UQÀM

Faculté des sciences

Université du Québec à Montréal

QOMSBOC

26th Québec and Ontario Mini-Symposium in Bioorganic and Organic Chemistry

Montréal – November 6 to 8, 2015

UQÀM

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All presentations and coffee breaks as well as the poster session and the mixer will be held in the UQÀM SH-building located at 200 rue Sherbrooke West, Montreal, Quebec, H2X 3P2. The banquet will take place at ITHQ.

Toutes les présentations et pauses-café ainsi que la session de posters et le cocktail de bienvenue se tiendront dans le pavillon SH de l'UQÀM, situé au 200 rue Sherbrooke Ouest, Montréal, Québec, H2X 3P2. The banquet will take place at ITHQ.

1- Welcome / Bienvenue

It is a pleasure to welcome you to the 26th Québec-Ontario Mini-Symposium in Bioorganic and Organic Chemistry. The QOMSBOC is the premier regional conference in the field in Ontario and Québec. This year, more than 200 participants will gather on the beautiful UQÀM sciences campus to discuss the latest developments in the field of organic and bioorganic chemistry. This symposium will include 21 oral presentations and 70 posters from 40 academic groups, 2 research centers and 3 companies, spawning accross 12 different universities. We will also have the privilege of hearing three keynote lectures given by Pr. Tristan Lambert from Columbia University, Pr. Matthew Shoulders from MIT, and Dr. Chris Senanayake from Boehringer Ingelheim, world-renowned scientists in the field. I would also like to thank our sponsors who are supporting this event and contributing to the training of the next generation of highly qualified scientists. This year, many of the sponsors will be present during the conference: I encourage everyone to go visit them during the coffee breaks, lunch and poster session. I am grateful to UQÀM, the faculty of sciences and the department of chemistry for supporting this event, and in particular to René Canuel, Danny Bolduc, Odette Desrosiers and Josée Savard. A special thanks to my colleagues René Roy, Sylvain Canesi, Mathieu Frenette, Benoit Daoust, Daniel Chapdelaine and Livain Breau and to the students who volunteered to organize this event. I also want to acknowledge Pr. Russ Viirre, Pr. Guillaume Bélanger and Pr. Pat Forgione for providing countless advice on the organization of this event. Finally, I would like to thank my very good friends Steve Bourgault and Isabelle Marcotte for their constant support during the preparation of the QOMSBOC.

I wish you all a fantastic conference and a wonderful time in Montréal! Bon symposium!

Alexandre Gagnon
Chair, QOMSBOC 2015

C'est un grand plaisir de vous accueillir à ce 26ième Mini-Symposium Québec-Ontario en chimie bioorganique et organique. Le QOMSBOC est un des événements les plus importants dans le domaine au Québec et en Ontario. Cette année, plus de 200 participants se réuniront sur le très beau campus de l'UQÀM pour discuter des derniers développements dans le domaine de la chimie organique et bioorganique. Ce symposium comprendra 21 présentations orales et 70 présentations par affiche provenant de 40 groupes de recherche académique, 2 centres de recherche et 3 compagnies, couvrant ainsi 12 universités différentes. Nous aurons aussi le privilège d'assister à des conférences plénières données par le Pr. Tristan H. Lambert de Columbia University, le Pr. Matthew D. Shoulders du MIT et le Dr. Chris Senanayake de la compagnie pharmaceutique Boehringer Ingelheim. J'aimerais aussi souligner le support financier de nos commanditaires qui soutiennent cet événement et qui contribuent ainsi à la formation de la prochaine génération de scientifiques hautement qualifiés. Cette année, plusieurs commanditaires seront présents pendant le colloque: je vous encourage à aller les rencontrer pendant les pauses-café, le lunch et la session d'affiches. J'aimerais aussi souligner le support de l'UQÀM, de la faculté des sciences et du département de chimie et plus particulièrement René Canuel, Danny Bolduc, Odette Desrosiers et Josée Savard. Un merci spécial à mes collègues René Roy, Sylvain Canesi, Mathieu Frenette, Benoit Daoust, Daniel Chapdelaine et Livain Breau ainsi qu'aux étudiants et étudiantes qui se sont portés volontaires pour organiser ce symposium. Je veux aussi remercier le Pr. Russ Viirre, le Pr. Guillaume Bélanger et le Pr. Pat Forgione pour les innombrables conseils sur l'organisation de cet événement. Finalement, je tiens à remercier mes bons amis Steve Bourgault et Isabelle Marcotte pour leur support continu dans la préparation de ce QOMSBOC.

Je vous souhaite un très beau colloque et un merveilleux temps à Montréal. Bon symposium!

Alexandre Gagnon
Président, QOMSBOC 2015

2- Sponsors / Commanditaires

We would like to acknowledge the generous financial support from our sponsors. Thank you for supporting this event and for contributing to the training of the next generation of highly skilled scientists.

Nous aimerions remercier nos commanditaires pour leur généreux support financier. Merci de supporter cet événement et de contribuer à la formation de la prochaine génération de scientifiques hautement qualifiés.

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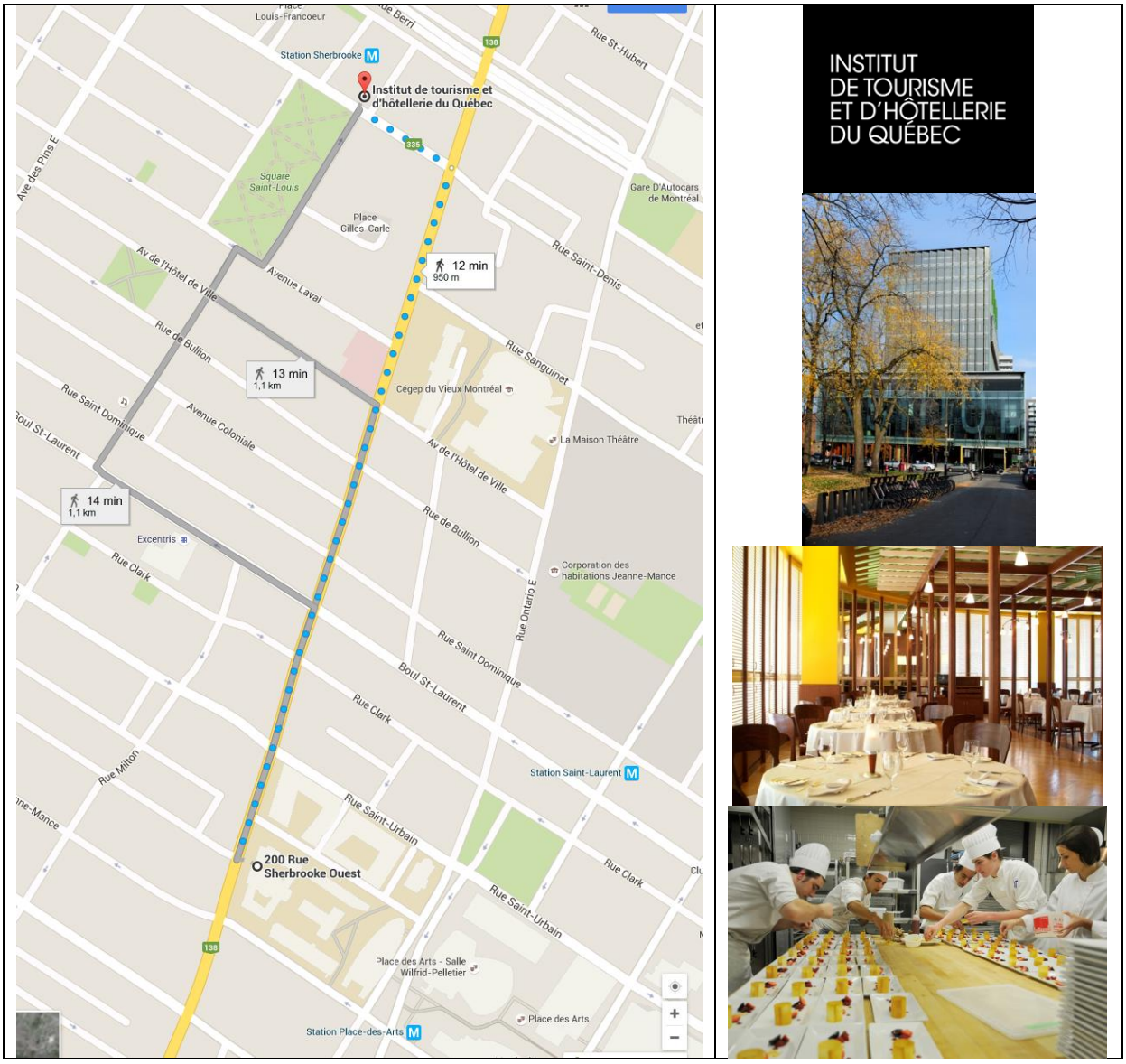
3- Banquet

The main focus of the QOMSBOC is to support our students by giving them a unique opportunity to present their work. Along with this philosophy, the banquet will take place at the Institut de Tourisme et d'Hôtellerie du Québec (ITHQ), a superb culinary school located at 3535 Rue Saint-Denis, Montréal, Qc, H2X 3P1 (514-282-5111). The ITHQ is approximately 15 minutes walking distance from the QOMSBOC venue. The ITHQ is also accessible by subway (Station Sherbrooke, orange line).

L'objectif principal du QOMSBOC est de donner une chance unique aux étudiants et étudiantes de présenter leurs travaux. En ligne avec cet objectif, le banquet aura lieu à l'ITHQ (Institut de Tourisme et d'Hôtellerie du Québec), une superbe école culinaire située au 3535, Rue Saint-Denis, Montréal, Qc, H2X 3P1. L'ITHQ est situé à moins de 15 minutes à pied du site du QOMSBOC. L'ITHQ est aussi accessible par le métro (Station Sherbrooke, ligne orange).



4- Program / Programme

Friday November 6, 2015			
19h00-22h00	Registration and mixer		SH-4800
Saturday November 7, 2015			
8h00-8h30	Registration		Hall SH
8h30-8h40	Opening remarks	Pr. Alexandre Gagnon - Organizer Pr. Livain Breau - Head of chemistry dpt., UQÀM	SH-2800
••• Session 1 - Chair: Pr. Mathieu Frenette, UQÀM			
8h40	**OR1**	Victoria Corless, University of Toronto	SH-2800
9h00	**OR2**	Henri Piras, Université de Montréal	
9h20	**OR3**	Ryan Ivanovich, University of Ottawa	
9h40	**OR4**	Sylvain Taillemaud, Université de Montréal	
10h00-10h20	**COFFEE BREAK**		SH-4800
••• Session 2 - Chair: Pr. Sylvain Canesi, UQÀM			
10h20	**OR5**	Philippe McGee, University of Ottawa	SH-2800
10h40	**OR6**	Jonathan Hughes, McGill University	
11h00	**KN1**	Dr. Chris Senanayake, Boehringer Ingelheim	
12h00-13h20	**LUNCH**		SH-4800
••• Session 3 - Chair: Pr. René Roy, UQÀM			
13h20	**OR7**	Vincent Albert, Université Laval	SH-2800
13h40	**OR8**	Dezhi Chen, Queen's University	
14h00	**OR9**	Clémence Hauduc, Université de Sherbrooke	
14h20	**OR10**	Alvin (Youngjin) Jang, University of Toronto	
14h40	**OR11**	Michel Prévost, IRCM	
15h00-15h20	**COFFEE BREAK**		SH-4800
••• Session 4 - Chair: Pr. Steve Bourgault, UQÀM			
15h20	**OR12**	Gaëtan Maertens, UQÀM	SH-2800
15h40	**OR13**	Kassandra Emberson, Brock University	
16h00	**KN2**	Pr. Matthew D. Shoulders, MIT	
17h00-18h30	**POSTER SESSION**		SH-4800
19h00-22h00	**BANQUET**	Institut de tourisme et d'hôtellerie du Québec (ITHQ) 3535, rue Saint-Denis, Montréal, Québec, H2X 3P1 1-514-282-5111 ext 4315	

Sunday November 8, 2015			
••• Session 5 - Chair: Pr. Livain Breau, UQÀM			
8h40	**OR14**	Richard Tran, University of Waterloo	SH-2800
9h00	**OR15**	Sébastien Cardinal, Université Laval	
9h20	**OR16**	Fei Chen, Concordia University	
9h40	**KN3**	Pr. Tristan H. Lambert, Columbia University	
10h40-11h00	**COFFEE BREAK**		SH-4800
••• Session 6 - Chair: Pr. Benoit Daoust, UQTR			
11h00	**OR17**	Yoann Schneider, Université de Sherbrooke	SH-2800
11h20	**OR18**	Zheng Huang, McGill University	
11h40	**OR19**	Martin Hébert, UQÀM	
12h00	**OR20**	Cynthia Crifar, Université de Montréal	
12h20	**OR21**	XiYe (Kaylie) Hua, University of Ottawa	
12h40-12h45	Closing remarks	Pr. Alexandre Gagnon - Organizer	

5- Plenary lectures and biographies / Conférences plénières et biographies

Dr. Chris H. Senanayake, Boehringer Ingelheim Pharmaceuticals

Dr. Chris H. Senanayake was born in Sri Lanka and received a B.Sc. degree (First Class) in Sri Lanka. After coming to the United States, he completed his M.Sc. at Bowling Green State University with Professor Thomas Kinstle in synthetic chemistry. He obtained his Ph.D. under the guidance of Professor James H. Rigby at Wayne State University in 1987 where he worked on the total synthesis of complex natural products such as ophiobolanes, and completed the first total synthesis of grosshemin in the guaianolide family. He then undertook a postdoctoral fellow with Professor Carl R. Johnson and worked on the total synthesis of polyol systems such as amphotericin B and compactin analogues, and the synthesis of C-nucleoside precursors.

In 1989, he joined the Department of Process Development at Dow Chemical Co. In 1990, he joined the Merck Process Research Group. After 6 years at Merck, he accepted a position at Sepracor Inc. in 1996 where he was promoted to Executive Director of Chemical Process Research. In 2002, he joined Boehringer Ingelheim Pharmaceuticals. Currently, he is the Vice President of Chemical Development and leading a group of highly talented scientists, engineers, and administrative staff located in Ridgefield, CT.

Dr. Senanayake's research interests focus on the development of new asymmetric methods for the synthesis of bioactive molecules and heterocycles and on catalytic, enzymatic, and mechanistic studies. He has published and lectured in the area of practical asymmetric synthesis and many disciplines of organic chemistry on how to develop drugs on an economical, greener and practical manner in large-scale operation for rapid development of drugs. He is co-author of more than 350 papers, patents and applications, book chapters and review articles in many areas of synthetic organic chemistry, drug development and design of improved chemical entities.

