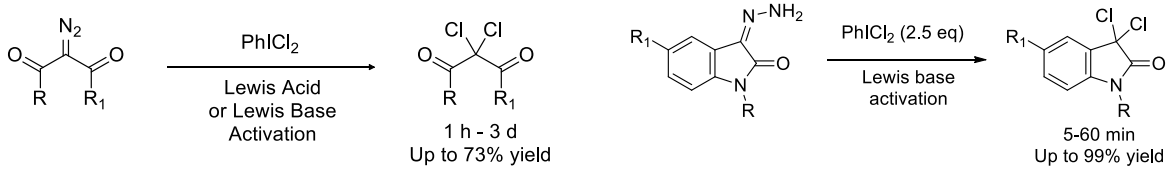
1. (a) Bleiholder, C.; Werz, D. B.; Köppel, H.; Gleiter, R., *J. Am. Chem. Soc.* **2006,** *128* (8), 2666-2674; (b) Bleiholder, C.; Gleiter, R.; Werz, D. B.; Köppel, H., *Inorg. Chem.* **2007,** *46* (6), 2249-2260; (c) Sanz, P.; Yáñez, M.; Mó, O., *J. of Phys. Chem. A* **2002,** *106* (18), 4661-4668. d) Cozzolino, A. F.; Dimopoulos-Italiano, G.; Lee, L. M.; Vargas-Baca, I., *Euro. J. Inorg. Chem.* **2013,** *2013* (15), 2751-2756.

OR3 The use of (dichloro)iodobenzene for the *gem*-dichlorination reactions of diazo- and hydrazone-containing compounds

Keith E. Coffey, Farhana Z. Abbas, Ryan E. Moreira, Graham K. Murphy*, Department of Chemistry, University of Waterloo, Waterloo, ON, N2J 3G1, gkmurphy@uwaterloo.ca

Hypervalent iodine reagents have been used historically as versatile reagents that allow for many unique transformations in organic chemistry. The α-functionalization of carbonyl compounds with hypervalent iodine reagents has been extended to allow for geminal transfer of both ligands from a single iodane on ylide containing compounds. Reactivity has been shown to proceed via a Lewis base or Lewis acid catalysis. The expansion of this chemistry from phenyldiazoacetate derivatives to a variety of 2-diazo-1,3-dicarbonyl compounds will be discussed in depth.

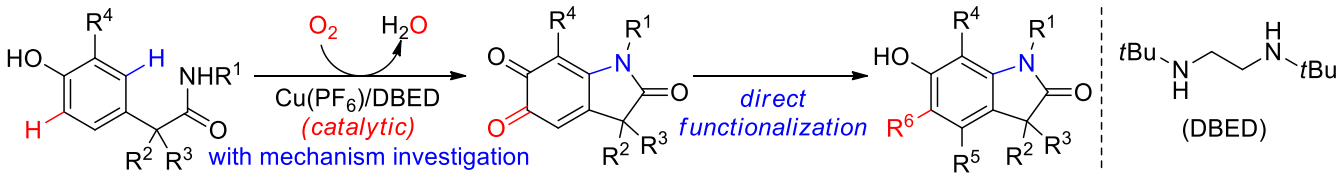
The use of suitable groups as diazo surrogates has also been explored through a tandem oxidation/chorination reaction. Functionalized hydrazone compounds are transformed efficiently to the corresponding *gem*-dichlorinated product upon reaction with (dichloro)iodobenzene under Lewis base catalysis. Methods using such reactivity as a deoxygenative halogenation approach will be discussed.



OR4 Adapting a catalytic aerobic dearomatization of phenols to the synthesis of oxindoles

Zheng Huang, Mohammad S. Askari, Kenneth V. N. Esguerra, Xavier Ottenwaelder, Jean-Philip Lumb* Department of Chemistry, McGill University, Montreal, QC, H3A 0B8, jean-philip.lumb@mcgill.ca

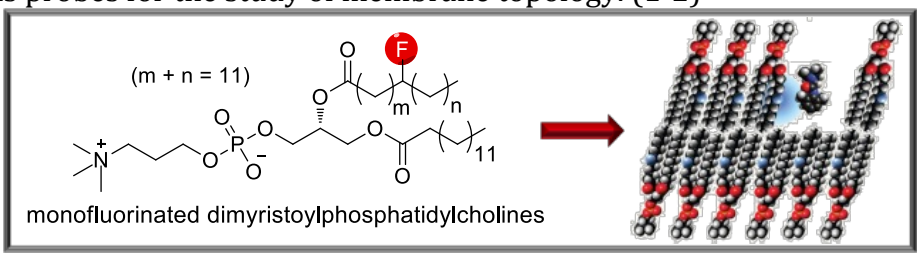
Nitrogen-containing heterocycles are fundamentally important to the function of pharmaceuticals, agrochemicals and materials. Herein, we report a biomimetic approach to the synthesis of oxindoles, which couples the energetic requirements of dehydrogenative C-N bond formation to the reduction of molecular oxygen (O_2). Our method is inspired by the ubiquitous biosynthesis of melanin pigments (melanogenesis), but diverges mechanistically from the biosynthetic polymerization. We provide mechanistic insight, which is characterized by a dehydrogenative C-N bond formation that does not require coordination of the nitrogen to a transition metal. Thus, our method tolerates a broad range of substituents on nitrogen, including aryl-, hetero-aryl- and alkyl-substituents. Our method is marked by a rapid increase in molecular complexity, which gives rise to the efficient synthesis of diversely substituted oxindole heterocycles.



OR5 Synthesis and properties of monofluorinated dimyristoylphosphatidylcholine derivatives: potential fluorinated probes for the study of membrane topology

Marie-Claude Gagnon, Michèle Auger* and Jean-François Paquin*, Département de chimie, Université Laval, Québec, QC, G1V 0A6, marie-claude.gagnon.24@ulaval.ca

Understanding the interactions between lipid membranes and drugs, peptides or proteins is of primary importance to determine their mechanism of action. In this context, nuclear magnetic resonance (NMR) is a method of choice to study their effects on model membranes. Since ^{19}F offers several advantages for NMR studies, we synthesized a variety of monofluorinated dimyristoylphosphatidylcholine derivatives (F-DMPC). The synthesis, but also FTIR and solid-state NMR studies will be presented. These results suggest that the presence of the fluorine atom does not significantly perturb the properties of the lipid bilayers and that these fluorinated lipids could be used as probes for the study of membrane topology. (1-2)



1. Guimond-Tremblay, J.; Gagnon, M.-C.; Pineault-Maltais, J.-A.; Turcotte, V.; Auger, M.; Paquin,* J.-F. *Org. Biomol. Chem.* **2012**, *10*, 1145-1148. 2. Gagnon, M.-C.; Turgeon, B.; Savoie, J.-D.; Parent, J.-F.; Auger, M.; Paquin,* J.-F *Org. Biomol. Chem.* **2014**, *12*, 5126-

OR6 Synthesis and *in vitro* assessment of chemically modified siRNAs containing 2'-ribose modifications and triazole linked backbone modifications

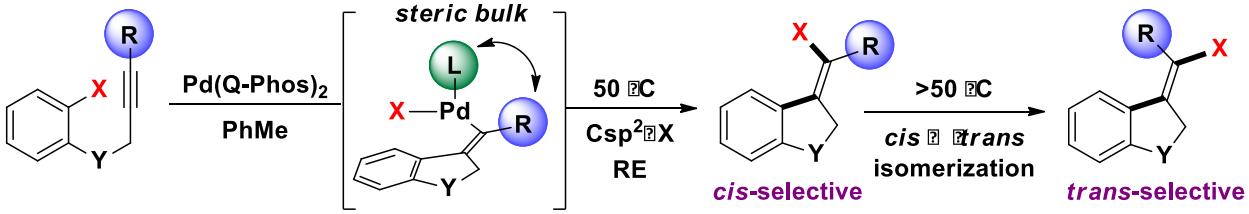
Gordon Hagen, and Jean-Paul Desaulniers*, Department of Chemistry, University of Ontario Institute of Technology. Oshawa. ON. L1H 7K4. Jean-Paul.Desaulniers@uoit.ca

Short interfering RNAs (siRNAs) are naturally occurring biomolecules used for post transcriptional gene regulation and therefore hold promise as a future therapeutic by controlling aberrant gene expression. However, there are many inherent problems with native RNA which can be overcome by chemical modifications. This project synthesizes unique chemically modified siRNAs by combining 2'-ribose sugar modifications with a triazole-linked backbone modification. Our lab has developed a synthesis of a triazole nucleic acid phosphoramidite, which is synthesized through the reaction of azido- and alkynyl- nucleic acid monomers via a copper(I)-catalyzed Huisgen [3+2] cycloaddition. Solid support phosphoramidite chemistry was used to incorporate these chemical modifications at various positions within the siRNA and their *in vitro* effects were evaluated through qPCR, cell viability, nuclease stability, and immunological ELISA assays. These modifications show enhanced activity and stability over natural siRNAs while improving upon inherent issues of toxicity, immunological activation, and off-target effects of unmodified siRNAs.

OR7 Stereodivergent synthesis of vinyl halides via palladium-catalyzed carbohalogenation of hindered alkynes

Christine M. Le, Perry J. C. Menzies, David A. Petrone, Mark Lautens*, Department of Chemistry, University of Toronto, Toronto, Ontario, M5S 3H6, mlautens@chem.utoronto.ca

In contrast to oxidative addition, the reductive elimination of carbon–halogen bonds from Pd^{II} complexes is rare elementary process when conventional ligands, such as triarylphosphines, are employed. Our group has previously reported the application of bulky, electron-rich Pd catalysts in the carboiodination reaction of alkenes to form alkyl iodides. We now report that by exploiting the synergistic steric effects between substrate and catalyst, an intramolecular Pd-catalyzed alkyne carbohalogenation can be realized, providing access to vinyl halides in a stereodivergent manner.[1] Mechanistic studies reveal that oxidative addition is a reversible process, thereby preventing catalyst deactivation and, more interestingly, enabling a thermodynamically-driven isomerization of the vinyl halide product at elevated temperatures.

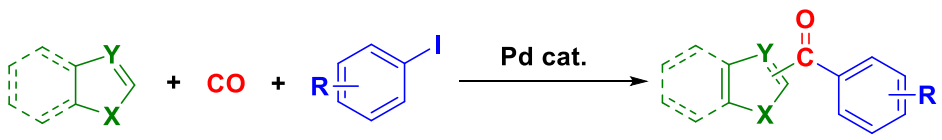


1. Le, C. M.; Menzies, P. J. C.; Petrone, D. A.; Lautens, M. *Angew. Chem. Int. Ed.* **2014**, accepted (DOI: 10.1002/anie.201409248).

OR8 Palladium-catalyzed carbonylative C-H functionalization of heterocycles

Jevgenijs Tjutrins, Bruce Arndtsen* Chemistry Department, McGill University, Montreal, Quebec, H3A 0B8, bruce.arndtsen@mcgill.ca

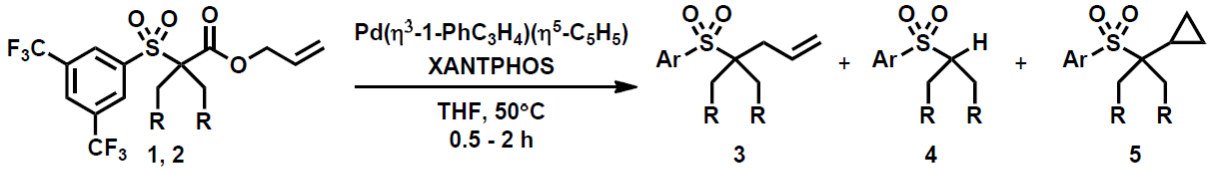
The palladium catalyzed C-H functionalization of arenes has become an important new approach in synthetic chemistry. Relative to classical cross coupling reactions, the direct functionalization of C-H bonds does not require stoichiometric organometallic reagents and/or pre-activated compounds, leading to greater efficiency, atom economy, and minimizing waste. While many transition metal catalyzed C-H arylation, alkylation, alkynylation reactions of arenes and heteroarenes have been developed, transition metal catalyzed carbonylative C-H functionalizations have not been extensively studied, presumably due to the inhibitory effect of CO on C-H activation. We describe here how the influence of ligands can be exploited to develop a general approach to carbonylative C-H functionalization, and allow, overall, palladium catalyzed carbonylative coupling of various aryl halides and heterocycles. The details of this reaction, catalyst development, mechanism and substrate scope will be discussed.



OR9 Palladium-catalyzed decarboxylative allylation of sulfones: method development and mechanistic insight

Monica A. Gill and Jeffrey M. Manthorpe* Department of Chemistry, Carleton University, Ottawa, ON, K1S 5B7, jeffey.manthorpe@carleton.ca

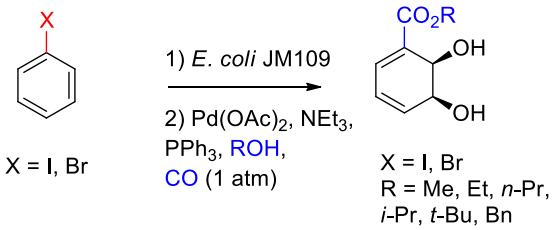
Metal-catalyzed decarboxylative allylation is a versatile and valuable set of reactions used by synthetic chemists. We have developed a Pd-catalyzed, sulfone-based variant to the typical substrates. The sulfone in **3** may be retained, or may be easily excised using a variety of C-S bond cleavage conditions. Using mild conditions, good yields for **3** were obtained for a range of substrates, **1**. A mechanistic investigation was initiated based on the unusual product distribution observed for the reaction of **2** (R = H). Current mechanistic understanding for these transformations does not account for the origin of the protonated product. Several deuterium labelled substrates have been prepared, with labels in both the allyl moiety and on the alkyl fragments, to probe the mechanism. The reaction development, substrate scope and mechanistic insight gained from the deuterium labelled substrates will be presented.



OR10 Palladium-catalyzed carbonylation of halo arene-*cis*-dihydrodiols to the corresponding carboxylates. Access to compounds unavailable by toluene dioxygenase-mediated dihydroxylation of benzoates.

Jordan Froese, Jason Reed Hudlicky and Tomas Hudlicky* Chemistry Department and Centre for Biotechnology, Brock University, , thudlicky@brocku.ca

A series of arene-*cis*-dihydrodiol carboxylates was prepared by palladium-catalyzed carbonylation of (1S, 2S-cis)-3-iodo-3,5-cyclohexadiene-1,2-diol, which is obtained in high titers by enzymatic dihydroxylation of iodobenzene. Both the free diol and the corresponding acetonide were subjected to this protocol to produce various arene-cis-dihydrodiol carboxylates that are unavailable by fermentation of the corresponding benzoates or are produced in low yields. The comparison of yields obtained from fermentation versus carbonylation was made for all compounds investigated. These arene-*cis*-dihydrodiol carboxylates were subsequently utilized to produce novel analogs of oseltamivir for biological testing, as well as in the pursuit of an efficient synthesis of tetrodotoxin.

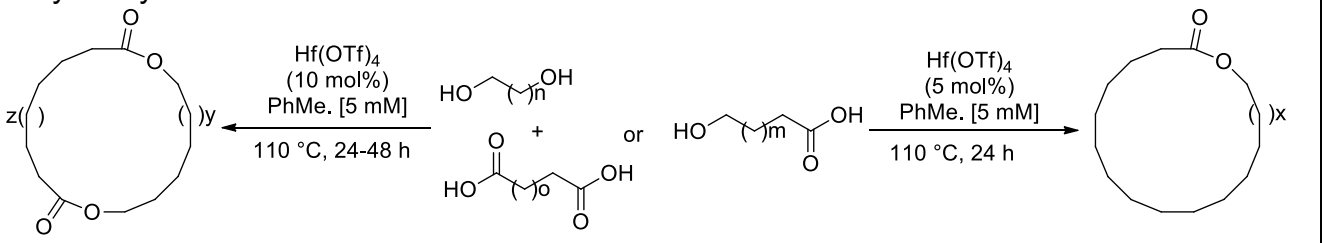


Froese, J.; Hudlicky, J.; Hudlicky, T. *Org. Biomol. Chem.* **2014**, *12*, 7810.

OR11 Development of a direct macrolactonization protocol via hafnium (IV) catalysis

Mylène de Léséleuc and Shawn K. Collins*, Département de Chimie, Center for Green Chemistry and Catalysis, Université de Montréal, Montréal, Qc, H3T 1J4

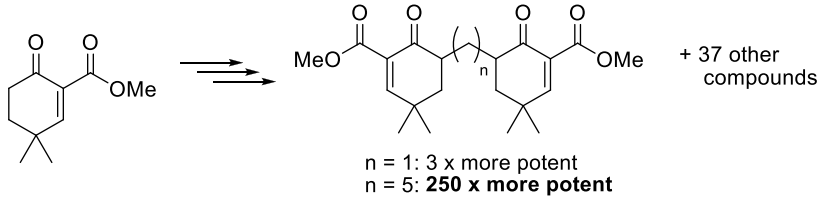
Macrolactones are important structural motifs in numerous chemical industries, in particular the pharmaceutical and cosmetic markets. However, the traditional strategy for the preparation of macrolactones remains cumbersome, often requiring stoichiometric or excess amounts of activating reagents. Consequently, stoichiometric quantities of by-products are generated. These are often toxic, environmentally damaging, and/or require tedious purification methods to remove them. Herein, we describe efforts to develop an efficient Hafnium-catalyzed direct macrolactonization between carboxylic acid and alcohol functionalities, generating only water as a by-product. This method is compatible with numerous functional groups, such as carbamates, tosylamines, silyl ethers, acetals and alkoxymethyl ethers.



OR12 New agonists of the Keap1 – Nrf2 pathway, a potential solution for oxidative stress related diseases

Ludovic Deny[1], Hussein Traboulsi[2], Martin V. Richter[2], Eric Marsault[3], Guillaume Bélanger[1]*
[1]Département de chimie, [2]Département de médecine and Centre de recherche du CHUS, [3]Département de pharmacologie, Université de Sherbrooke, QC, J1K 2R1, Guillaume.Belanger@USherbrooke.ca

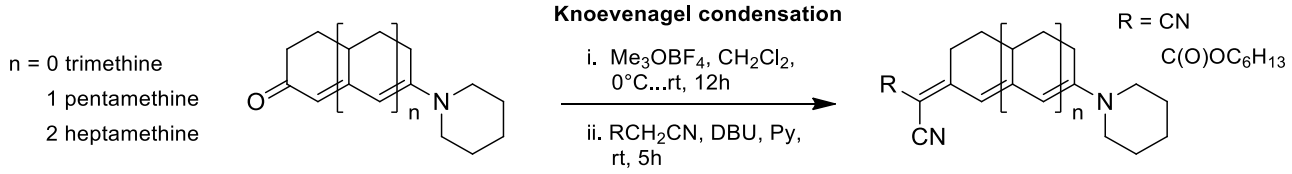
The Keap1/Nrf2 pathway is an essential component of the cell's antioxidant defense and possesses a therapeutic potential for diseases involving oxidative stress such as cancers, diabetes or neurodegenerative disorders. Keap1 is a cytosolic chaperone protein that sequesters the Nrf2 (Nuclear factor erythroid-related 2-like 2) transcription factor in the cytosol, preventing the transcription of genes associated with the ARE (Antioxidant Response Element). Keap1 is a cysteine-rich protein whose nucleophilic thiols can be modulated with small molecules. In this respect, Nazarov acceptors (see scheme) have raised our interest, based on the reasoning that a compound able to react with more than one cysteine could be highly potent and selective. Herein, we present a series of compounds aimed at understanding the synergy between two acceptors. We have identified the relative position (tether length and rigidity) of the electrophilic centers as a key parameter in activity. We strongly believe our study will help in the understanding of the Keap1/Nrf2 pathway.



OR13 Synthesis of new rigidified merocyanine dyes: A Knoevenagel condensation as the key step

Katharina Christina Kreß, Sabine Laschat and Holger S. Eichhorn*, Department of Chemistry and Biochemistry, University of Windsor, Windsor, ON, N9B 3P4, eichhorn@uwindsor.ca

Three series' of rigidified tri-, penta- and heptamethine merocyanine dyes were synthesized. A piperidyl moiety was chosen as the electron-donating substituent while the electron-accepting group was varied (ketone, malononitrile, and cyanoacetate). The synthesis of these compounds was less straightforward than expected and required the optimization of several steps, such as the final Knoevenagel condensation to the malononitriles and cyanoacetates. The 3D structures in solid state and in solution were elucidated by single crystal XRD and solution NMR spectroscopy, respectively, and compared to structures predicted by calculations at the B3LYP 6-311+G(d) level of theory (Gaussian 09). Absorption and emission spectroscopy revealed that the optical properties strongly depend on the length of the conjugated system and the strength of the acceptor group. Derivatives with the strong malononitrile acceptor approach the cyanine limit.

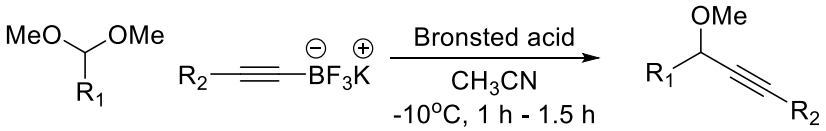


K. C. Kreß et al., *ChemPlusChem* **2014**, *79*, 223–232. DOI: 10.1002/cplu.201300308

OR14 Brønsted acid catalyzed synthesis of propargylic ethers from acetals using potassium alkynyl trifluoroborate salts

Matthew Baxter, Yuri Bolshan*, Faculty of Science, University of Ontario Institute of Technology, Oshawa, On. L1H 7K4, Yuri.Bolshan@uoit.ca

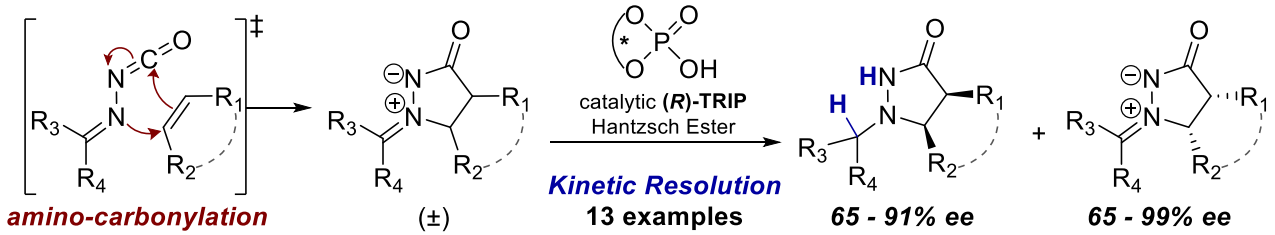
Brønsted acid catalysis has emerged as a powerful synthetic tool. However, the compatibility of carbon-based nucleophiles is the major limitation of acid-catalyzed reactions. In effort to expand the repertoire of nucleophiles that are compatible with Brønsted acids, we present a novel carbon-carbon forming methodology between acetals and potassium phenylacetylene trifluoroborate salts. Brønsted acid promotes *in-situ* formation of oxocarbenium ions that subsequently react with trifluoroborate salts to form propargyl ethers. This protocol features excellent functional group tolerance including nitrile, nitro and halogen functionalities.



OR15 Brønsted acid catalyzed kinetic resolution enables access to enantioenriched β-aminocarbonyl compounds from alkenes

A. Bongers, P. Moon and A. Beauchemin*, Department of Chemistry, Centre for Catalysis Research and Innovation, University of Ottawa. *andre.beauchemin@uottawa.ca

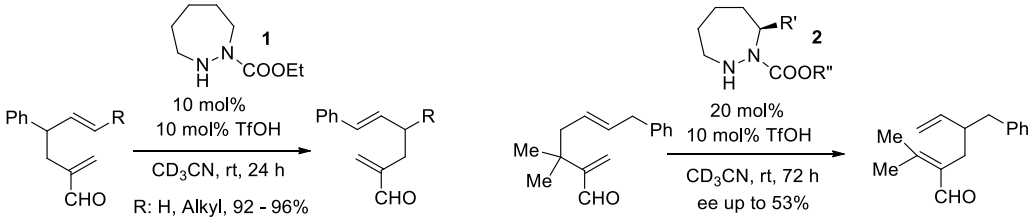
The aminocarbonylation of alkenes with blocked imino-isocyanates was recently developed by our group to synthesize a variety of *N,N*'-cyclic azomethine imines that are difficult to access by other methods.[1,2] Our cycloaddition approach gave racemic azomethine imines, which are oxidized precursors to pyrazolidinones and β-amino acid derivatives. To give us access to new enantioenriched β-amino carbonyls, we have developed a kinetic resolution for a broad scope of azomethine imines. The selective reduction (*s*=17-39) of one enantiomer, catalyzed by the chiral Brønsted acid (*R*)-TRIP, can provide both enantiomers of β-amino carbonyl compounds.



OR16 Development of diazepane carboxylate organocatalysts for asymmetric Cope rearrangement

Dainis Kaldre*, James L. Gleason, Department of Chemistry, McGill University, Montreal, Quebec, H3A 2K6, dainis.kaldre@mail.mcgill.ca

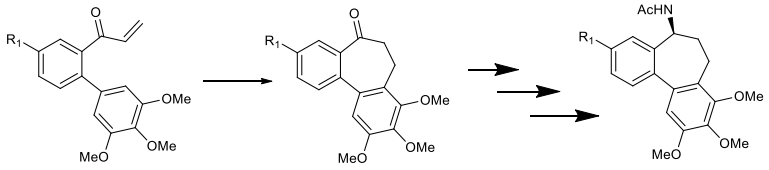
[3,3]-Sigmatropic rearrangements, particularly the Claisen and Cope rearrangements, have been extensively applied in organic synthesis. These reactions can generate two stereocenters in a single reaction that typically passes through a highly ordered transition state. Since their discovery, several metal and Lewis acid catalyzed variants have been developed. However, only a few organocatalyzed sigmatropic rearrangements are known. We have developed an organocatalyzed Cope rearrangement using diazepane carboxylate catalyst **1**, that shows remarkable rate acceleration compared to the simple thermal rearrangement. Subsequent studies have shown that organocatalysts of general structure **2**, can be used in a catalytic asymmetric Cope rearrangement. These studies have also revealed, that catalysts **1** and **2** are efficient in forming α-substituted iminium ions, and are currently being applied to Diels-Alder cycloadditions and Michael additions.



OR17 An enantioselective formal synthesis of '*iso'* NSC 51046 allocolchicine and related analogues via catalytic conjugate addition reactions

Mariam Mehdi, Sinisa Djurdjevic and James R. Green*, Department of Chemistry and Biochemistry, University of Windsor, Windsor, ON, N9B 3P4, jgreen@uwindsor.ca

The A-ring isomeric allocolchicine analogue, referred to as 'iso' NSC 51046 **(1a),** which was previously synthesized by intramolecular Nicholas reaction chemistry, has been shown to induce pro-death autophagy in pancreatic cancer cells and E6-1 leukemia cells without apparent affect on normal human fibroblasts. We have sought alternative methods for the synthesis of this compound and related analogues using catalytic conjugate addition reaction for the preparation of dibenzocycloheptane unit of these allocolchicines. The optimization studies and the scope of this methodology will also be addressed in this work.

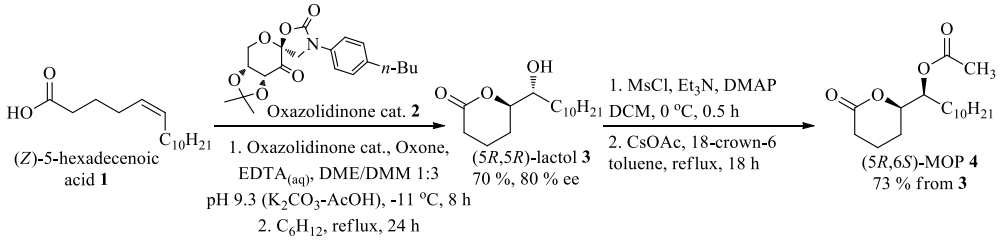


(1a), R_1 = OMe

OR18 Racemic and enantioselective total syntheses of mosquito oviposition pheromone from a naturally available unsaturated fatty acid

David Hurem, Travis Dudding*, Department of Chemistry, Brock University, St. Catharines, ON, L2S 3A1, tdudding@brocku.ca

Mosquito Oviposition Pheromone (MOP) is a potent oviposition attractant of gravid *Culex sp*. mosquitos. As part of our focus on asymmetric catalysis for the synthesis of natural products, we have developed a synthetic route to MOP from **1**. The key **3** intermediate was obtained in enantioenriched form *via* Shi's epoxidation, employing catalyst **2**. Alternatively, racemic *threo*-lactol was obtained using a lipase-mediated Prilezhaev epoxidation under mild oxidative conditions.[1] The desired relative geometry of the target **4** was obtained using a mesylation-substitution sequence. A dynamic kinetic transformation was attempted to set the desired relative geometry in the final product, however conversion of starting material was limited to ~30 % and lead primarily to the accumulation of a ketone intermediate that was suspected to function as a lipase inhibitor.



1. Hurem, D.; Dudding, T. *RSC Adv.* **2014**, *5*, 15552.

P01 Advanced strategies for efficient macrocyclic Cu(I)-catalyzed cycloaddition of azides

Bédard, A.-C. and Collins, S. K.,* Department of Chemistry, Center for Green Chemistry and Catalysis, University of Montreal, Montreal, QC, H3T 1J4, shawn.collins@umontreal.ca

The copper-catalyzed azide–alkyne cycloaddition reaction has become an important synthetic strategy for the preparation of macrocycles, particularly in medicinal chemistry, where the triazole can act as an amide isostere. Despite the wealth of applications, most macrocyclic CuAAC reactions still suffer from the slow rate of ring closing associated with conventional macrocyclization reactions. Consequently, long reaction times and high catalyst loadings can be required to obtain practical and efficient macrocyclization. We report the development of an efficient macrocyclic Cu(I)-catalyzed azide-iodoalkyne cycloaddition process that can be performed at relatively high concentrations using a phase separation strategy. Application of this reaction to continuous flow synthesis will be presented.