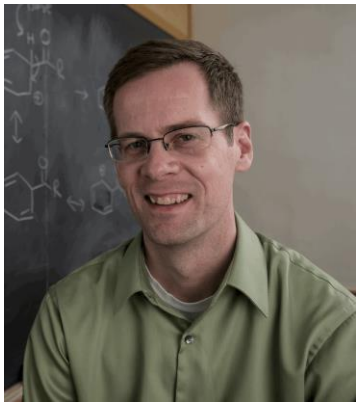
Pr. Senanayake demonstrated the ability to define and optimize chemical research and development strategies and tactics. He is able to "connect the dots" between the purely scientific and commercial perspectives and set up creative and effective strategies for new and proprietary products in ways that build value for the organization and create a competitive advantage. He is an Editorial Advisory Board member of the Organic Process Research & Development Journal. In 2008, he was the chairperson of Stereochemistry Gordon Conference. In 2010, he received the prestigious Siegfried gold medal award for development of practical processes for APIs and Process Chemistry. In 2011, he was appointed as an editorial board member of the Advance Synthesis and Catalysis Journal. In 2012, he was appointed as an Advisory board member of the Asian Journal of Organic Chemistry. In 2013 he was appointed as a Board of Editors for Organic Syntheses.

Pr. Matthew D. Shoulders, MIT

Matt Shoulders was born in Roanoke, VA in 1983 and received his B.Sc. from Virginia Tech in 2004. Later that year, he began graduate studies with Ron Raines at the University of Wisconsin-Madison, first as a Department of Homeland Security Graduate Fellow and later as an American Chemical Society Division of Medicinal Chemistry Fellow. Matt received his Ph.D. in 2009. From 2009-2012, he was an American Cancer Society Postdoctoral Fellow with Jeffery W. Kelly at The Scripps Research Institute in La Jolla, CA. In 2012, he joined the Chemistry Department at MIT as an Assistant Professor of Biological Chemistry. His numerous awards include the Smith Family Award for Excellence in Biomedical Research and being named the 56th Edward Mallinckrodt Jr. Foundation Faculty Scholar.

The Shoulders' group is particularly interested in developing and applying chemical biology tools and bioorthogonal chemistry to elucidate how cells dynamically adjust the molecular identities of proteins in response to dysregulated protein homeostasis. In this area, their initial focus is on cancer-related and stress-induced post-translational protein modifications such as N- and O-glycosylation. They also work to understand the etiologies of and develop new therapeutic strategies for incurable orphan diseases that derive from missense mutations to extracellular matrix proteins, such as osteogenesis imperfecta. These disorders are powerful models for entire categories of protein folding-related diseases. As they discover and characterize pathways involved in cellular protein folding, they also develop new chemical entities that modulate those pathways for the treatment of protein folding-related diseases.

Pr. Tristan H. Lambert, Columbia University



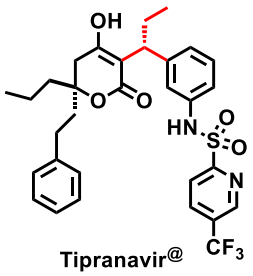
Tristan Lambert was born in Madison, Wisconsin in 1976 and received his B.Sc. from the University of Wisconsin at Platteville in 1998. That year, he began his graduate studies with David MacMillan at the University of California at Berkeley, and moved with MacMillan to Caltech in 2000 where he received his Ph.D. in 2004. From 2004-2006 he was an NIH postdoctoral fellow with Samuel Danishefsky at the Memorial Sloan-Kettering Cancer Center. In 2006, he joined the chemistry department at Columbia University and was appointed Associate Professor in 2011. He has received numerous awards, including the Alfred P. Sloan Fellowship, the Eli Lilly Grantee Award, and Young Investigator Awards from Abbott and Amgen.

From drug design to nanotechnology to materials and beyond, our modern society relies crucially on the ability to prepare complex molecules with atom level control over both connectivity and three-dimensional shape, a capacity enabled by the science of chemical synthesis. The goal of research in the Lambert group is to advance the field of organic synthesis by inventing transformative new reaction tools that will increase the speed, efficiency, and selectivity with which complex molecules may be constructed. To accomplish this goal, their efforts are focused on the development of new modes of chemical activation and novel concepts for catalysis. One of their primary interests has been in the study of aromatic ions, including cyclopropenium ions, tropylium ion, and cyclopentadienyl anions, for the purposes of reaction design and catalysis. Aromatic ions, those species that satisfy Hückel's rules for aromaticity by the formation of ionic charge, couple the high reactivity of carbon based ions with the accessible stability of aromatics, all within a highly tunable yet readily accessible framework. As such, they offer tremendous opportunities for the design of advantageous new synthetic methods. The Lambert group has been pioneering efforts to conceptualize and develop such opportunities.

KN1: Dr. Chris H. Senanayake, Boehringer Ingelheim Pharma - *Important Asymmetric and Catalytic Transformations for Drug Development*

Saturday November 7th, 11h-12h

During the past two decades, my process research group is involved in the development of truly efficient, reliable, greener and economically viable catalytic and asymmetric transformations for many drugs and drug candidates. The finding of effective asymmetric methodologies in a timely manner for important drug candidates has provided many advantages to produce complex APIs rapidly for clinical development. This lecture will be centered on several highlights of these methods for the synthesis of important drug candidates.



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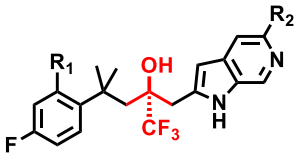
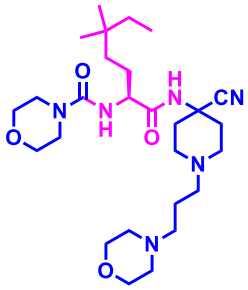
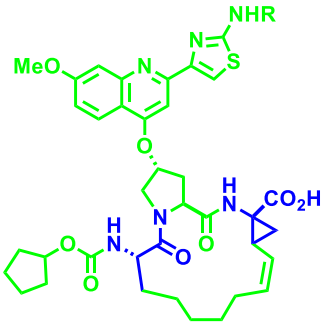


Glucocorticoid Agonists



Cathepsin S inhibitor



HCV Protease Inhibitor

X. Wang, Y. Xu, L. Zhang, D. Krishnamurthy, T. Wirth, T. Nicola, and C. H. Senanayake, *Org. Lett.* 2010, 12, 4412; V. Farina, C. Shu, X. Zeng, X. Wei, Z. Han, N. Yee, C. Senanayake *Org. Pro. Res. & Dev*. 2009, 2, 250; Shu, C.; Zeng, X.; Hao, M.-H.; Wei, X.; Yee, N. K.; Busacca, C. A.; Han, Z.; Farina, V.; Senanayake, C. H. *Org. Lett*. 2008, 10, 1303; Busacca, C.A.: Lorenz, J.C.; Grinberg, N.; Haddad, N.; Lee, H.; Li, Z.; Liang, M.; Reeves, D.; Saha, A.; Varsolona, R.; Senanayake, C.H. *Org. Lett*. 2008, 10(2), 341; Jon C. Lorenz, Carl A. Busacca, XuWu Feng, Nelu Grinberg, Nizar Haddad, Joe Johnson, Suresh Kapadia, Heewon Lee, Anjan Saha, Max Sarvestani, Earl M. Spinelli, Rich Varsolona, Xudong Wei, Xingzhong Zeng and Chris H. Senanayake. *J. Org. Chem*., 2010, 75, 1155; *Angew. Chem. Int. Ed.* 2010, 122, 6015; *J. Am. Chem. Soc.* 2010, 132, 7600. Han, Zhengxu S.; Herbage, Melissa A.;Mangunuru, Hari P. R.; Xu, Yibo; Zhang, Li; Reeves, Jonathan T.; Sieber, Joshua D.; Li, Zhibin; DeCroos, Philomen; Zhang, Yongda *Angew. Chem. Int. Ed.* 2013, 52(26), 6713-6717; Han Zhengxu S; Goyal Navneet; Herbage Melissa A; Sieber Joshua D; Qu Bo; Xu Yibo; Li Zhibin; Reeves Jonathan T; Desrosiers Jean-Nicolas; Ma Shengli *J. Am. Chem. Soc.* 2013, 135, 2474.

KN2: Pr. Matthew D. Shoulders, MIT - Chemical Biology Strategies for Mechanistic Delineation of Complex Cellular Protein Folding Pathways

Saturday November 7th, 16h-17h

A network of chaperones, quality control factors, and protein trafficking/degradation pathways has evolved to maintain proteostasis (a folded, functional, and properly localized proteome) in metazoan cells. Pharmacologic manipulation of these pathways holds great promise for delineating their mechanistic roles in resolving protein (mis)folding at the molecular level. Likewise, a detailed understanding of the proteostasis network could engender new therapeutic strategies for the treatment of protein misfolding- and aggregation-related diseases. A major challenge continues to be the lack of selective and potent chemical biology methods to manipulate and probe these pathways. We have developed several chemical genetic methods to regulate metazoan proteostasis with small molecules. Here, we discuss applications of those techniques for mechanistic studies elucidating how the proteostasis network modulates the folding and secretion of complex, proteinaceous components of the extracellular matrix. We also describe our surprising discovery that the proteostasis network regulates the molecular nature of client protein post-translational modifications by sugars. These studies provide mechanistic insights into how metazoan cells solve the protein folding problem, with important implications for human disease.

KN3: Pr. Tristan H. Lambert, Columbia University – Aromatic Ions for the Design of Highly Reactive Asymmetric Catalysts

Sunday November 8th, 9h40-10h40

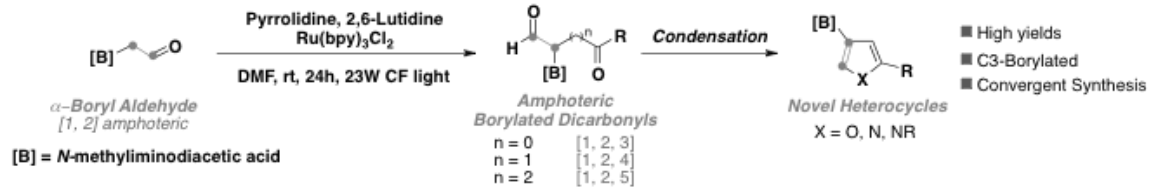
Our group is exploring the use of aromatic ions in catalysis. With this program, we are seeking to develop broadly applicable paradigms for substrate activation that capitalize on the unique reactivity of ionic aromatic motifs. This lecture will focus on our development of cyclopropenimines as a highly effective platform for enantioselective Bronsted base catalysis and pentacarboxycyclopentadienes (PCCPs) as a new class of enantioselective Bronsted acid catalysts.

6- Abstracts – oral presentations / Résumés – présentations orales

OR1 Synthesis of previously inaccessible borylated heterocycles using novel boron-containing amphoteric molecules

Victoria B. Corless, Piera Trinchera, Andrei K. Yudin*, Department of Chemistry, University of Toronto, Toronto, Ontario, M5S 3H4, ayudin@chem.utoronto.ca

Boron-containing compounds have shown utility in a broad range of applications however, one of the main limitations has been the restricted number of routes to functional organoboron derivatives. We have recently developed a novel approach to boron-containing 1,4-dicarbonyl compounds through photoredox-organocatalyzed α-alkylation of the parent α-MIDA boryl aldehyde.[1] These novel [1,2,4]-amphoteric molecules were subjected to double-condensation reactions, which resulted in a variety of synthetically challenging borylated heterocycles. This study demonstrates the utility of amphoteric reagents as a means for developing a flexible approach to highly functional organoboron compounds. Expansion of this work is currently being extended to include the synthesis of new [1,2,5]- and [1,2,3]-amphoteric dicarbonyl molecules, which will serve as additional intermediates to unconventional boron-containing heterocycles.

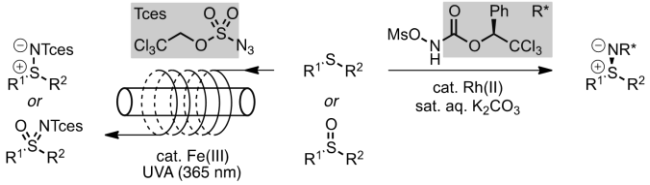


1. P.Trinchera, V.B. Corless, A.K. Yudin*, *Angew. Chem. Int. Ed.* 2015, 54 (31), 9038-9041.

OR2 Continuous Flow Processes for the Synthesis of Sulfilimines and Sulfoximines

Henri Piras and Hélène Lebel*, Département de Chimie, Université de Montréal, Montréal, QC, H3T 1J4, henri.piras@umontreal.ca

Sulfilimines and sulfoximines are valuable building blocks in medicinal chemistry, displaying biological activities when incorporated in pharmaceutical compounds.[1] Nonetheless, their chemistry remains largely underdeveloped, because of the lack of synthetic methods available in the literature. Our group has recently reported an efficient rhodium(II)-catalyzed synthesis of chiral sulfilimines and sulfoximines from thioethers and sulfoxides, using a chiral *N*-mesyloxycarbamate as a mild and practical electrophilic amination reagent.[2] We are currently exploring the photochemical decomposition of azide derivatives to produce sulfilimines and sulfoximines in continuous flow processes. Black-light blue UVA is used in the presence of catalytic amount of simple and commercially available iron(III) complexes. Results and limitations will be discussed during the presentation.

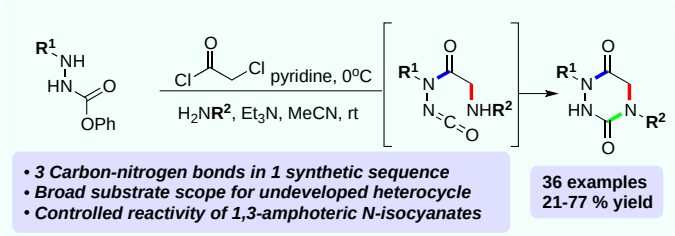


1. Lücking, U. *Angew. Chem., Int. Ed.* 2013, *52*, 9399. 2. a) Lebel, H.; Piras, H.; Bartholoméüs, J. *Angew. Chem., Int. Ed.* 2014, *53*, 7300. b) Lebel, H.; Piras, H. *J. Org. Chem.* 2015, *80*, 3572.

OR3 One-pot synthesis of aza-diketopiperazines enabled by controlled reactivity of *N*-isocyanate precursors

Ryan A. Ivanovich, Jean-Francois Vincent-Rocan, Eslam B. Elkaeed, André M. Beauchemin*
Department of Chemistry & Biomolecular Sciences, CCRI, University of Ottawa, Ottawa, ON, K1N 6N5

Nitrogen-substituted isocyanates (N-isocyanates) are a rare class of amphoteric isocyanates with high, but severely underdeveloped synthetic potential. We have recently shown that controlled reactivity of N-isocyanates can permit their use in various cascade reactions affording a diverse subset of heterocyclic derivatives.1 In these examples, the reaction sequence always began with generation and reaction of the N-isocyanate, neglecting the ability of the blocking groups to serve as hemilabile-protecting groups in cascade reactions. In this work we highlight that βN-acyl carbazates can act as blocked (masked) N-isocyanates, thus allowing a challenging intermolecular SN2 reaction of a primary amine to proceed while the N-isocyanate is "protected", and then cyclization once it is unmasked. This strategy is used to gain access to a rare heterocyclic class of molecules—aza-diketopiperazines—and greatly increase the diversity of available compounds.