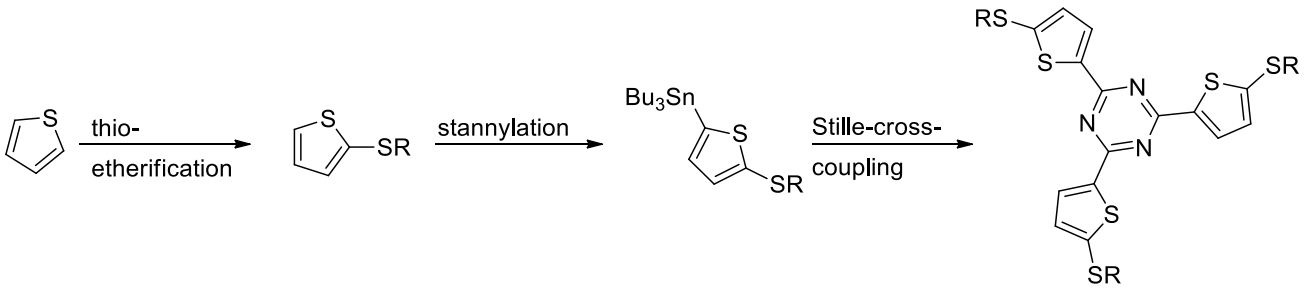
First demonstration of a macrocyclic CuAiAC process
Retained wide functional group tolerance, Catalytic copper
Simple experimental set-up/Relatively high concentrations
New sites for further functionalization

Bédard, A.-C., Collins, S. K.; *Org. Lett.* **2014**, *ASAP*. (10.1021/ol502415a)

P02 Synthesis of triazines trisubstituted with 2-alkylthiothiophenes

Vanessa Bellemore, Hi Taing, S. Holger Eichhorn*, Department of Chemistry and Biochemistry, University of Windsor, Windsor, ON, N9B 3P4, eichhorn@uwindsor.ca

Triazines substituted with three 5-membered ring heterocycles are interesting core structures for the preparation of dyes and self-organizing organic semiconductors because of their co-planar and donor-acceptor structures.[1,2,3] Presented here is the synthesis of 1,3,5-triazine substituted with 2-alkylthiothiophenes. The alkylthiothiophene is generated from thiophene in a one-pot two-step approach, stannylated, and finally cross coupled to cyanuric chloride *via* Stille-coupling. Also reported are the thermal and optical properties of the new donor-acceptor triazine derivatives.

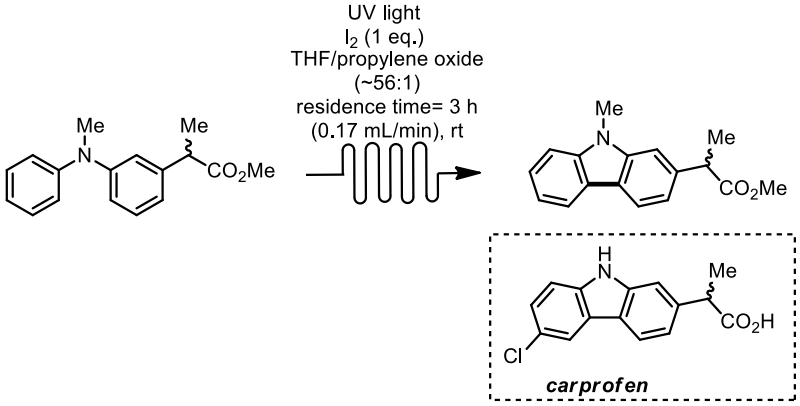


1) Misra, R. et al. *Tetrahedron.* **2013***, 54*, 5399-5402. 2) Weissberger, A. et al., *The Chemistry of Heterocyclic Compound.,* **1985**, *Part 1,* 151-165. 3) Liu, J. et al.*, Material Matters.* **2014**.

P03 U.V. Light mediated synthesis of carbazole: application of a U.V. reactor toward the construction of a carprofen analog.

Antoine Caron, Augusto César Hernandez Perez, Shawn K. Collins*, Department of Chemistry, University of Montreal, Montreal, Quebec, H3C 3J7,shawn.collins@umontreal.ca

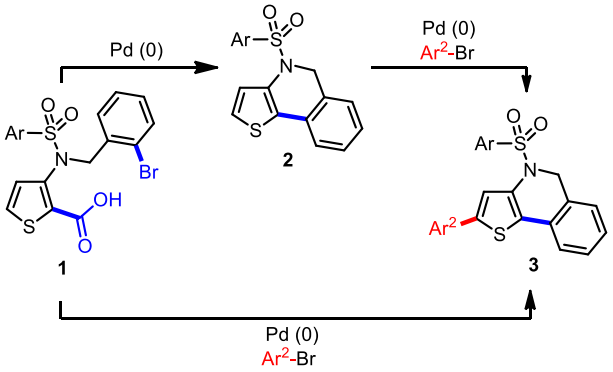
A continuous flow UV light reactor has been constructed using commercially available equipment, and its efficiency was demonstrated by performing a photocyclodehydrogenation reaction to prepare carbazole derivatives of the drug carprofen.



P04 Efficient access to thienoisoquinoline scaffolds: one-pot tandem palladium-mediated decarboxylative arylation and C-H activation.

Fei Chen, Nicolas Wong and Pat Forgione*, Department of Chemistry & Biochemistry, Concordia University, Montréal, QC, H4B 1R6 and Centre in Green Chemistry and Catalysis, Montreal, QC pat.forgione@concordia.ca

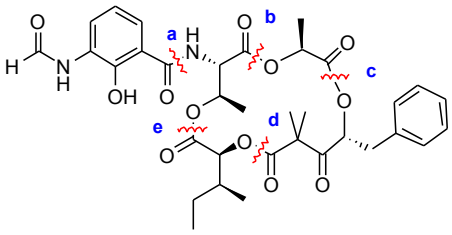
In 2006, Wyeth patented thienoisoquinoline scaffolds (**3**) that have potential therapeutic for inflammatory associated diseases. The reported synthetic pathway has an overall yield of 6% and involves 2 Suzuki reactions which requires pre-functionalization of starting materials and organoborons as coupling partners. We herein demonstrate an alternative five-step synthetic approach to the scaffolds. Our approach used the environmental friendly and more sustainable Pd-catalyzed decarboxylative coupling (**1**→**2**) and C-H activation (**2**→**3**). Furthermore, we were able to telescope the two palladium-catalyzed reactions into one-pot (**1**→**3**) to make our method even more efficient (35% ~ 63%) and straightforward. Preliminary mechanistic study on the regioselectivity of the thiophene C-H activation illuminates a competition between intra- and inter-molecular arylations.[1]



1 Chen, F.; Wong, N. W. Y.; Forgione, P.* *Adv. Synth. Catal.* **2014**, *356*, 1725–1730.

P05 Progress towards the chemical synthesis of prunustatin A.

Maja Wanda Chojnacka, Robert Alexander Batey*, Department of Chemistry, University of Toronto, Toronto, ON, M5S 3H6, rbatey@chem.utoronto.ca



Prunustatin A - key disconnections

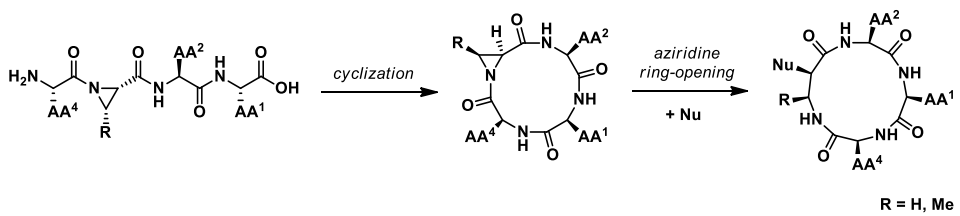
Prunustatin is a natural product that was recently isolated in small quantities from a fermentation broth from bacterial species *Streptomyces violaceoniger* and identified as a potent anticancer agent.[1] It displays low nanomolar activity against human fibrosarcoma - bone or soft tissue tumor. This natural product is not only a promising anticancer agent, but also an interesting and challenging synthetic target. Prunustatin may be synthesized through the amide coupling of the aromatic fragment (blastmycin head group) with the core macrocyclic structure (disconnection *a*). The synthetic strategy for the synthesis of the macrocycle is based on several ester bond disconnections *b*-*e* leading to four key fragments: two alpha-hydroxy acids, threonine, and an unusual beta-keto-gamma-hydroxy acid residue. The development of new methods to selectively synthesize the fragments will be discussed. Subsequent application of these methods towards the total synthesis of prunustatin will be presented.

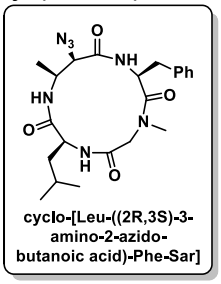
1. Umeda, Y.; Chijiwa, S.; Furihata, K.; Furihata, K.; Sakuda, S.; Nagasawa, H.; Watanabe, H.; Shin-ya, K. *J. Antibiot.* **2005**, *58*, 206-209

P06 The synthesis and regioselectivity of ring-opening of aziridine-containing cyclic tetrapeptides

Benjamin K. W. Chung, Christopher J. White, Conor C. G. Scully, Andrei K. Yudin* Department of Chemistry, University of Toronto, Toronto, ON, M5S 3H6, ayudin@chem.utoronto.ca

Aziridine-containing cyclic tetrapeptides represent an interesting class of substrates for highly regioselective aziridine ring-opening, yielding unexpected 13-membered $\alpha_3\beta$ macrocycles. The preparation of linear precursors on solid-phase using *N*-Fmoc-aziridine-2-carboxylic acids, as well as their cyclization and aziridine ring-opening will be presented. One azide-functionalized substrate, cyclo-[Leu-((2R,3S)-3-amino-2-azido-butanoic acid-Phe-Sar], exists in two distinct conformations, indicating a degree of flexibility in these systems. Structural elucidation via 2D NMR has demonstrated that the major conformation contains a *cis*-amide between the Phe/Sar residues, while the minor conformation is in an all-*trans* conformation. The rate of conformational exchange was determined using 2D Exchange Spectroscopy (EXSY) NMR.





1. White, C. J.; Yudin, A. K. *Org. Lett.* **2012**, *14*, 2898-2901.

P07 A more efficient reducing agent for the formation of Fab' antibody fragments

Victor Crivianu-Gaita, Alex Romaschin, and Michael Thompson*, Department of Chemistry, University of Toronto, Toronto, ON, M5S 3H6, victor.crivianu.gaita@mail.utoronto.ca

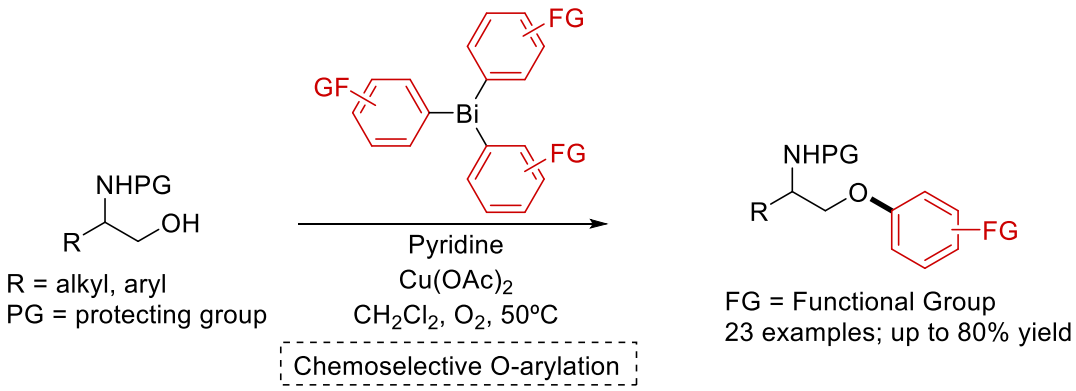
Antibodies are natural peptides produced by human bodies and many other living organisms. Application of these molecules ranges from cancer drug therapies all the way to biosensor coatings. A standard procedure for cleaving immunoglobin G antibodies involves a primary cleavage with the enzyme pepsin. This will produce an $F(ab)_2$ unit, cleaved below two important disulfide linkages in the hinge region of the antibody.
Currently, the most efficient reducing agent that will cleave an $F(ab)_2$ dimer into two Fab' fragments is dithiothreitol (DTT).[1] Reduction of the dimer over 90 minutes yields a conversion efficiency of approximately 55%. In this study, we describe a comparative analysis of the reducing capabilities of dithiobutylamine (DTBA) compared to DTT on $F(ab)_2$ dimers. The results of the study indicate that DTBA is significantly more efficient in the reduction of $F(ab)_2$ dimers – at 90 minutes, roughly 99% of the dimers have been reduced to Fab' monomer fragments.

1. Lu,* B.; Xie, J.; Lu, C.; Wu, C.; Wei, Y. *Anal. Chem.* **1995**, *67*, 83-87.

P08 Copper-catalysed *O*-arylation of *N*-protected 1,2-aminoalcohols using highly functionalized organobismuth reagents

Julien Dansereau, Pauline Petiot, Imene Khene, Tabinda Ahmad, Samira Saamali, Maxime Leroy, Francis Pinsonneault, Claude Y. Legault et Alexandre Gagnon*, Département de chimie, Université du Québec à Montréal, Montréal, Qc, H3C 3P8, gagnon.alexandre@uqam.ca

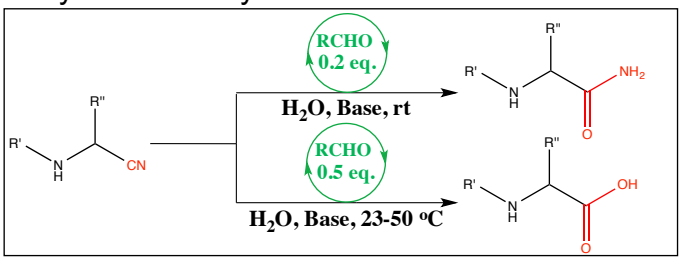
The *O*-arylation of 1,2-aminoalcohols using functionalized triarylbismuth reagents is reported. The reaction is promoted by substoichiometric amounts of copper acetate and operates under mild conditions. Good functional group tolerance is observed, giving access to a range of β-aryloxyamines. The accelerating effect provided by the amino group in the arylation reaction is investigated.



P09 Exploiting intramolecularity: Efficient catalytic hydrolysis of α-aminonitriles and α-aminoamides

Josh Derasp, Sampada Chitale, Bashir Hussain, Kashif Tanveer, Menachem Benzaquen, André M. Beauchemin* Dept of Chemistry, University of Ottawa, Ottawa, ON, K1N 6N5, jdera088@uOttawa.ca

Temporary intramolecularity is a powerful tool to achieve significant increases in reaction rates relative to intermolecular reactions (ca. 10^4 - 10^8).[1] We have demonstrated that the hydrolysis of α-aminonitriles can be achieved with simple carbonyl compounds as catalysts exploiting temporary intramolecularity. Use of 10-20 mol% of carbonyl compounds, specifically formaldehyde and glycolaldehyde, under basic conditions proved to have broad applicability and functional group tolerance. This was further developed to access α-aminoacids by the hydrolysis of the α-aminoamides using sub-stoichiometric quantities of the carbonyl catalyst. This work includes a rare study on the catalytic efficiency of carbohydrates, and shows that simple aldehydes, which are at the basis of chemical evolution, are *efficient* organocatalysts mimicking the function of hydrolase enzymes.

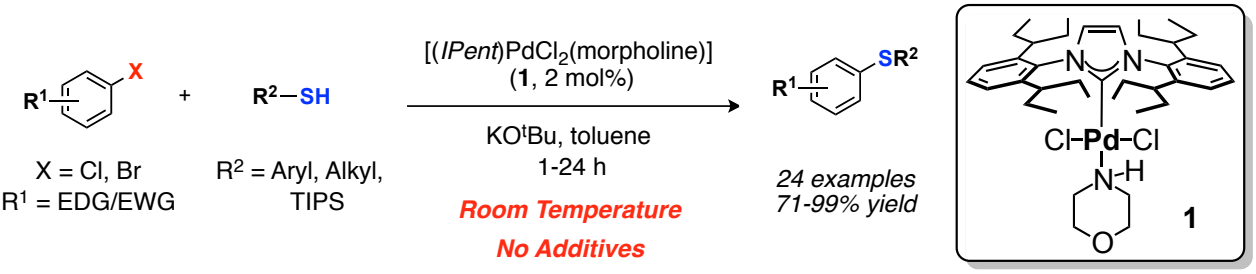


1. For a review, see: Tan, K.L. *ACS catalysis* **2011**, *1*, 877.

P10 [(IPent)PdCl$_2$(morpholine)]: A readily activated precatalyst for room-temperature, additive-free carbon–sulfur coupling

Jennifer L. Farmer, Matthew Pompeo, Alan J. Lough, Michael G. Organ*, Chemistry, York University, Toronto, ON, M3J 1P3, organ@yorku.ca

A series of new, easily activated NHC-Pd^{II} pre-catalysts featuring a trans-oriented morpholine ligand were prepared and evaluated for activity in carbon-sulfur cross-coupling chemistry. (*IPent*)PdCl$_2$(morpholine) (**1**) was identified as the most active pre-catalyst and was shown to effectively couple a wide variety of deactivated aryl halides with both aryl and alkyl thiols at, or near ambient temperature, without the need for additives, external activators, or pre-activation steps. Mechanistic studies revealed that, in contrast to other common NHC-Pd^{II} pre-catalysts, these complexes are rapidly reduced to the active NHC-Pd^0 species at ambient temperature in the presence of KO*t*Bu, thus avoiding the formation of deleterious off-cycle Pd^{II}-thiolate resting states.[1]

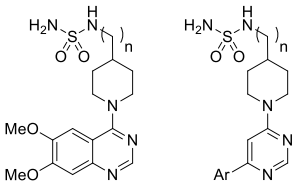


1. Farmer, J. L.; Pompeo, M.; Lough, A. J.; Organ, M. G. *Chem. Eur. J.* **2014**. (Just Accepted).

P11 Synthesis and *in vitro* activity of ectonucleotide pyrophosphatase/phosphodiesterase-1 inhibitors

Elsa Forcellini, Elnur Elyar Shayhidin, Marie-Chloé Boulanger, Ablajan Mahmut, Carole-Anne Lefevbre, Sophie Boutin, Xavier Barbeau, Patrick Lagüe, Patrick Mathieu* and Jean-François Paquin* Département de chimie, Université Laval, Québec, QC, G1V 0A6, jean-francois.paquin@chm.ulaval.ca

Calcific aortic valve disease (CAVD) is the most common heart valve disorder in United States and Western Europe. Thus far, there is no medical treatment to prevent the mineralization of aortic valves, only valve replacement when illness patient is far advanced.[1] Recent studies have shown that an increase of expression and enzymatic activity of ectonucleotide pyrophosphatase/phosphodiesterase-1 (ENPP-1) promotes mineralization process of aortic valve. In this context, ENPP-1 inhibition represents a major challenge. Herein, we will describe the synthesis of two categories of potential inhibitors in addition to their *in vitro* activity.[2]



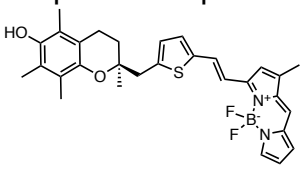
(1) Mathieu, P. *et al. J. Mol. Cell. Cardiol.* **2012**, *52,* 1191.
(2) Mathieu, P. *et al. Submitted.*

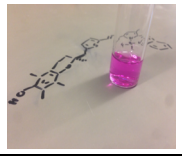
P12 Second generation of BODIPY-vitamin E: Synthesis and α-TTP binding studies of α-tocopherol-thienyl-ene-BODIPY

Mikel Ghelfi, Jeffrey Atkinson*, Department of Chemistry, Brock University, St.Catharines, Ontario, L2S 3A1, mikel.ghelfi@bluewin.ch

Vitamin E describes eight lipid soluble anti-oxidant molecules, the tocopeherols and tocotrienols. The main function of these compounds is the protection of the mammalian cell membrane by radical scavenging.
The mammalian body depends on external sources for vitamin E. After digestion, the vitamin E vitamer α–tocopherol is specifically transported from the liver into the cell membrane by a protein called α-tocopherol transfer protein (αTTP). Our group has designed fluorescent α-tocopherol derivatives to track the vitamin E transport by fluorescent microscopy in cells.

Our collaborators at Pittsburg University have recently found that vitamin E has important protective functions from peroxidative damage in mice brains. Neuronal- and brain dysfunctions have been observed in mice lacking vitamin E. For further brain studies, a novel fluorescent α-tocopherol analogue was synthesized with a higher fluorescents wavelength for deeper tissue penetration, which has shown a high specific affinity to αTTP.

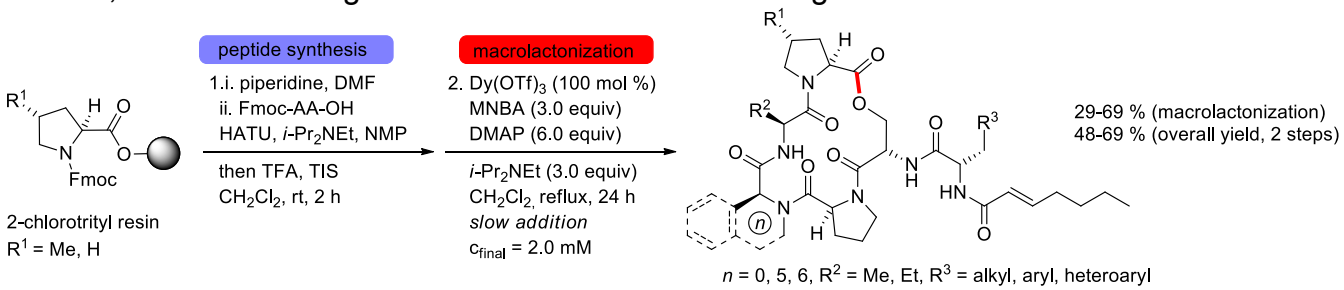




P13 Rapid synthesis of antibacterial A54556 acyldepsipeptide analogues using a two-step protocol employing solid phase peptide synthesis and a lanthanide-assisted macrolactonization reaction.

Jordan D. Goodreid, Eduardo Dos Santos, Robert A. Batey*, Department of Chemistry, University of Toronto, Toronto, ON, M5S 3H6, rbatey@chem.utoronto.ca

The A54556 acyldepsipeptides (ADEPs) comprise a small family of peptide-based natural products which have been found to exhibit potent antibacterial activity in the treatment of highly resistant gram-positive strains.[1] In recent years, these natural products (as well as related analogues) have gained widespread attention owing to their unprecedented antibacterial mechanism of action which targets a bacterial serine protease, ClpP. We have recently developed an efficient two-step protocol for the synthesis of ADEP analogues which utilizes a combination of solid and solution phase chemistry. Optimization of the macrolactonization method, as well as biological evaluation of different analogues will be discussed.



[1] Goodreid, J. D.; Wong, K.; Leung, E.; McCaw, S. E; Gray-Owen, S. D.; Lough, A.; Houry, W. A.; Batey, R. A. *J. Nat. Prod.* **2014**, *77*, 2170–2181 and references therein.

P14 Design and synthesis of type III pantothenate kinase inhibitors as potential antibacterial agents

Jinming Guan, Karine Auclair* Department of Chemistry, McGill University, Montreal, QC, H3A 0B8, karine.auclair@mcgill.ca

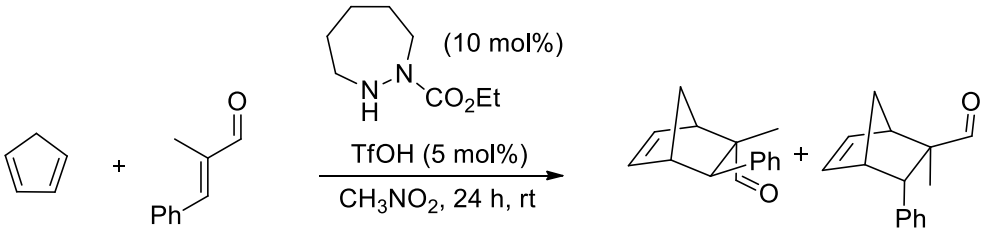
Pantothenate kinase (PanK), the enzyme catalyzing the phosphorylation of pantothenate using ATP, is the rate-limiting enzyme in the coenzyme A biosynthetic pathway. It has recently been suggested as a potential new target for developing antimicrobial drugs. For example, compounds that are substrates of type I PanK, such as pantothenamides, often inhibit the growth of *Escherichia coli*, while some inhibitors of type II PanK have an antibacterial activity towards *Staphylococcus aureus*. None of these molecules however have any effect on the growth of bacteria harboring only type III PanK. In fact no inhibitors or even alternate substrates have been reported for type III PanK. We will summarize our recent efforts to design inhibitors of *Pseudomonas aeruginosa* type III PanK.

P15 Diazepane carboxylate catalyzed Diels-Alder reactions of *α*-branched *α,β*-unsaturated aldehydes

Nicklas O.Häggman, Benjamin Zank, Dainis Kaldre and James L. Gleason*. Department of Chemistry, McGill University, Montreal, QC, H3A 0B8, jim.gleason@mcgill.ca

The Diels-Alder reaction is one of the most utilized reactions in organic chemistry and the iminium catalyzed Diels-Alder reaction of *α,β*-unsubstituted aldehydes, has been well studied. However, these catalysts typically are not compatible with *α*-branched aldehydes, most likely due to increased steric hindrance preventing iminium formation.

We have developed a 1,2-diazepane-carboxylate catalyst which together with an acid co-catalyst efficiently catalyzes the cycloaddition of sterically encumbered aldehydes. Use of this catalytic method provides high yields, great *exo*-selectivity and a wide substrate scope, exemplified by its ability to perform novel Diels-Alder reactions, such as *α*-methylcinnamaldehyde with cyclopentadiene (see figure). Chiral versions of the catalyst are currently under investigation and show promising preliminary results.



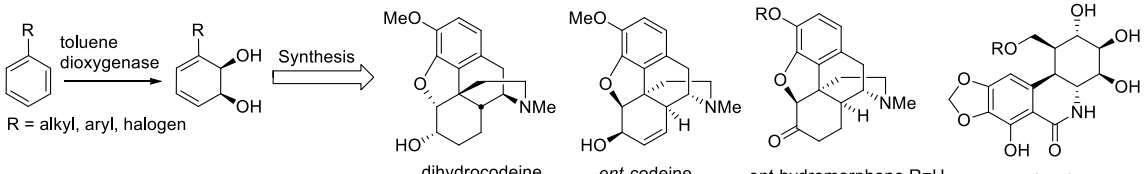
92% yield, 1:15 *endo:exo*

P16 Program in chemoenzymatic synthesis in the Hudlický group

John J. Hayward and Tomáš Hudlicky,* Department of Chemistry and Centre of Biotechnology, Brock University, 500 Glenridge Ave, St Catharines, ON L2S 3A1,

ABSTRACT –

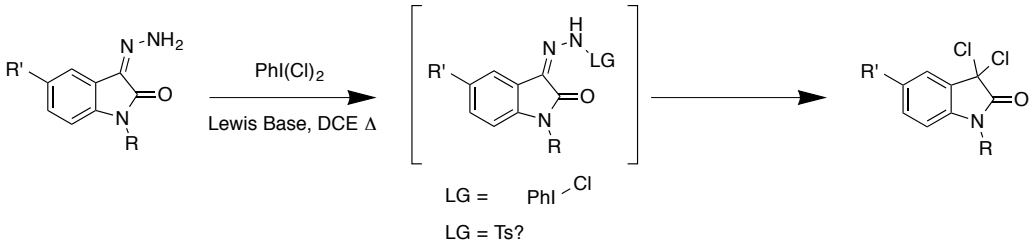
Current projects in the Hudlický research group involve the enzymatic dihydroxylation of aromatic compounds by a recombinant strain of *E. Coli* JM 109 (pDTG601A). Chirons derived from substituted aromatics are used in the total syntheses of the morphine alkaloids, idesolide, chiral polymers and aza-sugars, the synthesis of analogues of pancratistatin, and studies toward the total synthesis of vinca alkaloids and tetrodotoxin.



P17 α,α-Dihalogenation of 3-tosylhydrazonoxindole derivatives using aryl-λ^3-iodanes

Charlotte Hepples, Keith Coffey and Graham Murphy*, Department of Chemistry, University of Waterloo, Waterloo, ON, N2L 3G1, gkmurphy@uwaterloo.ca, chepples@uwaterloo.ca

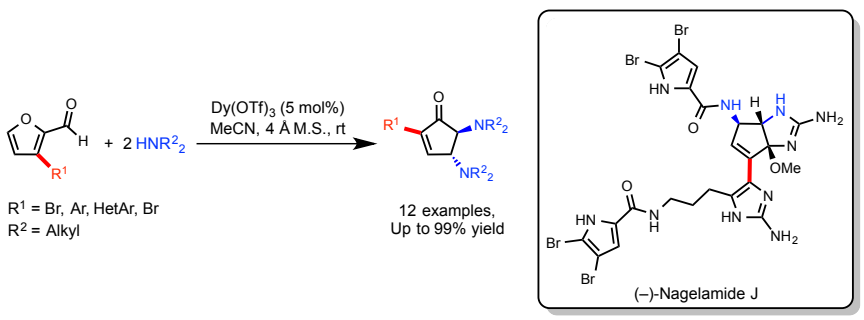
Hypervalent iodine reagents have been well documented in α-functionalization reactions of carbonyl compounds. Previously our group has shown that hypervalent iodine reagents are able to chemoselectively transfer ligands to diazo compounds, or their precursors, producing *gem*-dihalogenated products. This chemistry has been used to prepare a variety of 3,3-dihalogenated oxindole derivatives; an important class of biologically active compounds. Diazo- or hydrazone-bearing oxindoles were chlorinated through a deoxygenative chlorination method. Based on our proposed mechanism for this transformation, we believe a tosyl hydrazone to also be a suitable halogenation precursor. These would allow for shelf-stable alternatives to diazo compounds for use in functionalization chemistry, and may prove to be a useful alternative to the deoxygenative halogenation reaction. The development of this chemistry will be discussed.