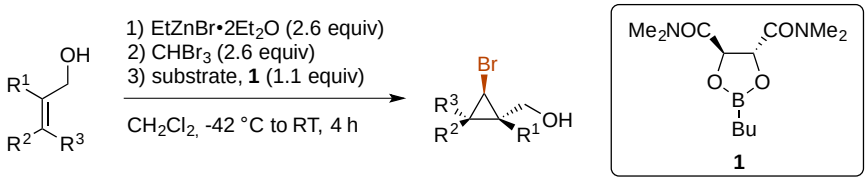


1. Vincent-Rocan, J.-F.; Ivanovich, R. A.; Clavette, C.; Leckett, K. Bejjiani, J. Beauchemin, A. M. *Chem. Sci.* **2015**, DOI: 10.1039/C5SC03197D.

OR4 Mechanism-driven Elaboration of an Enantioselective Bromocyclopropanation Reaction of Allylic Alcohols

Sylvain Taillemaud, Nicolas Diercxsens, Alexandre Gagnon and André B. Charette*,
Department of Chemistry, Université de Montréal, Montreal, QC, H3C 3J7,

Despite the fact that bromocyclopropanes are key intermediates toward the synthesis of complex cyclopropane architectures, only few methods currently exist to synthesize them in a stereospecific fashion. Using NMR spectroscopy to study and understand the structure and formation mechanism of the active intermediate, we were able to develop a highly efficient protocol for the stereoselective bromocyclopropanation of allylic alcohols. Unprecedently high yields were, therefore, obtained by making adjustments to reduce wastes and make the reaction more efficient.[1]

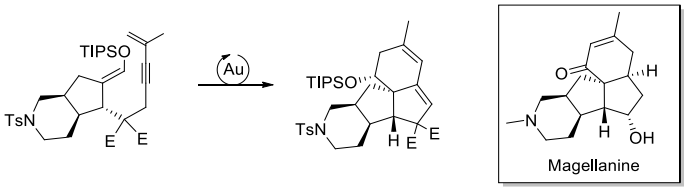


1. Taillemaud, S., Diercxsens, N., Gagnon, A., Charette, A. B., *Angew. Chem. Int. Ed.* **2015**, ASAP.

OR5 Synthesis of Angular and Fused Polycyclic Compounds with Au(I) Catalyst

Philippe McGee, Geneviève Bétournay and Louis Barriault*, Department of Chemistry, University of Ottawa, Ontario, K1N 6N5, Louis.Barriault@uottawa.ca

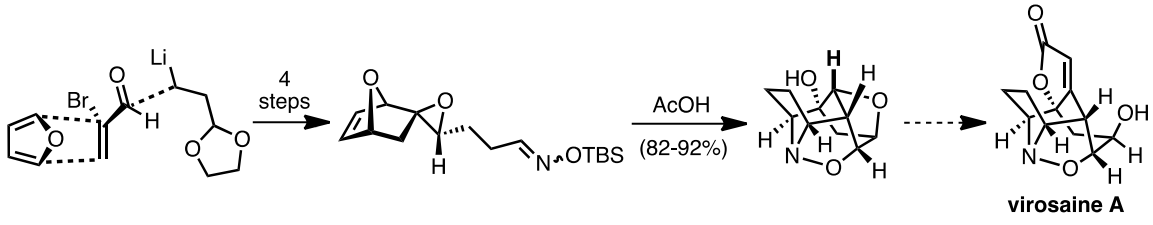
The development of new synthetic methods for the formation of carbon-carbon bonds is of paramount importance for the efficient synthesis of molecules having applications in medicine, material science, biofuels, etc. The high affinity of Au(I/III) salts to alkyne and allene moities in the presence of many other functional groups and combined by its ability to stabilize cationic charges provide tremendous opportunities for the discovery novel and useful reactions. We are currently investigating the potential of gold(I) catalysis to construct angular fused polycyclic cores by using the unique selectivity of Au(I) combined with a Prins cyclization. This will give access to functionalized polycyclic cores embedded in many complex bioactive natural products such as magellanine. Isolated from the the club moss *Lycopodium magellanicum* in 1976, this alkaloid is known to be an acetylcholinesterase inhibitor. Total synthesis of this angular natural product will be presented.



OR6 A concise approach to virosaine A

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

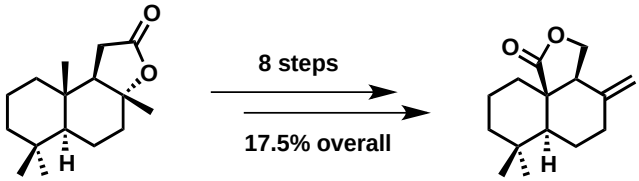
Securinega alkaloids are a small but varied class of natural products that have been associated with a number of biological activities. Virosaine A (isolated in 2012) contains the most highly caged skeleton of all the *Securinega* alkaloids. We report our efforts in developing a concise synthesis of virosaine A, highlighted by an efficient cascade reaction sequence to access the core of the natural product. Diels-Alder cycloaddition of furan and 2-bromoacrolein is followed by *in situ* nucleophile addition and epoxide formation to furnish the cascade precursor. In the cascade event, a Brønsted acid-initiated nucleophilic opening of the epoxide with a pendant oxime generates a nitrone that undergoes a facile [3+2] cycloaddition to give the polycyclic core in excellent yield. Efforts to employ a late-stage C-H functionalization/oxo-bridge cleavage to install the butenolide functionality will be discussed.



OR7 Concise and Scalable Enantioselective Synthesis of Antrocin by Remote Functionalization

Vincent Albert and John Boukouvalas*, Departément de Chimie, Université Laval, Quebec City, QC, G1V 0A6, John.Boukouvalas@chm.ulaval.ca

Antrocin (**1**) is an architecturally unusual antitumor sesquiterpene lactone isolated in tiny amounts from the Taiwanese medicinal fungus *Antrodia camphorata*. Antrocin efficiently suppresses the phosphorylation of Akt and its downstream effectors mTOR, GSK-3β, and NF-κB in cellular settings and displays potent antitumor activities in vitro and in vivo.[1] It is especially potent toward metastatic breast cancer cells, more so than the drugs doxorubicin and cisplatin.[1a] We shall present here the first enantioselective approach to **1**, which begins from readily available sclareolide (ca. $5/gram) and employs remote functionalization as a key step.



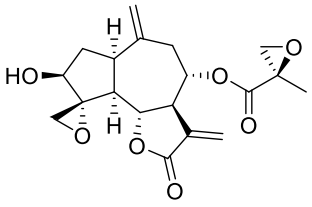
sclareolide **antrocin (1)**

1. (a) Yeh, C.-T.; Tzeng, Y.-M. et al., *Chem. Res. Toxicol*. **2011**, *24*, 238. (b) Tzeng, Y.-M. et al., *Carcinogenesis* **2013**, *34*, 2918.

OR8 Progress towards the Total Synthesis of Repin

Dezhi Chen, Tomass Baikstis, P. Andrew Evans*, Department of Chemistry, Queen's University, Kingston, ON, K7L 3N6, andrew.evans@chem.queensu.ca

Repin is a guaianolide isolated from *Acroptilon Repens*. It shows significant cytotoxic activities. The synthesis of the tricyclic core of repin with seven stereocenters will be presented. The synthetic approach features the palladium-catalyzed umpolung allylation, the rhodium-catalyzed [(3+2)+2] carbocyclization and radical alkylation/lactonization as the key steps.

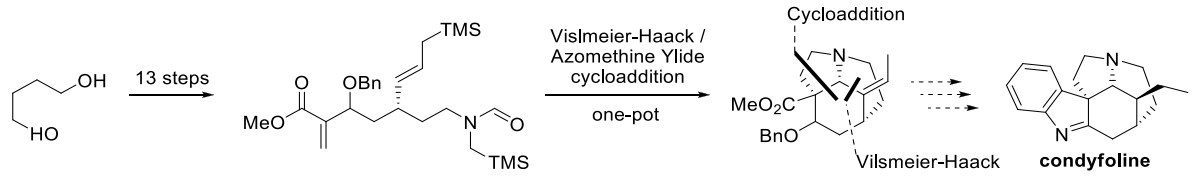


repin

OR9 General Approach Toward Aspidospermatan Alkaloids Using One Pot Sequential Intramolecular Vilsmeier-Haack Reaction and Azomethine Ylide Cycloaddition

Clémence Hauduc and Guillaume Bélanger*, Département de chimie, Université de Sherbrooke, Sherbrooke, QC, J1K 2R1, Guillaume.Belanger@USherbrooke.ca

For many years, chemists have been interested in increasing rapidly the molecular complexity to access complex molecules with short syntheses. Over the last years, our research group developed a one pot sequence of Vilsmeier-Haack cyclization and non-stabilized azomethine ylide intramolecular (3+2) cycloaddition to access the core of different alkaloids. In a single transformation, 3 cycles and 3 C-C bonds are generated from a linear chain with complete chemo- and diastereocontrol induced by a single stereocenter on the precursor. The latter was synthesized in only 13 steps. The different approaches towards the key step precursor, as well as the development of the key transformation will be presented, highlighting the efficiency of our sequential cyclization strategy. The cycloadduct represents a common intermediate to several members of the aspidospermatan alkaloids' family, such as condyfoline.

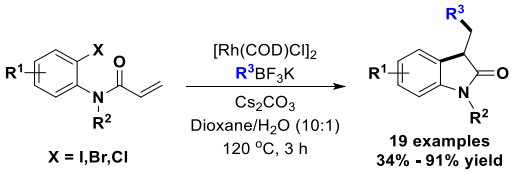


OR10 Rhodium catalyzed domino addition-enolate arylation: Generation of 3-substituted oxindoles via a rhodium(III) intermediate

Young Jin Jang, Hyung Yoon, Mark Lautens*, Department of Chemistry, University of Toronto, Toronto, Ontario, M5S 3H6, mlautens@chem.utoronto.ca

Transition metal catalyzed α-arylation has been a central focus of organic chemistry research due to its versatility and utility in the synthesis of a diverse array of medicinal targets and natural products. Since the seminal report by Semmelhack in 1973,[1] numerous variations have been developed incorporating transition metal catalysts such as palladium, copper and rhodium. Major drawbacks of current methods reside in the use of strong bases to generate the enolate nucleophile, and the incorporation of transition metal catalysts often suffer from poor selectivity towards mono-arylation, leading to decreased yields.

To circumvent these limitations, we developed a new rhodium catalyzed methodology. This cascade process involving a rhodium catalyzed 1,4 Hayashi-Miyaura conjugate addition, and the subsequent intramolecular α-arylation has been applied to the synthesis of medicinally relevant 3-substituted oxindoles.[2]



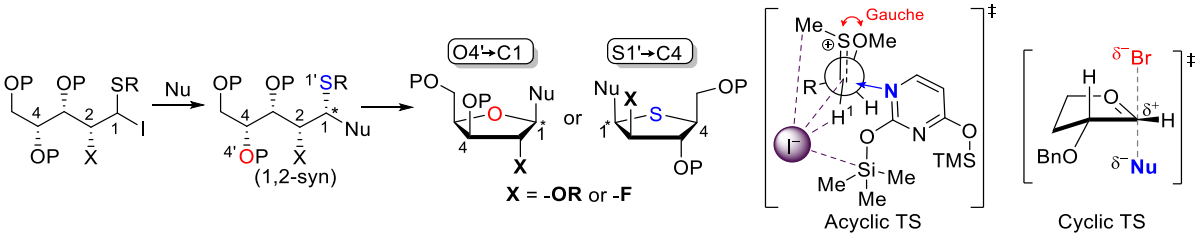
1. Semmelhack, M. F.; Stauffer, R. D.; Rogerson, T. D. *Tetrahedron Lett*. **1973**, *14*, 4519.

2. Jang, Y. J.; Yoon, H.; Lautens, M. *Org. Lett.* **2015**, *17*, 3895.

OR11 Diastereoselective Synthesis of Nucleoside Analogues from Cyclic/Acyclic Haloethers

Michel Prévost, Starr Dostie, Yvan Guindon*, Laboratoire de chimie bioorganique, IRCM, Montréal, Québec, H2W 1R7, yvan.guindon@ircm.qc.ca

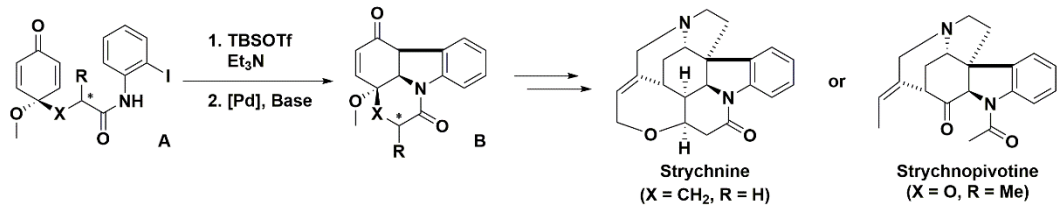
We will present the synthesis of thioaminals, which are useful intermediates that can undergo two different intramolecular cyclizations to yield members of an important class of anticancer and antiviral agents. Evidence to support a new model for acyclic N-glycosylations of α-alkoxyhalothioethers that provide high 1,2-syn control (anti-Felkin-Anh), opposite to what is found for additions to corresponding activated aldehydes, will also be discussed. The conformational preference observed by DFT calculation at the transition state level reveals interesting stereoelectronic effects and highlight key aspects of the reactivity of α-alkoxycarbenium precursors with heterobase nucleophiles. Studies of related substitutions involving cyclic haloethers will then be described. This work should help organic and medicinal chemists prepare nucleoside analogues and contribute to the comprehension of the outcome of N-glycosylation reactions.