P18 Synthetic studies of *trans*-4,5-diaminocyclopent-2-enones: Toward Nagelamide J.

Afton Hiscox, Kauan Ribeiro, and Robert A. Batey*, Department of Chemistry, University of Toronto, Toronto, ON, M5S 3H6, rbatey@chem.utoronto.ca

Our group recently reported the formation of 4,5-diaminocyclopent-2-enones from the mild, Lewis acid-catalyzed reaction of furfural and secondary amines. This rearrangement proceeds via a domino condensation/ring-opening/4π conrotatory electrocyclization, and gives rise to exclusively the *trans* diastereomer of the product.[1] This reaction served as the key step in our recent total synthesis of (±)-agelastatin A by forming the *trans*-diaminocyclopentane core of the natural product.[2] Herein we present our efforts to expand the scope of this methodology. We describe the synthesis of substituted *trans*-4,5-diaminocyclopent-2-enones from substituted 2-furaldehydes, as well as our strategy to access nagelamide J using this chemistry.



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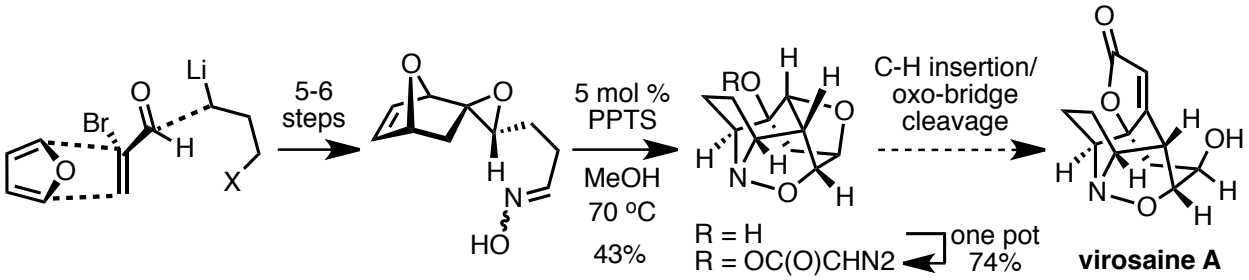
P19 A concise approach to Virosaine A using a cascade epoxide opening/nitrone cycloaddition sequence

Jonathan M. E. Hughes, James L. Gleason* Department of Chemistry, McGill University, Montreal, QC, H3A 0B8, jim.gleason@mcgill.ca

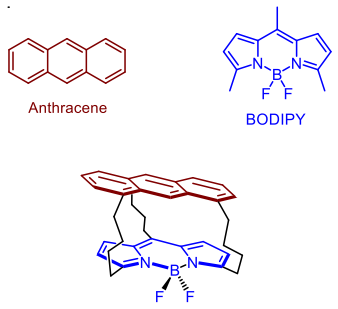
Securinega alkaloids are a small but varied class of natural products that have been associated with a number of biological activities. Virosaine A (isolated in 2012) contains the most highly caged skeleton of all the *Securinega* alkaloids. We report our efforts in developing a concise synthesis of virosaine A. Key features include *in situ* organolithium trapping of the sensitive *exo*-Diels-Alder adduct of furan and 2-bromoacrolein and an acid-catalyzed epoxide opening (via intramolecular oxime *N*-alkylation)/nitrone cycloaddition cascade. In this manner, our approach enables rapid access to the complex virosaine skeleton. Optimization of the route and efforts to employ a late-stage intramolecular C-H insertion/oxo-bridge cleavage to install the butenolide functionality will be discussed.



P20 Towards novel BODIPY cyclophanes for advanced materials applications

Burhan A. Hussein, Bryan D. Koivisto*, Department of Chemistry and Biology, Ryerson University, Toronto, Ontario, M5B 2K3, bryan.koivisto@ryerson.ca

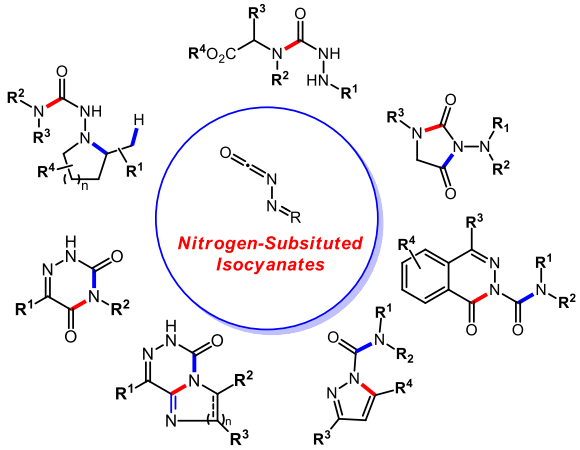
4,4-difluoro-4-bora-3a-4a-diaza-*s*-indacenes (BODIPYs) have been incorporated into a wide variety of advanced material applications due to their highly desirable properties, such as high absorption coefficients, sharp emission peaks exhibiting high quantum yields, and chemical stability under a wide range of conditions. This has led to materials that can be used for chemosensers, biological labeling agents, fluorescent switches, laser dyes, and organic sensitizers. This paper explores the synthesis of a novel cyclophane consisting of BODIPY and anthracene moieties designed to facilitate the study of these confined intramolecular π stacking effects.



P21 Nitrogen-substituted isocyanates in heteroaromactic chemistry: Synthesis of acyl pyrazoles and phthalazinones

Ryan Ivanovich, Jean-Francois Vincent-Rocan, André M. Beauchemin* Department of Chemistry & CCRI, University of Ottawa, Ottawa, ON, K1N 6N5, abeauche@uottawa.ca

Nitrogen-substituted isocyanates are a rare class of amphoteric building blocks with a synthetic potential that remains virtually untapped. These powerful intermediates can be generated *in situ* from bench-stable hydrazides and hydrazones. Recently, we have demonstrated that nucleophilic addition can be achieved under conditions that suppress dimerization, and yield different semi-carbazones.[1] Based on this, we reported the first cascade reactions using amino-isocyanates[2] and imino-isocyanates.[3] More recently, we have been interested in the synthesis of aromatic heterocycles using related reactivity. Latest results toward the synthesis of acyl pyrazoles and phthalazinones will be presented.

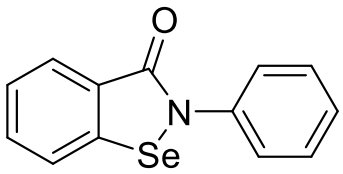


1: Garland, K.; Gan, W.; Depatie-Sicard, C.; Beauchemin, A. M. *Org. Lett.* **2013**, *15*, 4074-4077.
2: Clavette, C.; Vincent Rocan, J.-F.; Beauchemin, A. M. *Angew. Chem. Int. Ed.* **2013**, *52*, 12705-12708.
3: Vincent Rocan, J.-F, Clavette, C, Leckett, K. Manuscript submitted

P22 Investigation of reaction pathways toward the synthesis of ebselen and its derivatives

Vassilios Kanellis, Russell D. Viirre*,Chemistry and Biology , Ryerson, Toronto, ON M5B 2K3, rviirre@ryerson.ca

Ebselen is a synthetic selenium-containing organic compound that has been studied as a potential treatment for a number of conditions. Ebselen is an antioxidant, capable of scavenging peroxide and other reactive oxygen species. Our research is focused on the preparation of novel ebselen derivatives towards biologically active compounds with tunable redox properties and pharmacokinetics. Currently we are exploring different routes to synthesize ebselen, which are compatible with desired transformations of the ebselen scaffold including replacement of the phenyl group with different aryl or heteroaryl moieties as well as functional group substitution on the benzisoselenazolone ring. The pathways investigated include a recently published transition metal-mediated method[1] as well as a novel approach using isocyanates.

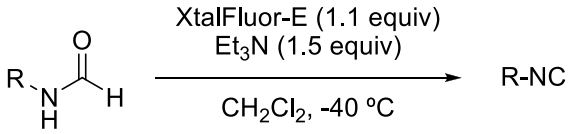


1.Balkrishna, S.J.; Bhakuni, B.S.; Chopra, D.; Kumar, S. *Org. Lett.*, **2010**, *12*(23), 5394-5397

P23 Synthesis of isocyanides through dehydration of formamides using XtalFluor-E

Massaba Keïta, Mathilde Vandamme, Olivier Mahé, Jean-François Paquin *, Département de chimie, Université Laval, Québec, QC, G1V 0A6, jean-francois.paquin@chm.ulaval.ca

Isocyanides (also called isonitriles) are key building blocks in organic synthesis.[1] They are well known for their use in Ugi reaction (or other multicomponent reactions), but they are also utilized in many other synthetic transformations and a few natural products contain this functionality. A straightforward approach for their preparation consists in the dehydration of formamide. Numerous reagents can affect this transformation. Unfortunately, some of these reagents are expensive and not available on large scale, in addition most are either hygroscopic, moisture sensitive, highly toxic or thermally unstable. Herein, we reported the formation of isocyanides from formamides using XtalFluor-E, $[Et_2NSF_2]BF_4$. A wide range of formamides can be used to produce the corresponding isocyanides in up to 99% yield. In a number of cases, the crude products showed good purity (generally >80% by NMR) allowing to be used directly in multi-components reactions.[2]



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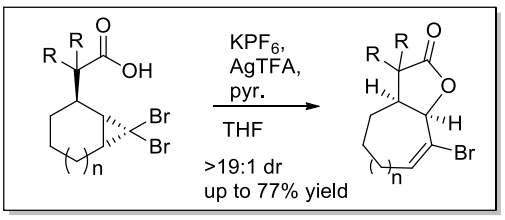
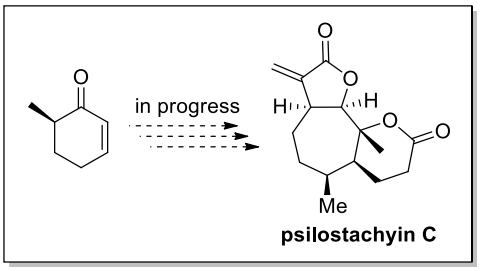
P24 Dibromocyclopropane opening/carboxylate trapping route for the sesquiterpene lactone natural products

Simon J. Kim; Robert A. Batey*, Department of Chemistry, University of Toronto, Toronto, Ontario, M5S 3H6. rbatey@chem.utoronto.ca

The sesquiterpene lactone natural products are medicinally relevant. For example, psilostachyin C enhances the anti-cancer activity of camptothecin. Therefore, we developed a highly diastereoselective route to these cores by dibromocyclopropane ring openings follow by carboxylate trappings. Current efforts are directed towards a total synthesis of psilostacyin C.

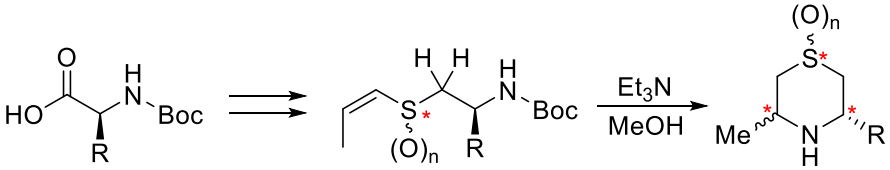




P25 A stereoselective study on the cyclization of 1-alkenyl β-aminoalkyl sulfoxides and sulfones

Monika R. Kulak, Tyler Mook, Stefan Söderman and Dr. Adrian Schwan* Department of Chemistry, University of Guelph, Guelph, ON, N1G2W1, schwan@uoguelph.ca

Research efforts focusing on organosulfur compounds have had wide implications in the understanding of organic synthetic reactions.[1] Nevertheless, there are still many areas to be studied, such as the stereoselectivity of cyclization of the cis forms of 1-alkenyl β-aminoalkyl sulfoxides and sulfones. The synthesis of this small family of compounds is proposed to take place through the manipulation of Boc-protected L-amino acids (**1**).The sulfoxide configuration may have an added effect on the stereoselectivity of the molecule. Hence, the given study is to explore the intramolecular cyclizations of *cis*-1-alkenyl β-aminoalkyl sulfoxides and sulfones (**2, 3**) in order to provide an insight into the stereochemistry of thiazine compounds. These products can have applications in medicinal chemistry.



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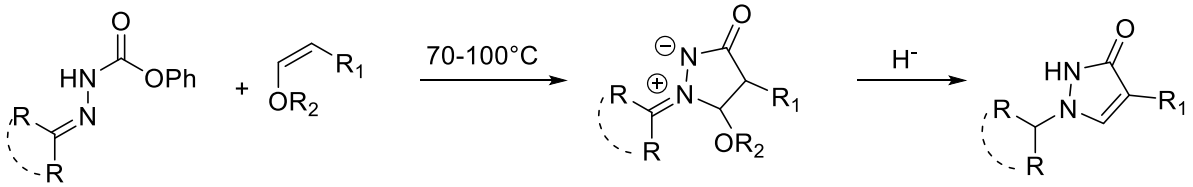
P26 Alkene aminocarbonylation with imino-isocyanates and derivatization into pyrazolones

Kaitlyn Lavergne, Amanda Bongers, André M. Beauchemin* Department of Chemistry, CCRI, University of Ottawa, Ottawa, Ontario, K1N 6N5, abeauche@uottawa.ca



Over the past few years, the Beauchemin group has been exploring reactivity of *N*-substituted isocyanates.[1] Our group recently developed a metal-free alkene aminocarbonylation with imino-isocyanates to form azomethine imines. Catalysis of this reaction using basic additives allowed milder reaction conditions with electron rich C=C bonds such as vinyl ethers. Efforts have also been made towards the derivatization of these azomethine imines into useful products. It was discovered that upon reduction and aromatization of azomethine imines, pyrazolones (Pharmaceuticals and agrochemicals) could be obtained providing a novel modular approach to these compounds. This reactivity was extended to include imino-isothiocyanates. Development efforts, reaction scope and preliminary results on aminothiocarbonylation will be discussed.

[1] Clavette, C.; Gan,W.; Bongers,A.; Markiewicz, T.; Toderian, A.; Gorelsky, S. I.; Beauchemin, A. M. *J. Am. Chem. Soc.* **2012**, *134*, 16111

P27 Multistage screening reveals a dual binding mode of thienopyrimidine bisphosphonates inhibitors of the human farnesyl pyrophosphate synthase and their remodeling to bind in an allosteric pocket

Chun Yuen Leung, Joris W. De Schutter, Jaeok Park, Yih-Shyan Lin, Zheping Hu, Albert M. Berghuis, and Youla S. Tsantrizos* Department of Chemistry, McGill University, Montreal, QC, H3A 0B8, Youla.Tsantrizos@mcgill.ca

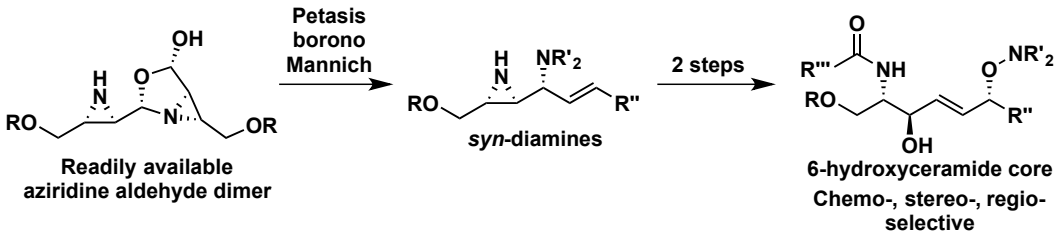
Human farnesyl pyrophosphate synthase (hFPPS) controls the post-translational prenylation of small GTPase proteins that are essential for cell signaling, cell proliferation, and osteoclast-mediated bone resorption. Inhibition of hFPPS is a clinically validated mechanism for the treatment of lytic bone diseases, including osteoporosis and cancer related bone metastases. Thienopyrimidine-based bisphosphonates (ThP-BPs) were previously identified as hFPPS inhibitors with low nanomolar potency.[1] A multistage screening protocol involving DSF, ITC, ^{1}H line broadening NMR, and X-ray crystallography revealed the dual binding mode of ThP-BPs to hFPPS. ThP-BPs were identified to bind to hFPPS in an allosteric pocket in the absence of the Mg^{2+} cofactor. Structural remodeling of these compounds led to the identification of a new monophosphonate chemotype that binds in an allosteric pocket of hFPPS.[2]

1. Leung, C.Y.; Park, J.; De Schutter, J.W.; Sebag, M.; Berghuis, A.M.; Tsantrizos*, Y.S. *J. Med. Chem.* **2013**, *56*, 7939-7950
2. De Schutter, J.W.; Park, J.; Leung, C.Y.; Gormley, P.; Lin, Y.-S.; Hu, Z.; Berghuis, A.; Poirier, J.; Tsantrizos*, Y.S. *J. Med. Chem.* **2014**, *57*, 5764-5776

P28 Stereocontrolled synthesis of 6-hydroxyceramide analogues from aziridine aldehyde dimers

Sean K. Liew, Andrei, K. Yudin*, Department of Chemistry, University of Toronto, Toronto, Ontario, M5S 3H6, ayudin@chem.utoronto.ca

6-hydroxyceramides, a class of sphingosine-derived lipids, were discovered in human skin in the 1990s, but their structure was confirmed only in 2003.[1] The exact role as well as the biosynthesis of these ceramides in the human body has yet to be elucidated. There are three reported total syntheses of the 6-hydroxyceramide scaffold, but all require extensive use of protecting groups to achieve chemoselectivity. The Yudin group's work on aziridine aldehyde dimers as chiral building blocks for synthesis has enabled the development of a chemo-, stereo-, and regio-selective synthesis of 6-hydroxyceramide analogues with minimal use of protecting groups. This presentation will outline our current progress towards these complex scaffolds using chiral *syn*-diamines derived from aziridine aldehyde dimers.[2]



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P29 Progress towards the total synthesis of Tedarene A

Marshall Lindner, Henri Delroisse, Thomas Malig, P. Nicholas Cooper, Adrian Schwan*, Chemistry Department, University of Guelph, Guelph, Ont., N1G 2W1

Tedarene A is a diarylheptanoid first isolated and characterized in 2012 from the marine sponge *Tedania ignis*. Featuring a diverse biological activity profile including antiprotozoal, antitumor, anti-inflammatory activities along with showing inhibitory effects on nitric oxide production, Tedarane A provides a synthetic challenge for the organic chemist.[1] Tedarene A is comprised of a diaryl ether bridge with a conjugated trans,cis-diene within the heptanoid system and features a chiral olefinic plane. Rapid ring flipping occurs so readily that isolation of pure enantiomeric atropisomers is difficult. The Schwan group is currently pursuing a total synthesis of Tedarene A with a synthetic scheme that involves a 1,3 sigmatropic rearrangement of a sulfinyl ester and a copper catalyzed Ullmann type biaryl ether coupling. Formation of the strained conjugated trans,cis- unsaturations will feature a Z-selective ring closing metathesis and a novel ozone friendly Ramberg-Backlünd protocol also developed by the Schwan group.[2]

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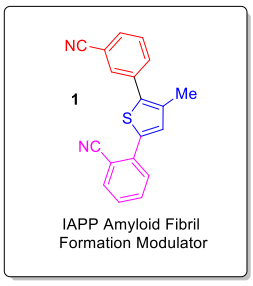
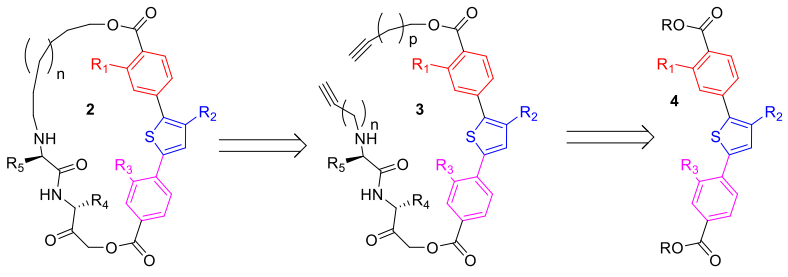
2 Söderman, S.C; Schwan, A.L. *Org. Chem.* **2012**, *77*, 10978-10984

P30 Design and synthesis of α-helical mimetic scaffolds for modulating protein-protein interactions

Daniel Mangel, Avid Hassanpour, Pat Forgione* Department of Chemistry and Biochemistry, Concordia University, Montreal, Quebec, H4B 1R6, pat.forgione@concordia.ca

Protein-protein interactions control the most important biological processes including signal transduction, metabolism, gene expression, cell cycle and apoptosis. It has been seen that a-helices play a key role in many of these interactions. Recently more attention has been given to modulating these interactions through the use of small molecule a-helix mimetic scaffolds. Towards this aim, we recently disclosed novel synthetic routes to target IAPP **(1)**.
We have designed pathways to macrocyclic aryl-substituted heteroaromatic scaffolds **(2)** through a palladium-catalyzed cross-couplings and macrocyclization strategy that support a range of diverse functional groups to target protein-protein interactions mediated through a-helical structures.





P31 Synthesis and study of intrinsic nucleobase quenchers

Augusto Matarazzo, Christie Ettles, Mckenry Charles, Mohamed Afifi, Robert H.E. Hudson* Department of Chemistry, Western University, London, ON, N6A 5B7, rhhudson@uwo.ca

Fluorescence quenchers are widely used in Förster resonance energy transfer (FRET) based molecular beacons to detect mutations within the human genome. Traditionally these quenchers are tethered to the end of an oligonucleotide strand because incorporating them in any other position will interfere with base pairing and thus decrease duplex stability.[1] The advantage of synthesizing a base pairing competent quencher is that it can be incorporated anywhere in an oligonucleotide strand and should not compromise duplex stability. Herein we report the synthesis and quenching studies of two novel intrinsic fluorescence quenchers, 5-(4-dimethylaminophenyl)azouridine and 6-{4-[(4-dimethylaminophenyl)azo]phenyl}pyrrolocytosine (DABCYLpC), that incorporate the key structural features of the universal quencher DABCYL. The key step in the synthesis of the azouridine was an azo coupling reaction between 5-diazouracil and *N,N*-dimethylaniline.[2] DABCYLpC was prepared in one pot via a Sonogashira reaction between a DABCYL modified alkyne and a suitably protected cytosine followed by a 5-endo-dig cyclization.[3] These quenchers will be further evaluated and optimized for use in molecular beacons as novel fluorescent probes.

1. Kramer, F.; Tyagi, S. *Nature Biotechnology.* **1996**, 14, 303.
2. Tsupak, E. B.; Shevchenko, M. A.; Tkachenko, Y. N.; Nazarov, D. A. *Russian Journal of Organic Chemistry.* **2002**, 38, 880.
3. Hudson, R. H. E.; Dambenieks, A. K.; Viirre, R. D.; *Synlett*. **2004**, 13, 2400.

P32 Prediction of μ-opioid receptor selectivity for β-Casomorphins using computational docking

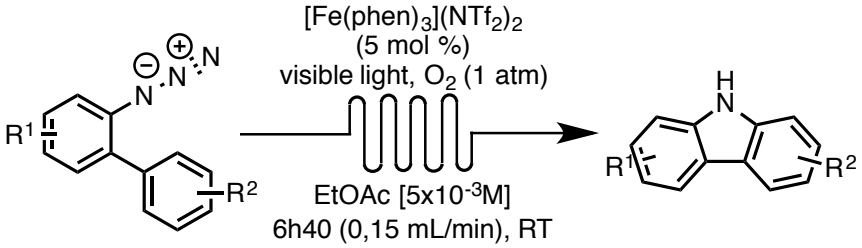
Christopher Oberc, Tony Yan, and Heather Gordon,* Department of Chemistry, Brock University, St. Catharines, Ontario, L2S 3A1, hgordon@brocku.ca

The opioid receptors were first identified in the 1960s. However it was not until 2012 that the crystal structures of these receptors were resolved. β-Casomorphins are peptide fragments of bovine milk protein that have been shown to bind to these receptors; preferentially to the μ receptor subtype. Using these crystal structures and the known binding affinity of β-casomorphins, computational docking experiments were carried out using GOLD to predict the conformation of β-casomorphins in the μ receptor and to determine the amino acids that account for the binding selectivity. While GOLD could differentiate binding affinities of rigid ligands used in control experiments, it could not differentiate binding affinities of highly flexible ligands such as β-casomorphins. Using a scoring approach based on individual amino acid, Glu229, Lys303 and Trp318 were found to be responsible for the binding selectivity of the β-casomorphins to the μ receptor.

P33 Photoredox catalysis employing Fe-based sensitizers: A visible-light-mediated synthesis of carbazoles

Shawn Parisien Collette, Augusto C. Hernandez-Perez, Shawn Collins*, Chemistry, University of Montréal, Montréal, Qc, H3T1J4, shawn.collins@umontreal.ca

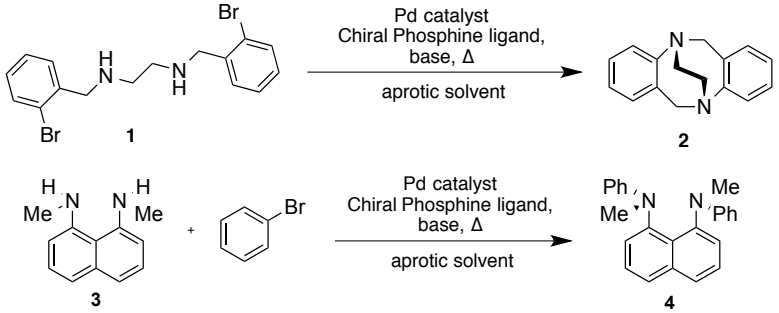
A photosynthetic preparation of carbazoles utilizing continuous flow, visible light, and a Fe-based sensitizer will be presented. The method is mild and efficient, affording a variety of carbazoles incorporating different substituents and heterocycles.



P34 Synthesis of candidate substrates for enantioselective Buchwald-Hartwig aminations.

Kevin Paul, Calvin Morier, Russell Viirre* Department of Chemistry & Biology, Ryerson University, Toronto, Ontario, M5B 2K3, rviirre@ryerson.ca

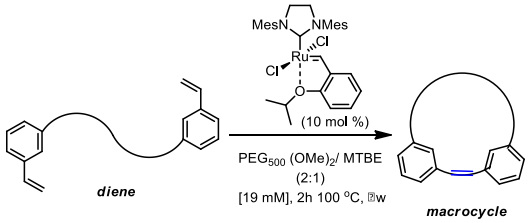
Enantioselective Buchwald-Hartwig amination will be pursued from bis(2-bromobenzyl)diamine and 1,8-bis(methylamino)naphthalene substrates synthesized from readily available starting materials. To achieve this, the substrate is reacted with various achiral Pd-phosphine complexes and bases in different solvents. Once the achiral reaction is optimized, an analogous enantioselective reaction will be undertaken with chiral phosphine ligands. This method has been used to desymmetrize malonamides. The enantiomeric products of these reactions could be used as asymmetric catalysts or selective non-nucleophilic bases. This work is part of an effort by the Viirre group to explore the underused potential of the Buchwald-Hartwig amination reaction in stereoselective synthesis.



P35 Macrocyclization at high concentrations: Phase separation applied to macrocyclic olefin metathesis

Michael Raymond, Michael Holtz-Mulholland, Shawn K. Collins*, Chemistry, Université de Montréal, Montréal, Québec, H3T 1J4, michael.raymond@umontreal.ca

Macrocycles are abundant in numerous chemical applications, however the traditional strategy for the preparation of these compounds remains cumbersome and environmentally damaging; involving tedious reaction set-ups and extremely dilute reaction media. Although a wide variety of synthetic strategies have been exploited for the synthesis of macrocycles, olefin metathesis has emerged as a preferential method for achieving cyclization due to the catalytic conditions, wide functional group tolerance and mild reaction conditions. The development of a macrocyclization strategy conducted at high concentrations is described which exploits phase separation of the catalyst and substrate, as a strategy to control dilution effects. A variety of macrocyclic skeletons could be prepared having either different alkyl, aryl or amino acids spacers. (1)



(1) Raymond, M.; Holtz-Mulholland, M.; Collins, S. K. *Chem. Eur. J.* **2014**, *20*, 12763-12767.

P36 Ring opening of tri-aryl substituted 5,6-dihydro-1,4-oxathiin S,S-dioxides

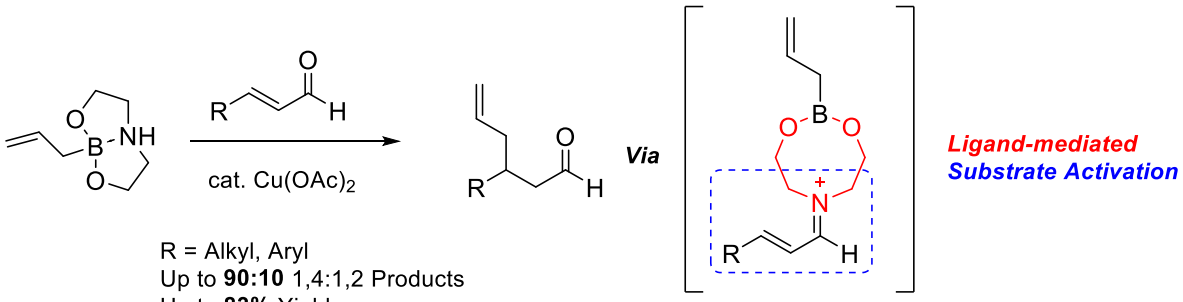
Erwin J. Remigio, Lilly U. Ho, Adrian L. Schwan*, Department of Chemistry, University of Guelph, Guelph, ON, N1G 2W1, schwan@uoguelph.ca

The Schwan group has recently communicated a proof-of-principle synthesis leading to aryl-substituted 5,6-dihydro-1,4-xathiin S,S-dioxides. Subsequent optimization of this chemistry has produced a library of oxathiins in yields up to 78%. However, the reaction creates a challenging separation problem, as it is accompanied with the formation of a β-keto sulfone by-product, predicted to arise from decomposition of the oxathiin in the reaction mixture. This presentation will outline the preparation of the oxathiins, whose purification was eventually achieved through a crystallization protocol. We will also outline methods to identify and fully characterize the β-keto sulfone by-product, which could also be formed independently through base induced decomposition of selected oxathiins. In addition, ring opened by-product was tested for conversion to an azathiin.