OR12 New Short Synthesis of Strychnine and Synthesis of Related Alkaloids

Gaëtan Maertens, Guillaume Jacquemot and Canesi Sylvain*, Laboratoire de Méthodologies et Synthèse de Produits Naturels, Université du Québec à Montréal, Montréal, Qc, Canada, H3C 3P8

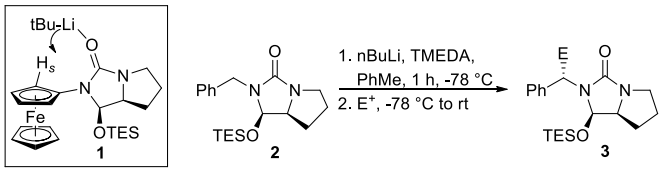
We present a new short synthesis of Strychnine as well as our recent works regarding the asymmetric synthesis of Strychnopivotine. We envisioned that both targets could derive from tetracycle B, which could be obtained by an aza-Michaël-enol-ether tandem process followed by a Heck-type coupling from dienone A. In the case of Strychnopivotine, where X is an oxygen atom and R is an alkyl, the corresponding tetracycle B is obtained in a diastereoselective fashion. After hydrolysis of the cetal-amide moiety at the end of the synthesis, this strategy should lead to an enantioselective avenue of the targeted compound. Both of these syntheses involve an oxidative dearomatization mediated by a hypervalent iodine reagent, a new aza-Michael-enol-ether tandem process, a Heck-type cyclization and a double reductive amination in cascade.



OR13 Use of the (1*R*,7a*S*)-1-((triethylsilyl)oxy)tetrahydro-1H-pyrrolo[1,2-c]imidazol-3(2H)-one chiral auxiliary as a ligand precursor for rhodium catalysis and a stereo determining group for *N*-benzyl substitution

Kassandra Emberson and Costa Metallinos*, Chemistry, Brock University, St. Catharines, ON, L2S 3A1, cmetallinos@brocku.ca

As part of ongoing research to expand the scope of L-proline hydantoin-derived chiral imidazolones for stereoselective induction of planar chirality in ferrocenes **1**, we have prepared the *N*-benzyl analogue **2**.[1,2] Standard lithiation of **2** followed by electrophile quench affords products **3** in yields ranging from 46-86% and up to 10:1 dr. The stereochemistry of the major diastereomer has been determined by X-ray crystallography of the benzophenone adduct (E = Ph_2COH). In addition, NMR spectroscopy and transmetalation studies of the stannane (E = $SnMe_3$) have revealed that the major diastereomers in all cases have the same relative stereochemistry. Recent efforts directed towards reaction optimization, and determining whether selectivity involves asymmetric deprotonation or asymmetric substitution will be presented.

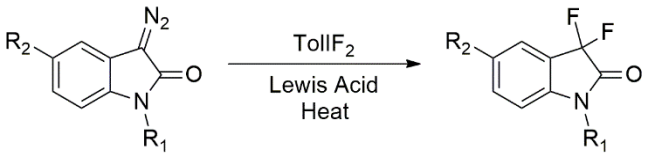


1. Metallinos, C.; John, J.; Zaifman, J.; Emberson, K. *Adv. Synth. Catal.* **2012**, *354*, 602.
2. Metallinos, C.; John, J.; Nelson, J.; Dudding, T.; Belding, L. *Adv. Synth. Catal.* **2013**, *355*, 1211.

OR14 Geminal Difluorination of Oxindole Derivatives

Richard Tran, Graham Murphy*, Department of Chemistry, University of Waterloo, Waterloo, ON, N2L3G1, graham.murphy@uwaterloo.ca

Reliable methods for the incorporation of fluorine into organic molecules are highly desired in medicinal chemistry. Current methods include electrophilic fluorination using reagents such as DAST or SelectFluor®, however, their drawbacks include toxicity, low stability or high costs. An alternative electrophilic fluorination strategy uses iodotoluene difluoride ($TolIF_2$), which exists as a stable solid, is not sensitive to moisture, and can be readily made from inexpensive reagents. We have reported α-carbonyl geminal difluorination on phenyldiazoacetate derivatives using $TolIF_2$ in good yield.[1] The fluorination protocol can be extended to similarly-appointed compounds such as 3-diazooxindole derivatives. The resulting 3,3-difluoroxindole compounds enjoy widespread interest in the pharmaceutical industry as they are biological active as anticancer agents. Studies towards efficient 3,3-difluorination of 3-diazo-2-oxindole derivatives using $TolIF_2$ will be presented.

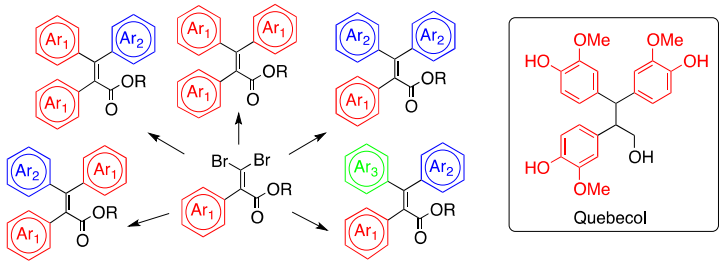


1. Tao, J.; Tran, R.; Murphy, G. K. *J. Am. Chem. Soc*., 2013, *135*, 16312.

OR15 New approach leading to various 1,2,2-triarylethene compounds : application to the total synthesis of a polyphenoclic compound found in maple syrup

Sébastien Cardinal, Jabrane Azelmat, Daniel Grenier, Normand Voyer*, Département de chimie et PROTEO, Université Laval, Québec, Qc, G1V 0A6, Normand.voyer@chm.ulaval.ca

We recently developed a new strategy to access 2,3,3-triarylacrylic acid esters, a class of 1,2,2-triarylethene compounds bearing an α,β-unsaturated ester functionality. Our approach implies the preparation of a *gem*-dibromoalkene precursor from a α-ketoester compound, followed by the installation of two aryl groups by Suzuki-Miyaura coupling reactions on the two C-Br bonds. Efficient conditions for double coupling and for stereoselective mono-coupling were found, in a way to give access to compounds with one, two or three types of aryl groups. This presentation will report the preparation of those compounds, as well as, the exploitation of this methodology for the total synthesis of quebecol[1], a polyphenolic compound found in maple syrup. New results on the anti-inflammatory activity of this natural product will also be discussed.

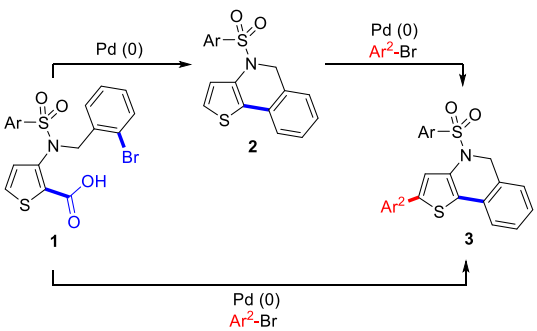


1. Cardinal, S., Voyer, N., *Tetrahedron Lett.* ***2013****, 54, 5178.*

OR16 One-pot Tandem Palladium-Catalyzed Decarboxylative Cross-Coupling and C-H Activation – An Efficient Method to Access to Thienoisoquinoline Scaffolds

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

Thienoisoquinoline scaffolds (3) are densely functionalized heteroaromatics with potential application in medicinal chemistry for inflammatory associated diseases as disclosed by Wyeth in 2006. The reported synthetic pathway involves two Suzuki reactions, which requires pre-functionalization of starting materials, with an overall yield of 6%. We herein demonstrate an alternative five-step synthetic pathway to access the thienoisoquinoline scaffolds. Rather than employing classic palladium-mediated cross-coupling methods, our approach used the environmental friendly and more sustainable palladium-catalyzed decarboxylative cross coupling (1→2) and C-H arylation (2→3) to produce the desired scaffolds. Furthermore, we were able to telescope the two palladium-catalyzed reactions into one-pot (1→3), that further increases the utility of this method (yield = 35% ~ 63%). Preliminary mechanistic studies of C-H activation on the regioselectivity of the thiophene illuminates a competition between intra- and inter-molecular arylations.[1]

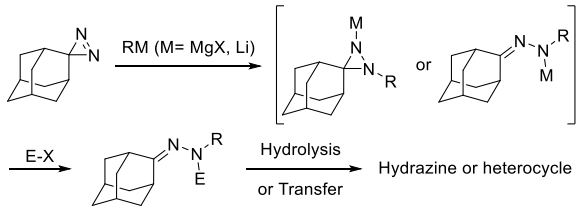


1- Chen, F.; Wong, N. W. Y.; Forgione, P.* *Adv. Synth. Catal.* 2014, *356*, 1725–1730.

OR17 Diazirines as Precursors of Electrophilic Nitrogen for the Synthesis of Disubstituted Hydrazines and Heterocyclic Compounds

Yoann Schneider and Claude Y. Legault*, Département de chimie, Université de Sherbrooke, Sherbrooke, QC, J1K 2R1, claude.legault@usherbrooke.ca

The *Umpolung* effect gives unusual properties to some functional groups, interesting for total synthesis. Diazirines have shown this effect, as a potential source of electrophilic nitrogen. Our group previously used this property for the synthesis of monosubstituted hydrazines, by nucleophilic addition of organolithium or organomagnesium reagents on the nitrogen. During our investigation of the nucleophilic addition process, we discovered an unusual rearrangement leading not only to monosubstituted diaziridines, but to monosubstituted hydrazones.[1] These results opened an opportunity to explore a strategy for the synthesis of *N,N'*-disubstituted diaziridines and *N,N*-disubstituted hydrazones. We were able to obtain the corresponding disubstituted hydrazines, as well as heterocyclic compounds, like *N*-amino pyrroles and *N*-protected indoles, with good yields.

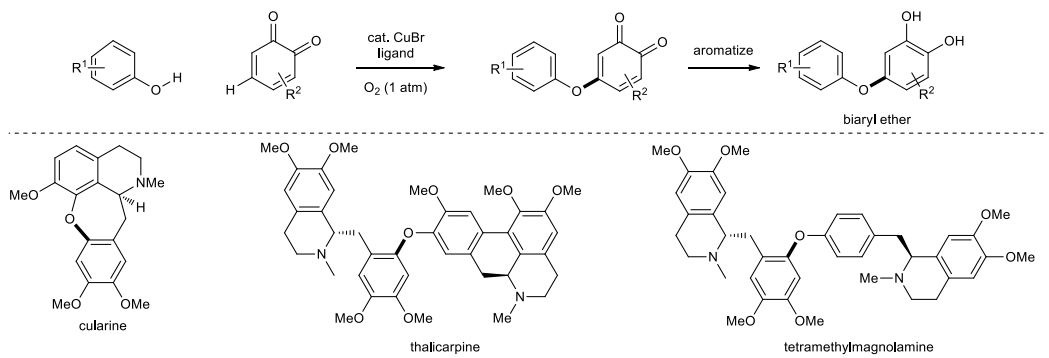


1. Schneider, Y.; Prévost, J.; Gobin, M.; Legault, C. Y. *Org. Lett.* **2014**, *16*, 596.

OR18 Unsymmetrical Biaryl Ether Synthesis by Copper-catalyzed Aerobic Phenol Addition to *ortho*-Quinone

Zheng Huang, Jean-Philip Lumb*, Department of Chemistry, McGill University, Montréal, QC, H3A 0B8, jean-philip.lumb@mcgill.ca

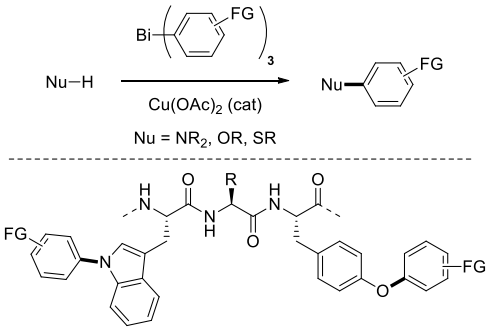
Biaryl ethers are present in many naturally products, drug molecules as well as functional material. Traditionally, these molecules are made by Ullmann coupling, generating one equivalent of the corresponding hydrogen halide as the byproduct. Our approach to biarylethers is a cross-dehydrogenative type coupling between phenol and ortho-quinone. The addition of phenol nucleophiles to ortho-quinone is challenging due to the weak nucleophilicity of oxygen atom, as well as the redox-exchange of the product catechol with starting quinone. We solve the problem by doing a direct oxidative coupling to generate the coupled quinone as product.



OR19 Towards Chemoselective Arylation Reactions of Peptides Using Triarylbismuthanes

Martin Hébert, Adrien Le Roch, Francis Pinsonneault, Marie-Jeanne Archambault, Alexandre Gagnon*, Département de Chimie, Université du Québec à Montréal, Montréal, Québec, H3C 2P8, gagnon.alexandre@uqam.ca

There is a need for general methods that lead to post-synthetic modification of peptides. Currently, few methods exist for the chemoselective arylation on specific amino acid residues. Organobismuth reagents have recently gained interest due to their versatility in bond formation, functional group tolerance, low cost and low toxicity related to the inorganic bismuth salt. Recently, our group has developed efficient arylation methods using highly functionalized trivalent arylbismuth reagents to form C–C, C–O and C–N bonds.[1] In particular, indoles, phenols and aminoalcohols have been successfully arylated in good to excellent yields via substoichiometric copper catalysis in mild conditions. As a result, this method will be further employed as a mean of selective arylation of polypeptides. In this presentation, we will discuss our progress in the development of arylation methods of peptides using triarylbismuthanes.

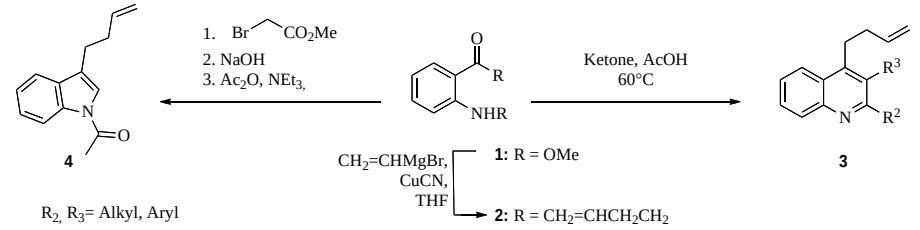


[1] a) Petiot, P.; Gagnon, A. *Eur. J. Org. Chem.*, **2013**, 5282; b) Crifar, C.; Petiot, P.; Ahmad, T.; Gagnon, A. *Chem. Eur. J.*, **2014**, *20*, 2755; c) Petiot, P.; Dansereau, J.; Gagnon, A. *RSC Adv.*, **2014**, *4*, 22255; d) Petiot, P.; Dansereau, J.; Hébert, M.; Khene, I.; Ahmad, T.; Samaali, S.; Leroy, M.; Pinsonneault, F.; Legault, C. Y.; Gagnon, A. *Org. Biomol. Chem.*, **2015**, *13*, 1322.