P37 Conjugate allylation of α,β-unsaturated aldehydes using air stable allyl diethanolamine boronate under Cu(II) catalysis

Pjotr C. Roest, Nicholas W. M. Michel and Robert A. Batey*, Department of Chemistry, University of Toronto, Toronto, ON, M5S 3H6, rbatey@chem.utoronto.ca

Despite recent advances in the field of conjugate additions, the conjugate allylation of α,β-unsaturated aldehydes remains a tremendous challenge. Classical methods of conjugate addition, including the Hosomi-Sakurai allylation and the use of organocuprates, have been shown to be ineffective for the conjugate allylation of aldehydes.[1] Considering the great versatility of the allyl group in organic synthesis, we have developed a novel method involving the Cu(II)-catalyzed conjugate addition of the air stable, crystalline allyl diethanolamine boronate. The proposed mechanism involves dissociation of the secondary amine from boron and subsequent iminium ion formation, followed by transmetalation and conjugate addition.



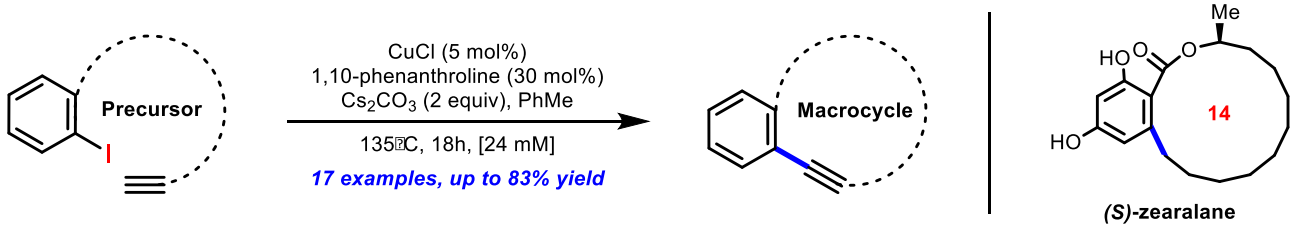
R = Alkyl, Aryl
Up to **90:10** 1,4:1,2 Products
Up to **83%** Yield

1. Majetich, G.; Casares A.; Chapman, D.; Behnke, M. *J. Org. Chem.*, **1986**, *51*, 1745–1753

P38 Cu(I)-Catalyzed macrocyclic Sonogashira-type cross-coupling protocol.

Jeffrey Santandrea, Anne-Catherine Bédard and Shawn K. Collins*, Département de Chimie, CGCC, Université de Montréal, Montréal, Québec, H3T 1J4, shawn.collins@umontreal.ca

Macrocyclic products are usually synthesized from a handful of known macrocyclization methods. Surprisingly, the Sonogashira coupling has yet to be a commonly used method to accomplish macrocyclizations, despite relatively mild reaction conditions. However, recent examples highlight the lack of practicality and effectiveness of this reaction on a large scale since significant amounts of palladium and stoichiometric amounts of copper in a dilute media are needed to afford benzolactones in poor yields. The development of a copper-catalyzed Sonogashira protocol performed at high-concentrations is described as an alternative to Pd-catalyzed methods to access a wider range of compounds and pharmaceutically relevant motifs such as polyketide-derived resorcylic acid lactones.[1]

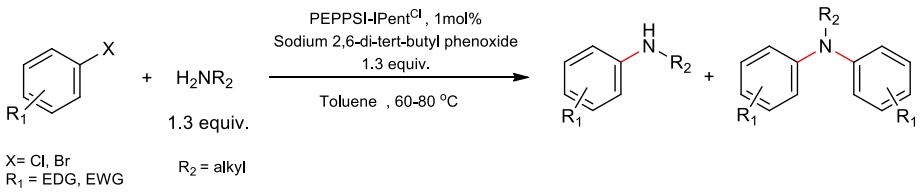


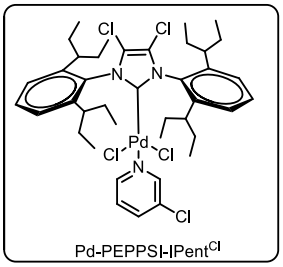
1. Santandrea, J.; Bédard, A.-C.; Collins, S. K. *Org. Lett.* **2014**, *16*, 3892-3895.

P39 Pd-PEPPSI-IPent^{Cl} in selective monoarylation of primary alkylamines

Sepideh Sharif, Richard Rucker, Michael G. Organ*, Chemistry, York University, Toronto, Ontario, M3J 1P3, organ@yorku.ca

The use of primary amines for the palladium catalyzed amination of aryl halides is often challenging as mixtures of both the secondary and tertiary anilines are often formed due to poor catalyst selectivity for the primary amine substrate over the secondary aniline product. Furthermore, the separation of these mixtures is often difficult and lowers the reaction's efficiency for producing the desired monoaryl amine. We now report that Pd-PEPPSI-IPent^{Cl}, a member of the Pd-PEPPSI pre-catalyst family, has shown high reactivity and good selectivity for this class of amination reaction through the use of sodium 2,6-di-tert-butyl phenoxide. The ability of this catalyst to affect the amination of 6- and 5-membered (hetero)aryl chlorides and bromides using simple and functionalized primary aliphatic amines is explored.



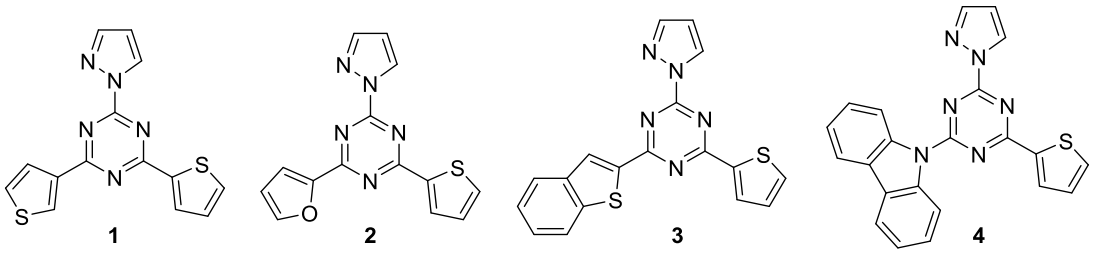


Pd-PEPPSI-IPent^{Cl}

P40 Low-symmetry triazines as new organic semiconductors and dyes

Hi Taing, Vanessa Bellemore and S. Holger Eichhorn* Department of Chemistry and Biochemistry, University of Windsor, Windsor, ON, N9B 3P4, eichhorn@uwindsor.ca

All previous studies on triazines substituted with 5-membered ring heterocycles have focused on symmetric derivatives that show high melting points and relatively low solubility. Presented here are low-symmetry triazines substituted with three different heteroaromatic groups (e.g. compounds **1** - **4**), which are potential organic semiconductors and dyes. Their synthesis involves the stepwise functionalization of each chlorine atom of cyanuric chloride with the heterocycle of interest via nucleophilic substitution or cross-coupling reactions. These planar compounds pack into columns in the crystalline state, are highly soluble, and melt well below 200 °C. HOMO-LUMO gaps may be reduced from about 3.7 eV to below 2.5 eV if strongly electron donating and accepting groups are attached.



P41 Organoboron catalyzed tandem ring opening and functionalization of epoxy alcohols

Kashif Tanveer and Mark S. Taylor*, Department of Chemistry, University of Toronto, Toronto, ON, M5S 3H4, mtaylor@chem.utoronto.ca

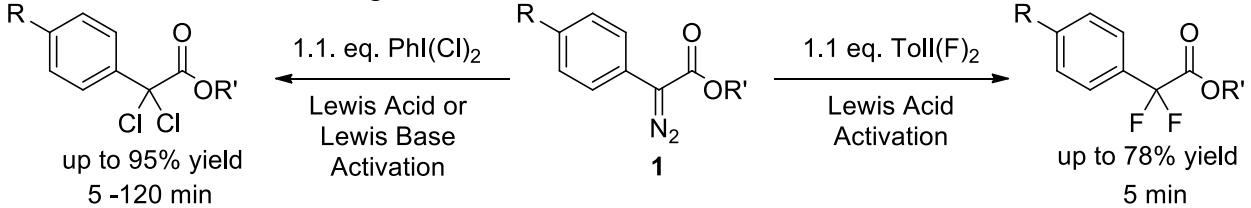
Epoxy alcohols are important synthetic intermediates that can be ring opened with a variety of nucleophiles. Selective manipulation of these intermediates requires regiocontrol in both the ring-opening step and the functionalization of the resulting diol. Our group has demonstrated that organoboron catalysts are capable of regioselective functionalization of polyols.[1] Building on this result, we now report the organoboron catalyzed tandem ring opening and functionalization of epoxy alcohols. The reaction proceeds in a stereospecific and regioselective manner, and enables rapid access to highly functionalized diol derivatives of potential utility for target-oriented synthesis.

1. Dimitrijević, E.; Taylor*, M.S. *ACS Catal.* **2013**, *3*, 945-962.

P42 Applications of hypervalent iodine reagents in synthesis: α,α-dihalogenation of carbonyl-containing compounds

Jason Tao, Graham Murphy*, Department of Chemistry, University of Waterloo, Waterloo, ON, N2J 3G1, gkmurphy@uwaterloo.ca, j3tao@uwaterloo.ca

While discovered over a century ago, new synthetic applications of hypervalent iodine (HVI) reagents are still being discovered today. Important types of reactions performed by HVI reagents include ligand transfer reactions, where a single carbon-(e.g., alkynyl or aryl) or heteroatom- (e.g., -Cl, -F, -OTs, -OAc) based group is transferred to a substrate per equivalent of iodane. Our research group found the reaction of (dihaloiodo)arenes ($PhI(Cl)_2$ and $TolI(F)_2$) and phenyldiazoester derivatives (**1**) transfers *both* halide ligands, affording geminally dihalogenated products. Initial studies found iodane-activation via Lewis acid (BF_3) or Lewis base catalysis (pyridine) was crucial for allowing these reactions to proceed rapidly with good yield/selectivity.[1] We have since began exploring the synthetic applications of these *gem*-difunctionalization methodologies. The results of these studies will be discussed.



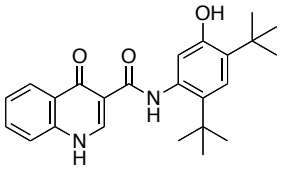
[1]Tao, J.; Tran, R.; Murphy, G.K. *J. Am. Chem. Soc.* **2013**, *135*, 16312-16315.

P43 Designing novel molecular probes for the treatment of Cystic Fibrosis

K. Toutah and R. D. Viirre*, Department of Chemistry and Biology, Ryerson University, Toronto, ON, M5B 2K3, <rviirre@ryerson.ca>

Cystic fibrosis is the most common fatal genetic disease affecting Canadian children and young adults. This chronic disease affects the aerodigestive tract by producing thick mucus, causing difficulty breathing and infections. Today, while all the available treatments for CF are only symptoms-based, a new compound called Ivacaftor has recently been developed and shows effectiveness in treating the underlying cause of the disease, genetic defects in a membrane protein: CFTR (Cystic Fibrosis Transmembrane conductance Regulator). Ivacaftor enhances channel opening, leading to improve lung function in mutated-CFTR CF patients. Unfortunately, Ivacaftor treats only 5% of CF patients. In order to design more broadly effective CF treatment, understanding the exact interactions between molecules like Ivacaftor and their binding site on the protein CFTR is essential.

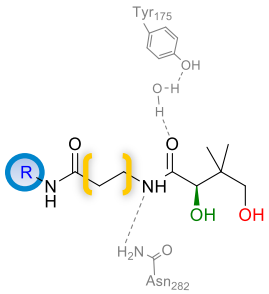
Toward this end, we are developing molecular probes based on Ivacaftor's structure which will enable unprecedented biochemical studies into the exact mode of action of drugs like Ivacaftor.



Ivacaftor

P44 Synthesis of pantothenamide mimics as potential antimicrobial agents activated by the coenzyme A pathway.

Elisa Tran, Annabelle Hoegl, Karine Auclair*, Department of Chemistry, McGill University, Montreal, Québec, H3A 0B8, Karine.auclair@mcgill.ca



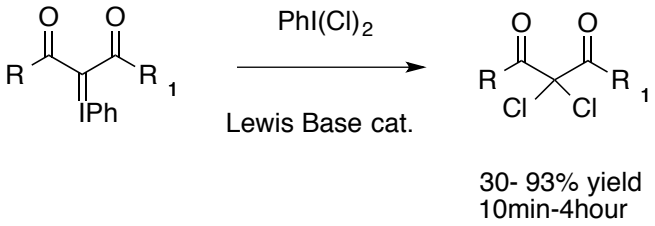
Antibiotics have been in use for decades to treat a range of infections caused by microorganisms. However, due to emerging drug resistance, the need for novel antimicrobial agents is crucial. Many members of the pantothenamide family of compounds show antibacterial and/or antiplasmodial activity.[1,2] A major focus of the Auclair group is to develop novel and more potent pantothenamide derivatives. The known mechanism of action for pantothenamides primarily involves transformation by the CoA biosynthetic enzymes to the corresponding CoA anti-metabolites, which affect downstream targets, such as the acyl carrier protein necessary for fatty acid synthesis.[3] We will discuss the synthesis and biological activity of triazole-containing pantothenamide mimics, where the triazole can act as an amide bioisostere, as well as to rigidify the molecule and decrease any entropic costs associated with binding.

1. Akinnusi, T. O.; Vong, K.; Auclair, K. *Bioorganic & medicinal chemistry* **2011**, *19*, 2696.
2. Hoegl, A., *et al.* Bioorganic & medicinal chemistry letters **2014**, *24*, 3274.
3. Villiers, M., *et al.* FEBS 2013, DOI: 10.1111/febs.13013.

P45 α,α- Dichlorination of α-carbonyl stabilized iodonium ylides

Tina Tuck*, Jason Tao and Graham Murphy*, Department of Chemistry, University of Waterloo, Waterloo, ON, N2J 3G1, gkmurphy@uwaterloo.ca, tntuck@uwaterloo.ca

Hypervalent Iodine (HVI) reagents are capable of ligand transfer reactions of various groups. The transfer of single ligands to carbonyls form α-substituted products has been well documented. *α*,*α*-Dihalogenation of carbonyl-stabilized diazo compounds has been achieved through the reaction with dihaloiodoarenes $TolIF_2$ and $PhICl_2$, and catalytic Lewis acid or Lewis base. Reactions of heavily stabilized diazo compounds occur at significantly decreased rates and yields, and surrogates for the diazo group have been sought. We have found iodonium ylides to be good surrogates for the diazo group, and this poster will display the use of iodonium ylides as substrates in the α,α-dihalogenation reaction.