OR20 Copper-catalyzed cascade addition route to Quinolines and Indoles from Anthranilate as common starting material

Cynthia Crifar, Fenja Duecker, Aurélie Dörr, William D. Lubell*, Department of Chemistry, University of Montreal, C.P. 6128, Succursale Centre-Ville, william.lubell@umontreal.ca Montreal, Quebec H3C 3J7

Focused on the diversity-oriented synthesis of heterocycles, we have pursued the preparation of two important classes of medicinally relevant compounds from a common intermediate. Quinolines and indoles are commonly found in biologically active molecules, such as quinine and serotonin. Efficient methods for making quinolines and indoles are of critical interest particularly in medicinal chemistry. The copper-catalyzed cascade addition of vinylmagnesium bromide on methyl anthranilate provides quantitatively ketone 2 without need of amine protection. Employing this common starting material, we have pursued the synthesis of quinolines and indoles. Solvent-free Friedlander synthesis converted 2 into 4-substituted quinolines 3 in 52-100% yields[1]. 3-Substituted indoles 4 have also been prepared from amino ketone 2. Double bond functionalization gives access to diversify heterocycle systems 3 and 4. Recent progress in the development of these methods to synthesize quinolines and indoles will be presented.

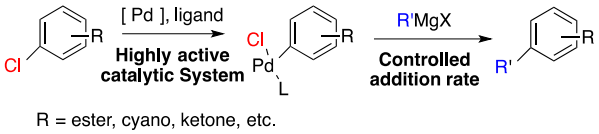


far, C.; Dörr, A. A.; Lubell, W. D. *Tetrahedron Letters* **2015**, *56*, 3451.

OR21 Inherent vs. Apparent Chemoselectivity: Expanding the Scope of Grignard Reagents in Cross-Coupling

XiYe (Kaylie) Hua, Jeanne Masson-Makdissi, and Stephen G. Newman*, Department of Chemistry & Biomolecular Sciences, University of Ottawa, Ottawa, ON, Xhua096@uottawa.ca

Catalytic C–C bond formation in cross coupling reactions continue to be a major focus in catalysis research for the production of fine chemical, pharmaceuticals, agrochemicals and organic materials. The use of boronic acid nucleophiles (the Suzuki reaction) is particularly common because they are stable and selective nucleophiles. However, from a green chemistry perspective, they are less desirable than the use of Grignard nucleophiles (the Kumada reaction), which are frequently intermediates in the synthesis of boronic acids. The perceived chemoselectivity issue of Grignard reagents has limited their direct use in cross-couplings and other catalytic reactions. In the interest of expanding the scope of the Kumada reaction, we have developed a procedure that minimizes over-reactivity of Grignard reagents with sensitive functional groups. By controlling the addition rate of Grignard, the inherent relative rates of selectivity-determining transmetallation vs. side reactions can be achieved.



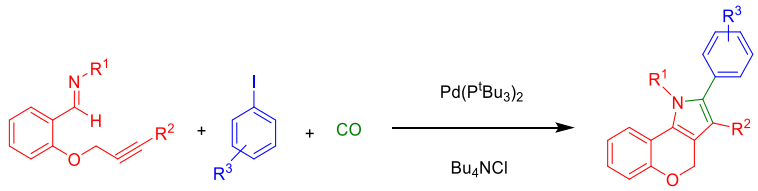
R = ester, cyano, ketone, etc.

7- Abstracts – posters / Résumés – affiches

P01 Palladium Catalyzed Multicomponent Synthesis of Polycyclic Pyrroles from Aryl Iodide, CO and Alkyne-Tethered Imines

Neda Firoozi, Bruce A. Arndtsen*, Department of Chemistry, McGill University, Montreal, QC, H3A 0B8, bruce.arndtsen@mcgill.ca

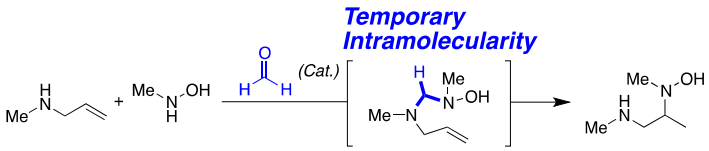
The synthesis of pyrrole-fused heterocycles has become an important field of research owing to their diverse biological properties. One approach to these products is via the intramolecular cycloaddition of mesoionic 1,3-oxazolium-5-oxides (Münchnone) with alkynes. However, these Münchnones are typically prepared via a multistep protocol, which can limit accessibility to modified versions of products. In this work, polycyclic pyrroles have been synthesized by palladium catalyzed reaction of alkyne-tethered imines, CO and aryl iodides. This transformation is proposed to proceed via the in situ, carbonylative generation of Münchnones, which undergo rapid alkyne cycloaddition. The design of catalysts for this reaction, its mechanism, and the diversity of pyrrole products available, will each be discussed.



P02 Accelerating Challenging Intermolecular Reactions in Water: A New Role For Formaldehyde in Prebiotic Chemistry

Mohammad P. Jamshidi, Melissa J. MacDonald, André M. Beauchemin*, Department of Chemistry and Biomolecular Sciences, CCRI, University of Ottawa, Ottawa, ON, K1N 6N5

Over decades, scientists have been trying to explain how life as we know it today emerged from simpler building blocks such as: HCN, NH_3, CH_4, aldehydes, etc. By definition, the reactions required to synthesize more complex structures are intermolecular, for which, there is an entropic penalty. Intermolecular reactions are inherently slow at low concentrations, and faster, more concentrated reactions could have dictated how chemical evolution occurred. Herein, we demonstrate that formaldehyde, a key prebiotic molecule, is able to catalyze a challenging intermolecular reaction in water, operating only through temporary intramolecularity. Interestingly, formaldehyde is already a well established crosslinking *reagent*,[1] and reports have dictated that its concentration was as high as 0.02M on primitive earth.[2] Consequently, we embarked on a study of this intermolecular hydroamination using water-soluble reagents at low concentrations, with formaldehyde as a focus point.

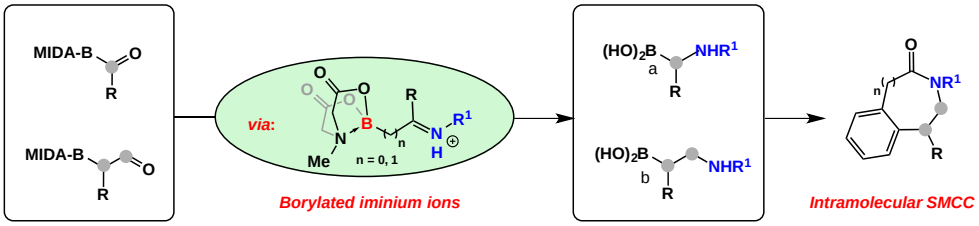


1. a) Kool, E. T. *et al. Nat. Chem.* **2015**, 7, 752. b) Auble, D. T. *et al. Science*, **2013**, 369. c) Marutzky, R. *et al. Chem. Rev.* **2010**, 110, 2536. 2. a) Cleaves, H. J. *Precambrian Res.* **2002**, 32, 209.

P03 Linking Amines with Boron-Containing Fragments: A General Route to α- and β-Aminoboronic Acid Derivatives

Diego B. Diaz, Conor C. G. Scully, Shinya Adachi, Sean K. Liew, Piera Trinchera, Jeffrey D. St. Denis, and Andrei K. Yudin*, Department of Chemistry, UofT, Toronto, ON, M5S 3H6

As part of a program aimed at the discovery and application of boron-based amphoteric molecules, we have developed a general method to connect boron- and nitrogen-containing fragments. Our strategy is based on the capacity for α-boryl aldehydes[1] and acyl MIDA boronates[2] to undergo reductive amination with various types of amines, including both linear and cyclic peptides. As a result, our methodology enables access to new classes of boropeptides such as, β-aminoboronic acids and macrocycles with borylated side chains. This presentation will highlight the salient features of our late-stage approach to introduce carbon-boron bonds into stereochemically complex and heteroatom-rich environments, enabling further functionalization of the sp^3-aminoboronic acid derivatives using intramolecular Suzuki-Miyaura cross-coupling (SMCC).

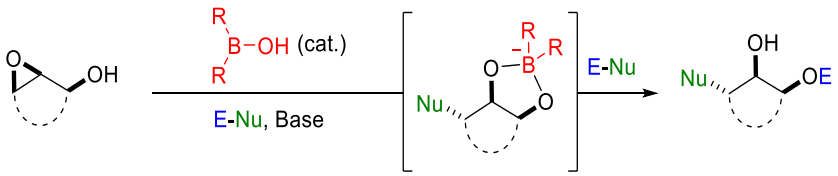


1) St. Denis, J. D., He, Z.; Yudin, A. K. *ACS Catal.* **2015**, *5*, 5373–5379. 2) He, Z.; Trinchera, P.; Adachi, S.; St Denis, J. D.; Yudin, A. K. *Angew. Chem. Int. Ed.* **2012**, *51*, 11092–11096.

P04 Organoboron catalyzed ring opening and functionalization of epoxy alcohols

Kashif Tanveer, Kareem Jarrah, Mark S. Taylor*, Department of Chemistry, University of Toronto, Toronto, ON, M5S 3H6, mtaylor@chem.utoronto.ca

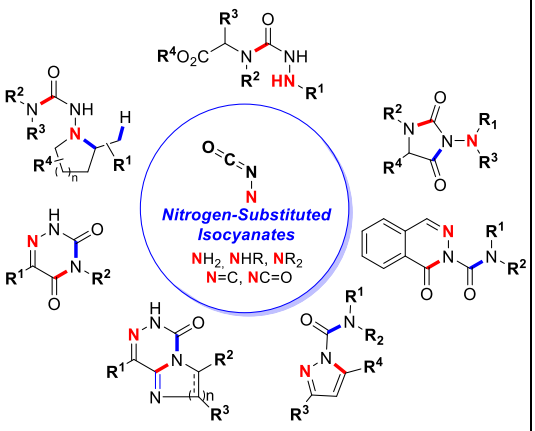
We report that 2,3-epoxy alcohols can undergo tandem ring-opening and diol functionalization by using organoboron based catalysts. This transformation directly generates *O*-functionalized halogenated diols from 2,3-epoxy alcohols with high levels of regioselectivity for both the ring-opening and *O*-functionalization steps.



P05 Cascade reactions of nitrogen-substituted isocyanates: A new tool in heterocyclic chemistry

Jean-François Vincent-Rocan, Ryan. A. Ivanovich, Christian Clavette, Kyle Leckett, Julien Bejjani, André M. Beauchemin,* Department of Chemistry and Biomolecular Sciences, University of Ottawa

Nitrogen substituted isocyanates (*N*-isocyanates) are a rare class of amphoteric intermediates with untapped synthetic potential. Given the importance of the N-N-C=O motif in pharmaceuticals and agrochemicals, we envisioned that *N*-isocyanates could provide new disconnections, and a unified approach to assemble N-N-C=O containing heterocycles. Building on our previous work for the synthesis of saturated heterocycles[1] and amino-hydantoins,[2] we developed tools that allowed access to a variety of heteroaromatic cores using cascades reactions of blocked (masked) *N*-isocyanates. The synthesis of phtalazinones, pyrazoles and azauracils will be discussed.



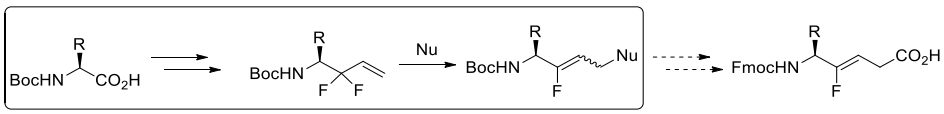
Rare and amphoteric intermediates
***In-situ* generation, controlled reactivity**
Diverse cascade reactions, over 100 examples

1) Clavette, C.; Vincent-Rocan, J.-F.; Beauchemin, A. M. *Angew. Chem. Int. Ed.* **2013**, *52*, 12705.
2) Vincent-Rocan, J.-F.; Clavette, C.; Leckett, K.; Beauchemin, A. M. *Chem. Eur. J.* **2015**, *21*, 3886.

P06 A Versatile Approach Towards the Synthesis of Monofluoroalkene-based Dipeptide Isosteres

Myriam Drouin, Sébastien Tremblay, Audrey Gilbert and Jean-François Paquin*, Département de chimie, Université Laval, Québec, QC, G1V 0A6, jean-francois.paquin@chm.ulaval.ca

Solid state ^{19}F NMR is a useful tool to study biological events such as protein interactions with biological membranes.[1] Given the fact that monofluoroalkenes are non-hydrolyzable peptide bond mimics,[2] we wish to explore their potential use as backbone molecular probes. Our progress towards the synthesis of monofluoroalkene-based dipeptide isosteres based on synthetic methods previously developed in our laboratory will be discussed.[3]

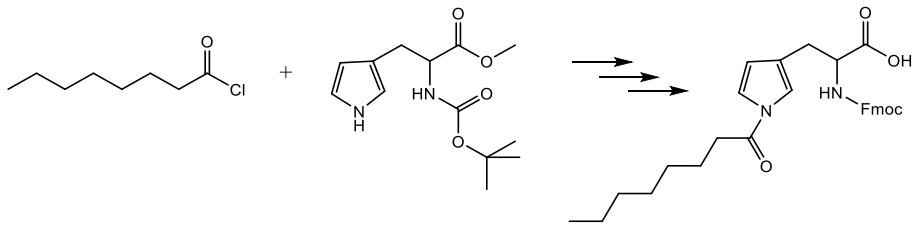


(1) Ulrich, A. S. *Prog. Nucl. Magn. Reson. Spectrosc.* **2005**, *46*, 1. (2) Choudhary, A.; Raines, R.T. *ChemBioChem* **2011**, *12*, 1801. (3) (a) Pigeon, X.; Bergeron, M.; Barabé, F.; Dubé, P.; Frost, H.N.; Paquin, J.-F. *Angew. Chem. Int. Ed.* **2010**, *49*, 1123. (b) Bergeron, M.; Johnson, T.; Paquin, J.-F. *Angew. Chem. Int. Ed.* 2011, *50*, 11112. (c) Bergeron, M.; Guyader, D.; Paquin, J.-F. *Org. Lett.* **2012**, *14*, 5888. (d) Hamel, J.-D.; Drouin, M.; Paquin, J.-F. *J. Fluorine Chem.* **2015**, *174*, 81.

P07 Probing the effect of protein carbonylation on amyloid formation with site-specifically modified peptide derivatives

Margaryta Babych, Phuong Trang Nguyen and Steve Bourgault*, Département de chimie, UQÀM, Montréal, QC, H3C 3P8

Non-enzymatic post-translational modifications of a protein can lead to dramatic changes in the chemical nature of amino acid side chains. These modifications in the primary sequence often leads to major perturbation of protein conformation and function(s). In type II diabetes, carbonylation can trigger the misfolding and aggregation of the islet amyloid polypeptide (IAPP)[1]. We recently revealed by LC-MS/MS analysis that the main site of IAPP carbonylation is the imidazole group of the histidine residue located at position 18. To address the role of this modification in the pathway of amyloid formation, we site-specifically modified the His side chain with an alkane analogue of 4-hydroxynonenal, which is the major product of polyinsaturated fatty acids peroxydation[2]. In this presentation, we will discuss two synthesis strategies: solution synthesis and solid-phase synthesis.

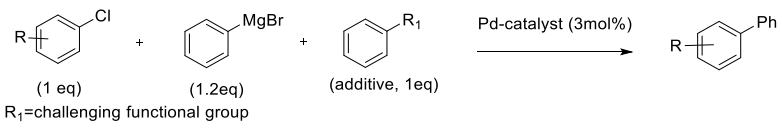


1. Liu, W. et al. *Journal of Cell Science*., **2000**, 113:635-641.
2. Qahwash, I. et al. *The Journal of Biological Chemistry* **2007** 282 (51):36987–36997.

P08 A Robustness Screen Approach to Identifying Functional Group Incompatibilities in the Kumada Cross-Coupling

Jeanne Masson-Makdissi, XiYe (Kaylie) Hua, Stephen G. Newman*, Department of Chemistry, University of Ottawa, Ottawa, ON, K1N 6N5, stephen.newman@uottawa.ca

The Kumada coupling was the first biaryl cross-coupling reaction developed, allowing C-C bond formation between a Grignard reagent and an aryl, alkyl or vinyl halide via Pd or Ni catalysis. Despite its effectiveness, chemists shy away from using this method due to chemoselectivity issues that arise from the high reactivity of the Grignard. However, which functional groups can be tolerated in this transformation have not been clearly identified in the literature, hindering applications. In interest of expanding the scope of the Kumada coupling, we decided to use the inexpensive and time-efficient “robustness screen” method introduced by Glorius *et al*.[1] This data is then used to identify limitations that may be overcome by reaction design, optimization, and ligand development.



1) Glorius *et al. Nature Chemistry*, **2013**, 5, 597-601.

P09 Online Reaction Monitoring: New Insights into the Mechanisms of 3-Methylpentanoic Acid with Meldrum's Acid

Martine Monette, Anna L. Dunn, Anna Codina*, David A. Foley, Brian L. Marquez and Mark T. Zell. *Bruker UK Limited, Banner Lane, Coventry CV4 9GH, United Kingdom. Anna.Codina@bruker.com

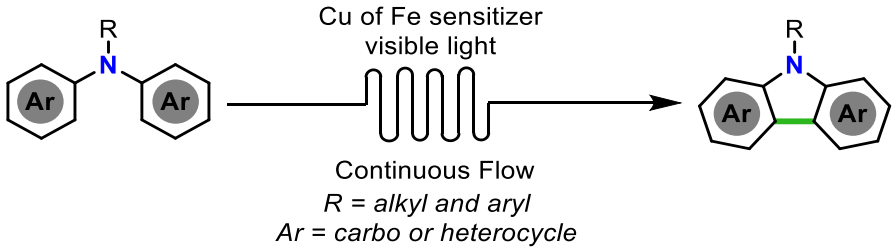
Process analytical technology (PAT) is routinely used to monitor reactions; however, most monitoring methods require some type of calibration step to normalize the output to relate concentration versus time.[1] Even then, it may not be readily apparent which species in the reaction matrix are responsible for a given change in analytical response. NMR overcomes these limitations as it inherently provides a quantitative signal response based on the number of nuclei, and it is the primary structural elucidation tool for small molecule characterization.[2] Online NMR spectroscopy is a powerful tool for organic process monitoring and understanding reaction mechanisms. Multiple designs systems have been reported which take advantage of the ability to track reaction progression in real-time with minimal disturbance to the reaction matrix.[3] Herein, we demonstrate the use of online NMR spectroscopy for the mechanistic understanding and comprehensive analysis of the reaction of 3-methylpentanoic acid with Meldrum's acid.[4]

1. Chanda A., Foley D.A, *Org. Process Res. Dev.*, **2015,** *19*, 63.
2. Holzgrabe U., *Prog. Nucl. Magn. Reson. Spectrosc.*, **2010**, *57*, 229.
3. Foley D.A., Bez E., Codina A., Colson K.L., Fey M., Krull R., Piroli D., Zell M.T., Marquez B.L., Anal. Chem., **2014**, *86*, 12008.
4. Dunn A.L, Codina A., Foley D.A, Marquez B.L., Zell M.T., *Magn. Reson. Chem.,* DOI: 10.1002/mrc.4317.

P10 Progress Toward New Photochemical Systems Using Fe-Based Sensitizers and O_2

Shawn Parisien Collette, Augusto C. Hernandez-Perez, Shawn K. Collins,* Center for Green Chemistry and Catalysis, Department of Chemistry, Université de Montréal, Mtl, Qc, H3T1J4, shawn.collins@umontreal.ca

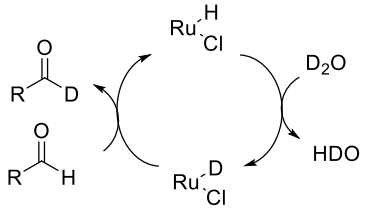
A photochemical synthesis of heterocycles employing photoredox catalysis has been developed that avoids the disadvantages associated with other traditional UV light mediated methods. The novel catalysis employs a copper-based sensitizer. Efforts to employ Fe-based sensitizers will be discussed. The use of a continuous flow strategy results in efficient use of oxygen as a stoichiometric oxidant, short reaction times and increased yields.



P11 Ruthenium Catalyzed Deuteration of Aldehydes with Methanol-d_4 and Deuterium Oxide

Wanying Zhang, Eric Isbrandt, Mohammad P. Jamshidi, Stephen Newman,* Department of Chemistry, University of Ottawa, Ottawa, ON, K1N 6N5, wzhan017@uottawa.ca

Deuterium-labeled compounds have useful applications in organic and bioorganic mechanistic studies.[1,2] Deuterated aldehydes are particularly useful, but current methods of synthesis pose significant challenges and limitations.[3] The catalytic properties of the ruthenium catalyst, $RuHCl(CO)(PPh_3)_3$, were explored to perform a direct H/D exchange on aldehydes, avoiding the need for multi-step synthesis. Methanol-d_4 and D_2O were found to be successful deuterium sources for the exchange. Moderate deuteration could be obtained in a single experiment, while iterative one-pot experiments allowed high deuterium incorporation to occur. Reaction optimization and scope evaluation will be discussed.

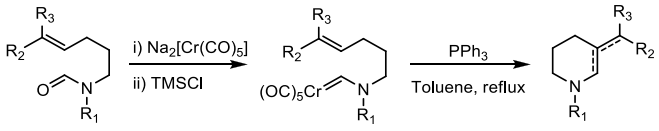


1. Bai, W.; Lee, K.-H.; Tse, S. K. S.; Chan, K. W.; Lin, Z.; Jia, G., *Organometallics.* **2015,** *34* (15), 3686-3698.
2. Krishe, M. J., Shibahara, F.; Bower, J. F., *J Am Chem Soc.* **2008,** 130(43), 14120-14122.
3. Spletstoser, J. T.; White, J. M.; Georg, G. I., *Tetrahedron Letters.* **2004,** *45* (13), 2787-2789.

P12 Toward a Catalytic Cyclisation of Chromium Aminocarbene Tethered to Alkenes

Kevin Assouvie and Claude Spino*, Département de chimie, Université de Sherbrooke, Sherbrooke, Québec, J1K 2R1, Claude.Spino@USherbrooke.ca

We have designed a methodology for the synthesis of *N*-heterocyclic compounds using chromium aminocarbenes tethered to alkenes of different electronics. We have discovered that we can modulate the reactivity of the chromium aminocarbene toward the double bond with the use of triphenylphosphine[1]. It is possible to access pyrrolidines, piperidines, isoquinolines and other *N*-heterocyclic motifs using this method. One of the major issues is the use of a stoichiometric amount of chromium hexacarbonyle which is toxic, not eco-friendly and expensive. There is no example to date of a catalytic use of metallic chromium to prepare *N*-heterocyclic compounds. We here present our efforts toward the developement of a catalytic use of metallic chromium to catalyse the cyclisation of chromium aminocarbene tethered to alkenes.

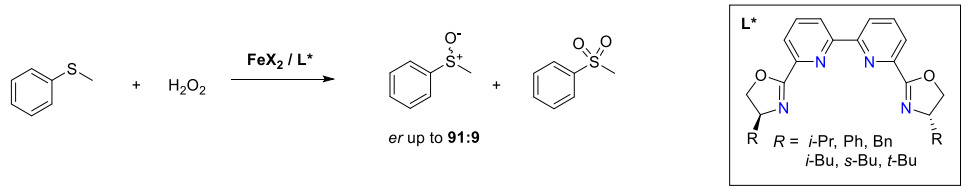


1) M. Déry, K. Assouvie, N. Heinrich, I. Rajotte, L.-P. D. Lefebvre, M.-A. Legault, C. Spino. *Org. Lett.*, **2015**, *17* (5), pp 1312–1315.

P13 New Chiral Bis(oxazolinyl) Bipyridine Ligands and Application in the Iron Catalyzed Asymmetric Oxidation of Sulfides Using Hydrogen Peroxide

Angela Jalba, Guillaume Levitre and Thierry Ollevier*, Département de chimie, Pavillon Alexandre-Vachon, Université Laval, 1045 avenue de la Médecine, Québec (Québec) G1V 0A6. E-mail: thierry.ollevier@chm.ulaval.ca

Chiral sulfoxides are important compounds for the preparation of biologically active compounds or as chiral ligands in enantioselective catalysis. The asymmetric oxidation of sulfides using chiral metal catalysts and H_2O_2 is one of the best ways to prepare enantio-enriched sulfoxides because these oxidizing systems can generally be applied to a wide range of substrates, and only a catalytic amount of the metal complex is necessary. Following our studies in iron catalyzed asymmetric catalysis,[1] C_2 symmetrical bis-(oxazolinyl)bipyridine chiral ligands, used with FeX_2 and H_2O_2, were found to be very effective in the asymmetric oxidation of aromatic sulfides. The synthesis and the application of such systems for the asymmetric oxidation of thioanisole will be presented.

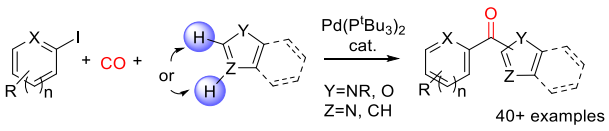


[1] a) Ollevier, T.; Plancq, B. *Chem. Commun.* **2012**, *48*, 2289-2291; b) Plancq, B.; Ollevier, T. *Chem. Commun.* **2012**, *48*, 3806-3808; c) Lafantaisie, M.; Mirabaud, A.; Plancq, B.; Ollevier, T. *ChemCatChem* **2014**, *6*, 2244-2247; d) Ollevier, T.; Keipour, H. in Topics in Organometallic Chemistry (Ed. E. Bauer), Springer, Heidelberg, 2015.

P14 An Electrophilic Approach to the Palladium-Catalyzed Carbonylative C–H Functionalization of Heterocycles

Jevgenijs Tjutrins, Bruce A. Arndtsen*, Department of Chemistry, McGill University, Montreal, Quebec, H3K 0B8, bruce.arndtsen@mcgill.ca

Palladium catalyzed C-H functionalization reactions have shown to be an attractive approach in synthetic organic chemistry, with applications ranging from synthesis of pharmaceuticals to complex polymeric materials. Compared to cross coupling reactions, these methods can be more efficient and atom economical, since they do not require prefunctionalizion of the substrates. While many transition metal catalyzed C-H arylation, alkylation, reactions of arenes and heteroarenes have been developed, transition metal catalyzed carbonylative C-H functionalizations of such substrates have not been extensively studied, presumably due to the inhibitory effect of CO on C-H activation. Herein we describe a novel palladium catalyzed approach to intermolecular carbonylative C-H functionalization of various heterocycles to generate aryl-(hetero)aryl ketones using stable, commercially available reagents.

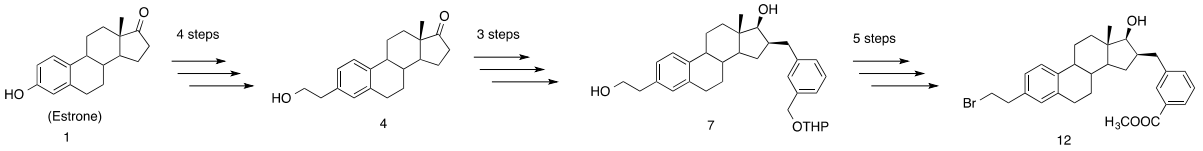


Tjutrins, J.; Arndtsen, B. A. *J. Am. Chem. Soc.* **2015**, *137*, 12050.

P15 Chemical Synthesis and Characterization of 3-(2-Bromoethyl)-16β-(*m*-carbomethoxybenzyl)-17β-hydroxy-1,3,5(10)-estratriene

Maxime Lespérance, René Maltais, Marie-Claude Trottier, Donald Poirier*, Laboratory of Medicinal Chemistry, CHU de Québec – Research Center and Université Laval, Québec, QC, maxime.lesperance.1@ulaval.ca

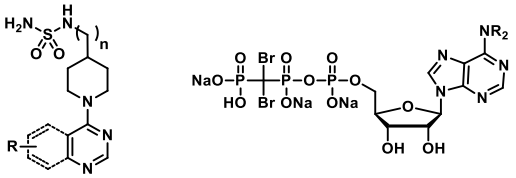
Steroid chemistry continues to be an active field in medicinal chemistry and organic synthesis, which supports the development of new steroidal drug candidates. In our continuing effort to identify bioactive molecules, we developed a new synthetic route for the synthesis of steroidal ester derivative **12** starting from the natural product estrone **1.** The first four steps (phenolic activation, vinylation, epoxidation and regioselective epoxide opening) lead to the formation of the key ethylalcohol intermediate **4**. The subsequent introduction of a benzylic side-chain at position-C16 through an aldolic condensation, a stereoselective reduction of the resulting conjugated ketone and a catalytic hydrogenation provided **7**. Five additional steps (bromation, THP hydrolysis, Jones'oxidation, ketone reduction and methylation) were necessary to obtain **12**. In summary, a synthesis of twelve steps provided the desired steroid derivative **12** in an overall yield of 6.4%. The detailed synthesis and complete characterization of final compound **12** will be presented.



P16 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 the United States and Western Europe. Thus far, there is no pharmaceutical 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 (ENPP1) promotes the mineralization process of the aortic valve. In this context, ENPP1 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*, 1191-1202.
(2) Shayhidin, E. E.; Forcellini, E.; Boulanger, M.-C.; Mahmut, A.; Dautrey, S.; Barbeau, X.; Lagüe, P.; Sévigny, J.; Paquin, J.-F.; Mathieu, P. *Br. J. Pharmacol.* **2015**, *172*, 4189-4199.