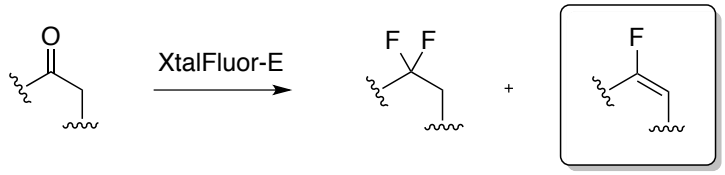


[1]Tao, J.; Tran, R.; Murphy,G.K.. *J.Am. Chem. Soc.* **2013**, 135, 16312-16315.

P46 Towards the direct synthesis of monofluoroalkenes from ketones using XtalFluor-E

Mathilde Vandamme, Eliane Soligo and Jean-François Paquin*, Département de chimie, Université Laval, Québec, QC, G1V 0A6, jean-francois.paquin@chm.ulaval.ca

The monofluoroalkene is a useful motif in medicinal chemistry since it can be used as a peptide bond isostere. Several synthetic methods exist but numerous challenges still remain (e.g. stereocontrol, length of synthesis).[1] Therefore, it would be attractive to develop a simple and straightforward approach to this motif. Interestingly, monofluoroalkenes are often observed as side-products of the deoxofluorination reaction of ketones.[2] Herein, we will describe our ongoing effort to synthesize monofluoroalkenes directly from ketones using XtalFluor-E ($[Et_2NSF_2]BF_4$). Optimization of the reaction conditions and preliminary scope of this transformation will be presented.



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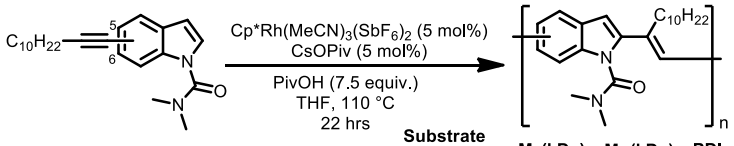
2. Beaulieu, F.; Beauregard, L.-P.; Courchesne, G.; Couturier, M.; Laflamme, F.; L'Heureux, A. *Org. Lett.* **2009**, *11*, 5050.

P47 Atom-efficient synthesis of (PPV)-type conjugated polymers by rhodium (III)-catalyzed hydroarylation of alkynes

Luke Vanderzwet, Alina Bielak, Geoffrey DeVisser, Derek Schipper*, University of Waterloo, Chemistry, University Of Waterloo, Waterloo, ON, N2L 3G1, dschipper@uwaterloo.ca

Conjugated polymers composed of alternating aromatic and alkene repeated subunits, such as poly(p-phenylene vinylene) and its derivatives, are one of the most important examples of organic semiconductors utilized in electronic applications. Nonetheless, the investigation of polymers containing this motif have been hindered by the lack of polymerization reactions capable of accesing them and the limited functional group tolerance of these reactions. Here, we present the utilization of the hydroarylation transformation, the formal addition of an arene C-H bond, across an alkyne as an alternative polymerization strategy. The optimization and intial scope for the polymerization reaction will be presented.

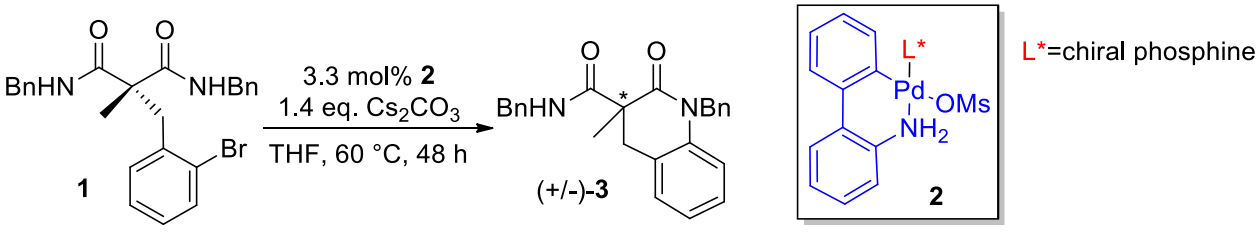


Substrate Substitution:	M_n(kDa)	M_w(kDa)	PDI
5-position	15	24	1.6
6-position	18	29	1.6

P48 Synthesis of chiral Pd-phosphine complexes for use in enantioselective C−N cross-coupling

Nande Wright, Russell Viirre*, Department of Chemistry and Biology, Ryerson University, Toronto, ON, M5B 2K3, rviirre@ryerson.ca

Enantioselectivity in the Buchwald-Hartwig cross-coupling reaction can be facilitated through the use of a chiral catalyst in special cases. For instance, prochiral malonamides can undergo intramolecular *N*-arylation, as previously investigated in the Viirre group.[1] Our present work is focused on the synthesis of chiral Pd-phosphine precatalysts **2**, analogous to those developed by Buchwald, towards increased selectivity and activity in the cyclization reaction. While biaryl phosphines are widely used, structural information of specific reaction intermediates within the catalytic cycle remains, to some extent, elusive. Obtaining a crystal of an amide-bound intermediate is desired; this may facilitate the understanding of the origin of selectivity and could lead to the development of more effective catalysts for this class of reaction.

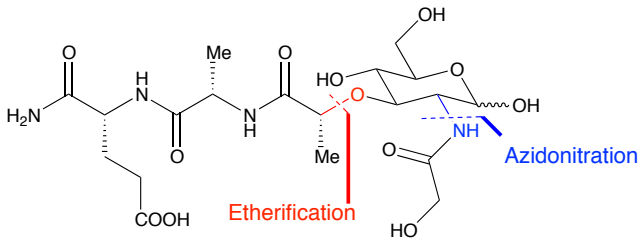


1. Viirre,* R.; Porosa, L. *Tetrahedron Lett.* **2009**, *50*, 4170–4173

P49 Synthesis of *N*-glycolyl muramyl dipeptide

Shuo Xing, Prof. James Gleason*, Department of Chemistry, McGill University, Montreal, Quebec, H3A0B8, jim.gleason@mcgill.ca

A novel synthetic route leading to *N*-glycolyl muramyl dipeptide (MDP), a bacterial glycopeptide of particular interest in studies of nucleotide-binding oligomerization domain-containing protein 2 (NOD2), is described. The synthetic strategy hinges on the alkylation of benzylidene-protected glucal with 2-bromopropionic acid and thus circumvents a challenging and non-reproducible S_N2 step at the *C*-3 position of glucosamine derivatives. The subsequent sequence includes an azidonitration and an unusual azide reduction/acylation step via an aza ylide/oxaphospholidine intermediate. This approach generates a protected *N*-glycolyl MDP that can be either subjected to a one-step global deprotection or differentially deprotected to obtain further derivatives.

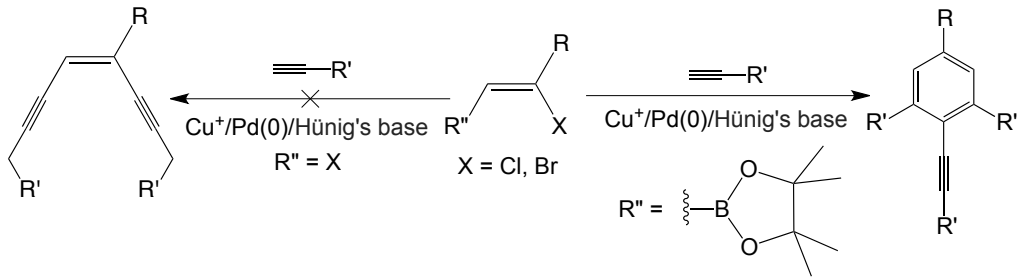


N-Glycolyl Muramyl Dipeptide

P50 Discovery of unusual reactions while attempting the Sonogashira reaction

Ravi Shekar Yalagala, Ningzhang Zhou, Tony Yan*, Department of Chemistry, Brock University, St. Catharines, Ontario, L2S 3A1, tyan@brocku.ca

During our attempts to synthesize substituted enediynes, coupling reactions between terminal alkynes and 1,2-*cis*-dihaloalkenes under the Sonogashira conditions failed to give the corresponding substituted enediynes. Under these conditions, terminal alkynes underwent self-trimerization or tetramerization reactions.[1] In an alternative approach to access substituted enediynes, treatment of alkynes with trisubstituted (*Z*)-bromoalkenyl-pinacolboronates was found to give 1,2,4,6-tetrasubstituted benzenes.[2] Substrate scopes for these two reactions were investigated.

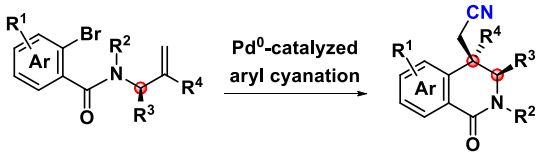


1. Yalagala, R. S.; Zhou, N.; Yan, H. *Tetrahedron Lett.***2014**, *55*, 1883.
2. Yalagala, R. S.; Yan, H. *Tetrahedron Lett.***2014**, *55*, 4830.

P51 Diastereoselective Pd-catalyzed domino Heck-type aryl cyanation of enantioenriched *N*-allyl carboxamides

Hyung Yoon, David A. Petrone, Mark Lautens*, Davenport Research Laboratories, Department of Chemistry, University of Toronto, Toronto, ON, M5S 3H6, Hyung.yoon@mail.utoronto.ca

The development of methods which efficiently introduce nitriles into complex organic scaffolds is an important objective due to their high synthetic utility. Traditionally, the nitrile incorporation is achieved through strategic pre-installation or nucleophilic cyanation. Drawbacks to these methods include decreased overall step economy and the difficulty encountered with efficiently displacing sterically encumbered leaving groups, respectively. We previously reported the formal synthesis of (+)-corynoline which utilized a key nucleophilic cyanation of a hindered neopentyl iodide produced by our Pd-catalyzed aryliodination methodology, which required excess KCN and crown ether under forcing conditions in order to proceed.[1] To overcome this challenging step, we envisioned a direct Pd-catalyzed arylcyanation to obtain the key nitrile intermediate. This poster will highlight our development of the Pd-catalyzed domino Heck-type arylcyanation of chiral *N*-allyl carboxamides which forges complex dihydroisoquinolinone cores, and represents an overall improvement to the formal synthesis of (+)-corynoline.

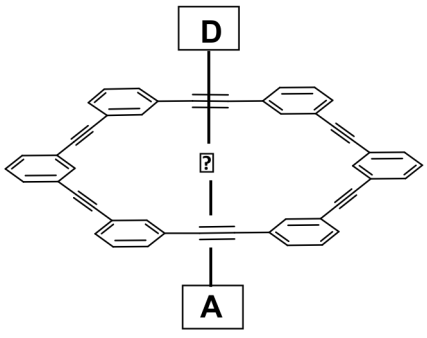


1. Petrone, D. A.; Yoon, H.; Weinstabl, H.; Lautens M. *Angew. Chem. Int. Ed.* **2014**, *53*, 7908.

P52 Supramolecular dye architectures for efficient DSSC devices

Muhammad Yousaf and Bryan D. Koivisto* Department of Chemistry and Biology, Ryerson University, 350 Victoria Street, Toronto, Ontario, M5B 2K3, bryan.koivisto@ryerson.ca

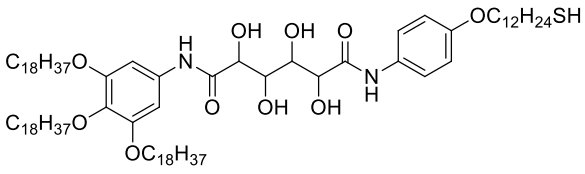
The most efficient next-generation photovoltaic cell is the low-cost dye-sensitized solar cell (DSSC) which incorporates a dye molecule as a light absorber. Recently metal-free organic dyes have received considerable attention owing to their diverse array synthesis and competitive efficiency when compared to Ru-based inorganic dyes. Organic dyes are comprised of a redox-active donor/chromophore (**D**) that is coupled through a conjugated linker (**π**) to an acceptor (**A**) capable of anchoring to TiO_2 (i.e. D-π-A motif). Fine tuning each of these components can shift the absorption spectrum increasing the overall device efficiency. This research is focused on the synthesis of shape-persistent phenylene-acetylene macrocycles. These macrocycles can be attached orthogonally to the D-π-A motifs through a novel BODIPY π spacer (see picture). This dye design should improve the DSSC performance by allowing the two-photon absorption and also by reducing the rate of recombination.



P53 New ligands for monolayer protected metal nanoparticles

Jonathan K. Yu, Omar Zghal, S. Holger Eichhorn*, Department of Chemistry and Biochemistry, University of Windsor, Windsor, ON, N9B 3P4, eichhorn@uwindsor.ca

Organic ligands are main contributors to the physical properties and chemical functionalities of monolayer protected metal nanoparticles (MNPs). They serve in applications such as catalytic systems and surfactants. However, critical deficiencies of these monolayer protected MNPs include ligand desorption and inaccessibility to the active metal surface for catalysis. Presented here are the syntheses of novel organic ligands **1** and **2** that we expect to provide larger stability to the MNP and additional functionality such as the capability of cross-linking for **1** and the formation of self-organizing structures for **2**. Synthesis of ligand **1** involves protection of the alcoholic groups, stepwise conversion of the acid groups of mucic acid to amides, thiolation, and deprotection of the alcoholic groups and thiol. Ligand **2** is generated by amide coupling of the aniline and benzoic acid precursors followed by deprotection of the thiol.



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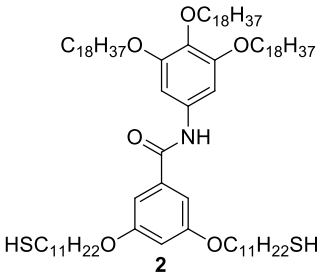

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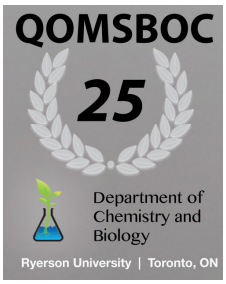
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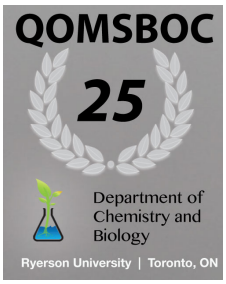
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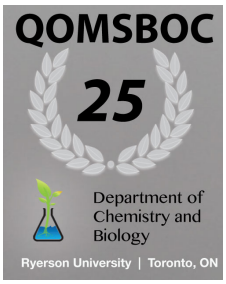
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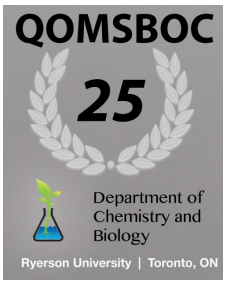
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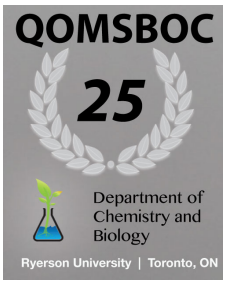
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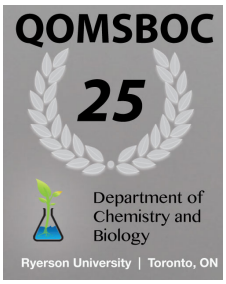
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