P17 ZMPSTE24 protease inhibitors as senescence agonists for cancer chemotherapy

Dimitrios Xanthopoulos‡, Alexios N. Matralis‡, Geneviève Huot¶, Gerardo Ferbeyre¶ and Youla S. Tsantrizos‡*, ‡Department of Chemistry, McGill University, Montreal, Quebec, H3A OB8, ¶Département de biochimie et médecine moléculaire, Université de Montréal, Montreal, Quebec, H3T 1J4, youla.tsantrizos@mcgill.ca

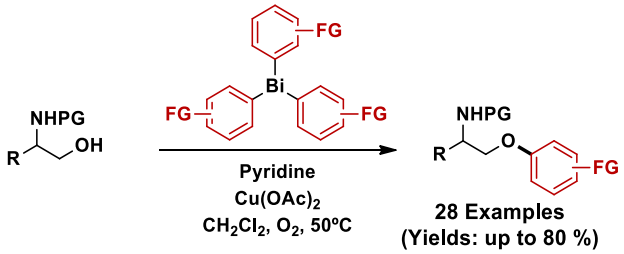
ZMPSTE24 is a zinc metalloproteinase responsible for the maturation of the nuclear envelope filament lamin A. Inhibition of ZMPSTE24 leads to accumulation of the precursor protein, pre-lamin A, leading to premature cell senescence. Cellular senescence is an attractive way of combating cancer since, unlike apoptosis, it is a permanent cell cycle arrest that halts tumorigenesis and activates an antitumor immune response.[1,2]
To date, selective inhibitors of ZMPSTE24 have not been identified. Interestingly, some HIV-1 protease inhibitors were accidently found to also inhibit ZMPSTE24 with low micromolar potency.[3] Based on structural features of these inhibitors, we initiated SAR studies, synthesizing and testing a library of 35 analogues.
We identified compounds that cause the accumulation of pre-lamin A and inhibit proliferation of osteosarcoma cells (U2OS), but do not inhibit the proliferation of normal fibroblasts (IMR90). The synthesis and biological evaluation of these compounds will be discussed.

1. Quigley, A. et al. Science, **2013**, 339, 1604.
2. Cairney, C. J., et al., Drug Discov. Today, **2012**; 17: 269-276.
3. Coffinier, C. et al. Proc. Natl. Acad. Sci. USA. **2007**, 104, 13432.

P18 Copper-Catalyzed *O*-Arylation of *N*-Protected 1,2-Aminoalcohols using Functionalized Organobismuth Reagents

Tabinda Ahmad and Alexandre Gagnon*, Département de chimie, UQÀM, Montréal, QC, H3C 3P8, Canada. Corresponding email address: alexandre.gagnon@uqam.ca

An efficient protocol for the copper-catalyzed *O*-arylation of *N*-protected 1,2-aminoalcohols using functionalized triarylbismuth reagents was developed. Catalytic amount of copper acetate promoted a C–O cross-coupling reaction under mild conditions. This reaction tolerates a wide diversity of functional groups giving access to a range of β-aryloxyamines which are important for the synthesis of medicinally relevant compounds and natural products.



1. Pauline Petiot, Julien Dansereau, Martin Hébert, Imene Khene, Tabinda Ahmad, Samira Samaali, Maxime Leroy, Francis Pinsonneault, Claude Y. Legault and Alexandre Gagnon, *Org. Biomol. Chem.*, **2015**, *13*, 1322-1327.
2. Cynthia Crifar, Pauline Petiot, Tabinda Ahmad and Alexandre Gagnon, *Chem. Eur. J.*, **2014**, *20*, 2755-2760.

P19 Can strong solvents like DMSO and DMF be used as injection solvents in reversed-phase flash chromatography?

Sab Hussaini, Bob Bickler*, Technical Specialist, Biotage, 10430 Harris Oaks Blvd., Suite C, Charlotte, NC USA 28269, USA Email : Bob.Bickler@biotage.com

Synthesis reactions are often conducted using DMSO and other highly solvating solvents (NMP, DMF) because their high boiling points allow for higher reaction temperatures. Retrieving the synthetic products from these solvents through evaporation, however, is nearly impossible and back extraction can be challenging.
Chromatographic purification should be an ideal method but because of these solvents' physical properties (density, viscosity, and high UV cutoff) many chemists shy away from them fearing high pressures or diminished separations.
In this poster we show the results of using both DMSO and DMF as dissolution solvents and provide guidelines for using them successfully in reversed-phase flash purification.

P20 Synthesis of azapeptide modulators of the prostaglandin $F_{2\alpha}$ receptor as potential therapeutics for prevention of preterm labour

F. Mohammadpour,[a] S. Chemtob,[b] X. Hou[b], W. D. Lubell[a*], [a]Département de chimie and [b]Département de Pédiatrie, Université de Montréal, P.O. Box 6128, Succursal Centre-ville, Montréal, QC H3C 3J7, Canada, william.lubell@umontreal.ca

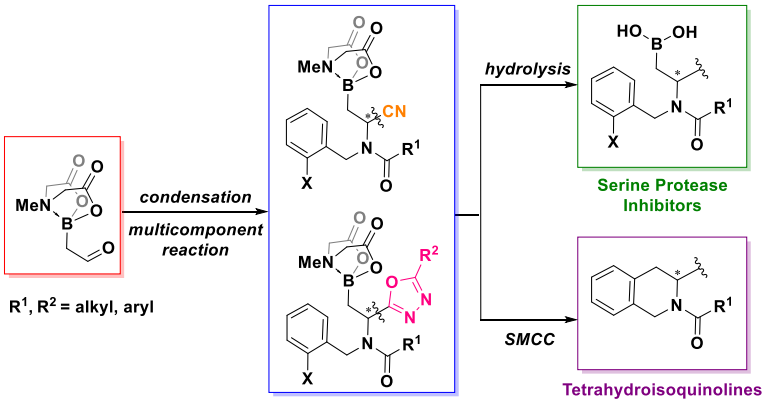
Preterm delivery accounts for nearly three quarters of all perinatal mortality, and the incidence of preterm birth has risen continuously over the last 30 years indicating the need for new therapeutics to safely inhibit uterine contractions and prolong pregnancy. Targeting the prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) receptor (FP) to design therapeutic agents based on peptide leads, we have found aza-amino acyl proline analogues[1] that reduce $PGF_{2\alpha}$-induced uterine contractions and modulate G protein signaling. Our presentation will focus on structure-activity relationships of these azapeptide modulators that are being pursued featuring alkylation of aza-glycinyl-proline analogues, and copper-catalyzed reactions on aza-propargynylglycinyl residues.

1. Bourguet, C. B.; Goupil, E.; Tassy, D.; Hou, X.; Thouin, E.; Polyak, F.; Hebert, T. E.; Claing, A.; Laporte, S. A.; Chemtop, S.; and Lubell, W. D. *J. Med. Chem.* **2011**, *54*, 6085-6097.

P21 Modular assembly of heteroatom-rich sp^3-boron-containing molecules as a versatile platform towards heterocycle synthesis

Joanne Tan, Julia Stille, Tatiana Rogova, John R. Frost and Andrei K. Yudin*, Department of Chemistry, University of Toronto, Toronto, Ontario, M5S 3H6, ayudin@chem.utoronto.ca

α-Boryl aldehydes, developed by our lab, have been subjected to many chemoselective transformations while displaying unusual protecting group stability.[1] Herein, we describe the synthesis of novel boron-containing molecules from α-boryl aldehydes using condensation-driven chemistry. These molecules contain heteroatom-rich motifs that are commonly found in serine protease inhibitors. The enantioselective synthesis and biological evaluation of these molecules will also be highlighted. In addition, these molecules participate in Suzuki-Miyaura cross coupling (SMCC) to afford tetrahydroisoquinolines (TIQ). This strategy provides a facile and modular approach towards inhibitor design and TIQ functionalization.

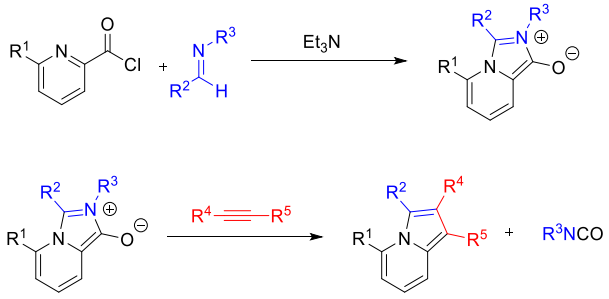


1. a) He, Z; Yudin, A. K. *J. Am. Chem. Soc.* **2011**, *133*, 13770-13773. b) St. Denis, J. D.; He, Z.; Yudin, A. K. *Org. Biomol. Chem.* **2012**, *10*, 7900-7902. c) St. Denis, J. D.; Zajdlik, A.; Tan, J.; Trinchera, P.; Lee, C. F.; He, Z.; Adachi, S.; Yudin, A. K. *J. Am. Chem. Soc.* **2014**, *136*, 17669-17673.

P22 Synthesis and Reactions of Mesoionic Imidazolium Heterocycles

H. Erguven, B.A. Arndtsen*, Chemistry Department, McGill University, 801, Sherbrooke Street West, Montreal, QC, H3A 2K6; bruce.arndtsen@mcgill.ca

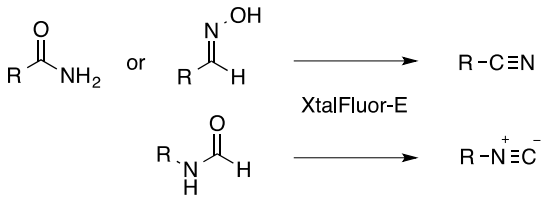
Munchnone-like dipoles are known for their cycloaddition reactivitiy towards dipolarophiles. Nitrogen-containing substituted heterocycles can be synthesized by utilizing this method. In this work, a new type of dipole and its reactivity towards dipolarophiles is investigated. Mesoionic imidazolium heterocycles can be obtained by reacting an imine with 2,6-pyridinedicarbonyl dichloride in the presence of a base. As the other 1,3-dipoles, these dipoles can react with dipolarophiles such as alkynes. This approach opens a new way to synthesize substituted indolizines. A number of different 1,3-dipoles and cycloadducts have been prepared and characterized.



P23 Utilization of XtalFluor-E as Dehydration Agent for the Synthesis of Nitriles and Isonitriles

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

Nitriles and isonitriles are key building blocks in organic synthesis. Nitriles are useful for the preparation of various compounds, including pharmaceuticals, agrochemicals and materials, while isonitriles are required for many synthetic transformations (e.g. Ugi reaction). The dehydration of amides, aldoximes and formamides is the common method for the preparation of these compounds. Numerous reagents can affect this transformation, but most of these suffer from drawbacks, as uncontrollable reactivity, high cost, instability, and toxicity. Herein, we described the formation of nitriles from both amides and aldoximes, and isonitriles from formamides, using XtalFluor-E ($[Et_2NSF_2]BF_4$). In the two cases, excellent yields were obtained (up to 99%) under mild conditions for a wide range of substrates.

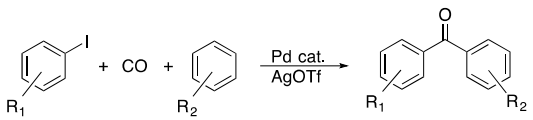


1. Keïta, M.; Vandamme, M.; Mahé, O.; Paquin, J.-F. *Tetrahedron Lett.* **2015**, 56, 461.
2. Keïta, M.; Vandamme, M.; Paquin, J.-F. *Synthesis* **2015**, DOI: 10.1055/s-0034-1378881.

P24 Direct Intermolecular Carbonylative C–H Functionalization of Unactivated Arenes

R. Garrison Kinney, Bruce A. Arndtsen* Department of Chemistry, McGill University, Montreal, Qc, Canada, H3A 0B8, bruce.arndtsen@mcgill.ca

Diaryl ketones represent an important class of compounds in the production of biologically relevant molecules and other useful chemicals. Classic synthetic routes to these compounds rely on Friedel-Crafts chemistry, or a palladium catalyzed carbonylative cross coupling reaction of Ar-X and M-Ar. Both methods rely on pre-synthesized highly reactive reagents, decreasing the overall efficiency of the desired transformation and generating extraneous waste. A direct carbonylative C-H functionalization of these arenes would allow access to diaryl ketones without the need for prefunctionalization. While there are minimal examples of functionalizing more activated arenes[1], to our knowledge, there are no examples of the direct intermolecular carbonylative functionalization of very benign arenes, such as benzene. An efficient method for the carbonylative functionalization of benzene and benzene derivatives has been developed. This reaction is thought to proceed through an unusual, highly electrophilic, aroyl triflate intermediate.

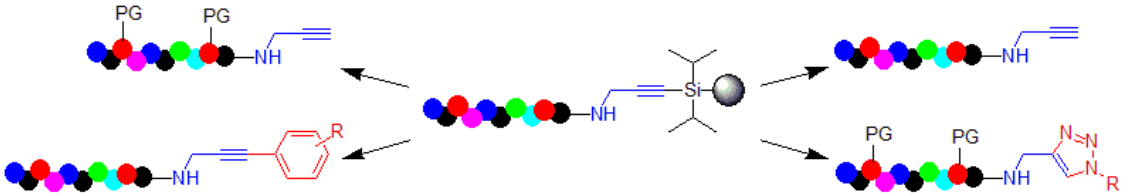


1. a) Arndtsen, B. A. *et al J. Am. Chem. Soc.* **2015**, *137*, 12050. b) Beller, M. *et. al. Angew. Chem., Int. Ed.* **2010**, *49*, 7316. c) Larock, R. C. *et. al. J. Org. Chem.* **2002**, *67*, 5616. d) Skrydstrup, T. *et. al. Chem. Commun.* **2015**, *51*, 1870.

P25 Silyl-Based SAM-Linkers for the Preparation of *C*-terminally Modified Peptides

M. Strack[†,‡], W. D. Lubell[†], N. Metzler-Nolte[‡], H. B. Albada[‡,*], [†] Département de Chimie, Université de Montréal, Canada; [‡]Inorganic Chemistry I, Ruhr-University Bochum, Germany.

The application of peptides across the chemical landscape creates an ongoing interest to develop novel strategies for the synthesis of their C-terminal analogs. The new family of **S**ilyl-based **A**lkyne **M**odifying (**SAM**)-Linkers responds effectively to the challenges in the preparation of C-terminal modified peptide conjugates. Compatible with Fmoc-based solid-phase peptide synthesis, the novel SAM2-linker enables the convenient preparation of propargylamides that have been used in one-pot procedures to prepare 1,2,3-triazole analogs. In this contribution, recent advancements in the preparation and utilization of SAM-linkers will be presented.

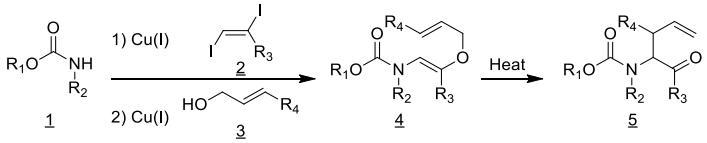


1. a) Strack, M. *et al*. *J. Org. Chem.*, **2012**, *77*, 9954. b) Strack, M., Metzler-Nolte N., Albada, H. B. *Org. Lett.*, **2013**, *13*, 3126. c) Strack, M., Metzler-Nolte N., Albada, H. B. *Synthesis*, **2014**, *46*, 2293.

P26 Synthesis of γ,δ-Unsaturated α-Aminoketones Using a Tandem Copper-Catalyzed Vinylation Reaction Followed by a Claisen Rearrangement

Simon Ricard, Benoit Daoust and Alexandre Gagnon*, Département de chimie, UQÀM, Montreal, Qc, H3C 3P8, gagnon.alexandre@uqam.ca

Up to now, copper-catalyzed coupling reactions between nitrogenated compounds and vinyl diiodides were given very little attention and only few intramolecular examples can be found.[1] The interest of using the latter as coupling partner is to easily access β-nitrogenated vinyl iodides which can undergo a subsequent coupling reaction. Daoust's group developed an efficient method for the preparation of non-natural α-amino acids from amides by successive C-N and C-O functionalizations of *trans*-diiodoethene (2, R_3=H) followed by a Claisen rearrangement.[2] In this project, we wish to extend this method to carbamates (1), non-symmetric vinyl diiodides (2) and various allylic alcohols (3) in order to synthesize highly functionalized allyl vinyl ethers (4) which can be rearranged into γ,δ-unsaturated α-aminoketones (5). In this presentation, we will discuss our progress in the optimization of the method and its application to different substrates.

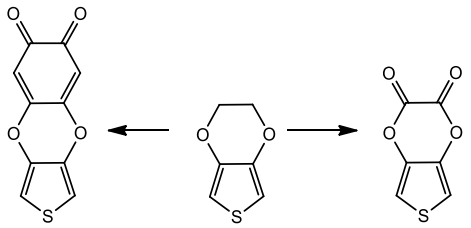


1. Jiang, B. *et al. Org. Lett.*, **2008**, *10*, 2737. 2. a) Daoust, B. *et al. Tetrahedron Lett.*, **2008**, *49*, 4196. b) Ricard, S. *et al. Manuscript in preparation*, **2015.**

P27 Cathode material for lithium ion battery based on functionnalized poly(3,4-ethylenedioxythiophene) (PEDOT)

Danny Chhin, Steen Brian Schougaard*, Department of chemistry, UQÀM, Montreal, QC, H2X 2J6, steenbs2@yahoo.com

Demanding applications such as electric vehicle and stationary energy storage are pushing the energy and power density limits of current inorganic intercalation material for lithium ion battery. Therefore, there is high interest in exploring new electrode materials which exhibits high energy density, fast kinetics, electrochemical stability while possessing high electronic and ionic conductivity. Of particular interest is PEDOT which is a polymer known to be highly stable and highly conductive. By adding conjugated carbonyl moieties on PEDOT, additional capacity can be obtained from the reversible reduction of carbonyl functionalities.[1] In this presentation, we will present our progress in synthesizing PEDOT with added conjugated carbonyl functionalities.



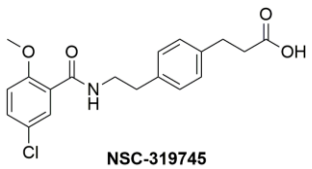
1. Song, Z., and Zhou, H. Energy Environ. Sci., **2013**, *6*, 2280–2301.

P28 Investigation Around the DNMT Activity of Selected NSC Series

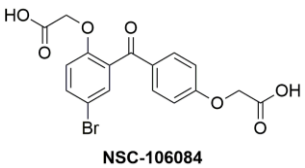
M. Leroy, M. Roy-Collinet, A. Kabro, H. Lachance and A. Gagnon*, gagnon.alexandre@uqam.ca, Departement chimie, UQAM, H2X 2J6, Qc, Montréal

Epigenetics is the study of the chromosomal mechanisms that induce inheritable changes in gene expression without alteration of the DNA sequence. These modifications translate into changes in the chromatin structure that favor or inhibit gene expression. DNA methylation is a stable but reversible epigenetic modification that occurs at position 5 of cytosine. This process is catalyzed by DNA Methyltransferases (DNMTs). The inhibition of DNMTs can lead to reactivation of tumor suppressor genes via their demethylation. Thus, the DNMTs constitute an attractive target for drug development. The current marketed drugs that inhibit DNMTs are analogues of nucleosides that present major liabilities. New potent and bioavailable non-nucleoside inhibitors of DNMTs are thus needed. We recently reported our investigation on NSC-319745.1 In this presentation, we will discuss our results on the structure-activity relationship of two NSC compounds: NSC-319745 and NSC-106084.

[1] Med. Chem. Commun., 2013, 4, 1562.



NSC-319745

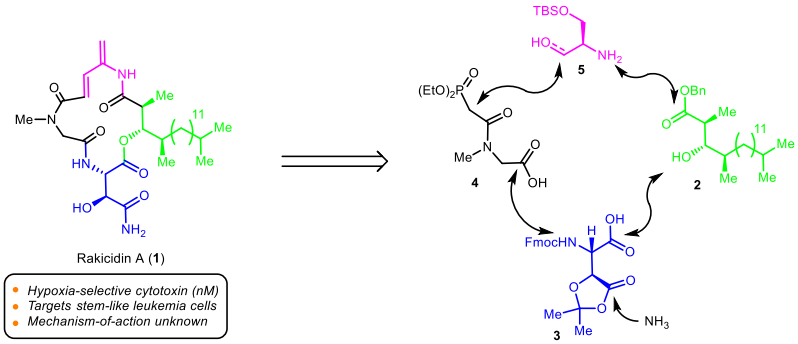


NSC-106084

P29 Total Synthesis of the Natural Depsipeptide Rakicidin A

Michail Tsakos,[a,b] Lise L. Clement,[b] Eva S. Schaffert,[b] Frank N. Olsen,[b] Sebastiano Rupiani,[b] Nikolaj L. Villadsen,[b] Kristian M. Jacobsen,[b] Rasmus Djurhuus,[b] and Thomas B. Poulsen[b]*
[a] Chemistry Department, McGill University, Montreal, QC, H3A 0B8. [b] Department of Chemistry, Aarhus University, 8000 Aarhus C, Denmark. thpou@chem.au.dk

Rakicidin A (**1**) is a natural macrocyclic depsipeptide that displays nanomolar cytotoxicity in cancer cells with selectivity towards hypoxic cancer cells and stem-like leukemia cells with an as yet unknown mechanism-of-action. Structurally, Rakicidin A is characterized by a complex architecture comprising a *β*-hydroxy fatty acid side chain, and three unnatural amino acids: namely sarcosine, *β*-hydroxyasparagine and a vinylogous dehydroalanine. Our synthetic route to **1** features an organocatalytic cross-aldol reaction to complete the stereo-triad in fragment **2**, a highly hindered esterification reaction between fragments **2** and **3**, a Horner-Wadsworth-Emmons reaction to construct the macrolactone and an alcohol elimination to form the exocyclic double bond.

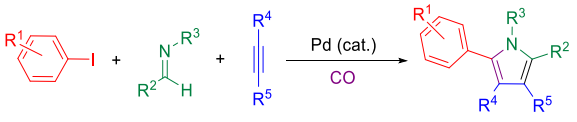


1. (a) Yamazaki, Y. *et al*. *Biol. Pharm. Bull.*, **2007**, *30*, 261. (b) Takeuchi M. *et al. Cancer Sci.*, **2011**, *102*, 591.

P30 From aryl iodides to 1,3-dipoles: a multicomponent route for the synthesis of pyrroles

Gerardo Martin Torres and Bruce A. Arndtsen*, Department of Chemistry. McGill University, 801 Sherbrooke Street West, Montreal, QC, H3A OB8, bruce.arndtsen@mcgill.ca

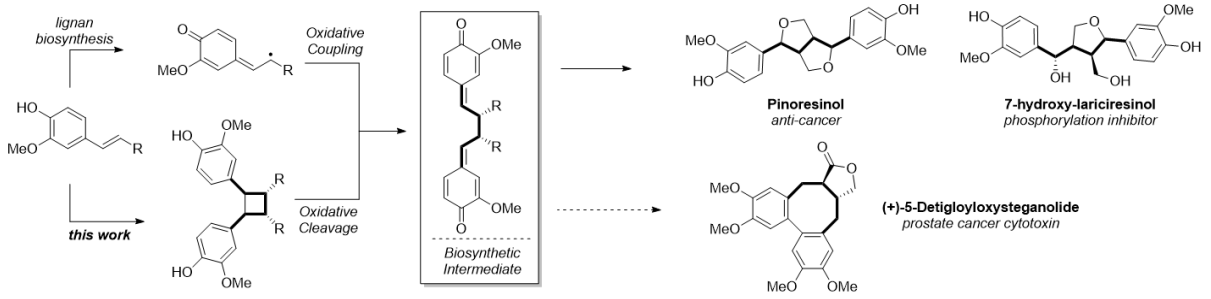
Pyrroles have found use in a broad variety of areas, ranging from components in biologically relevant compounds, to materials science and polymers. Nevertheless, approaches to construct pyrroles, especially highly substituted variants typically require multistep synthesis. These can be time consuming, create significant waste with each step, and make the generation and tuning of pyrroles an involved, iterative process. In recent years, multicomponent synthesis has arisen as an attractive route to prepare complex products from simple building blocks. In this work, a palladium catalyzed multicomponent synthesis of pyrroles is presented. The building blocks in this reaction are all simple: imines, aryl iodides, alkynes and CO, and are coupled together in a one pot, palladium catalyzed cascade. The mechanism of this transformation, catalyst design, reaction intermediates, and the diversity of pyrrole products available, will each be discussed.



P31 Utilizing an oxidative cyclobutane fragmentation in an efficient, biomimetic synthesis of lignan natural products

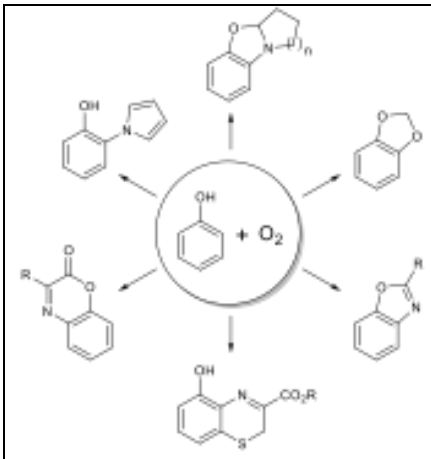
Anna K. F. Albertson, Jean-Philip Lumb*, Department of Chemistry, McGill University, Montreal, QC, H3A 0B8, jean-philip.lumb@mcgill.ca

Lignans comprise a vast array of highly oxygenated, polyaromatic natural products with important biological activities. Despite their significant structural diversity, the biosynthesis of lignans begins with the oxidative coupling of simple propenyl phenols. Attempts to mimic the biosynthetic coupling of such phenols have suffered from poor regio- and chemoselectivity. Recently, we demonstrated a novel method of accessing both furan and furanofuran lignans, utilizing the oxidative ring-opening of a cyclobutane. Here, we present the extension of this strategy to the synthesis cyclooctadiene natural products, such as the prostate cancer cytotoxin, (+)-5-Detigloyloxysteganolide C.



P32 Catalytic Aerobic Oxidation of Phenols as a Unified Approach for the Synthesis Heterocycles

Kenneth Virgel N. Esguerra, Matthew W. Halloran, Wenbo Xu, Jean-Philip G. Lumb*, Department of Chemistry, McGill University, Montreal, Quebec, H3A 0B8, jean-philip.lumb@mcgill.ca



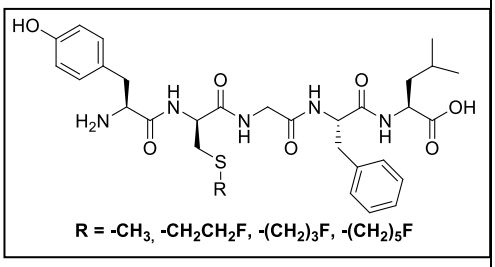
Heterocycles are ubiquitous in nearly all facets of applied chemistry. However, the majority of routes for their synthesis require cross-coupling reactions that utilize pre-functionalized starting materials, excess reagents and expensive rare-earth metal catalysts. We have developed a biomimetic approach for the synthesis of highly oxidized aromatic rings that employs *in situ* generation of *ortho*-quinones from simple phenols using molecular oxygen as the stoichiometric oxidant, generating water as the only by-product. This atom-economic transformation tolerates a vast array of functional groups, occurs at ambient temperature and utilizes an inexpensive copper catalyst. Applications to the synthesis of various nitrogen-, sulfur- and oxygen-containing heterocycles, including benzoxazoles, benzoxazinones, benzothiazines and N-arylated pyrroles will be described.

P33 Design, Synthesis and Evaluation of Selective ^{19}F-Enkephalin Analogs; A First Step in the Development of PET Tracers for DOP Imaging

Azadeh Pirisedigh, Yves Dory*, Louis Gendron*, Brigitte Guérin*, Dept de Chimie, Pharmacologie-Physiologie, Médecine Nucléaire et Radiobiologie, U. Sherbrooke, Sherbrooke, QC, J1H 5N4.

Opioid receptor imaging has proven valuable in disease management (pain, epilepsy, neurodegeneration, and addiction), drug administration and dosage studies. Only one opioid PET tracer with pronounced selectivity for delta opioid receptor (DOP) is currently available for application in humans; the [^{11}C-Me]naltrindole. However, this tracer cannot be used for quantitative measurements. Highly potent and selective PET tracers are therefore needed to further progress in this field[1]. Our objective is to prepare potent radiolabelled peptide-based DOP agonists for PET imaging studies. Our approach consists in labeling enkephalin analogs with more hydrophobic [^{18}F]-prostethic group to achieve high specific activity and facilitate/increase their stability and transport across the BBB.

We have successfully prepared a series of Tyr-D-Cys(S(CH_2)$_n$F)-Gly-Phe-Leu derivatives bearing ^{19}F-alkyl chains (n=2,3,5). The non-radioactive analogs showed excellent receptor binding affinity for DOP and their lipophilicities ($LogD_{7.4}$ values) increased with the chain length (from 0.04 to 0.95). Further *in vitro*/*in vivo* experiments with ^{18}F-labeled peptides as potential PET imaging agents are warranted.

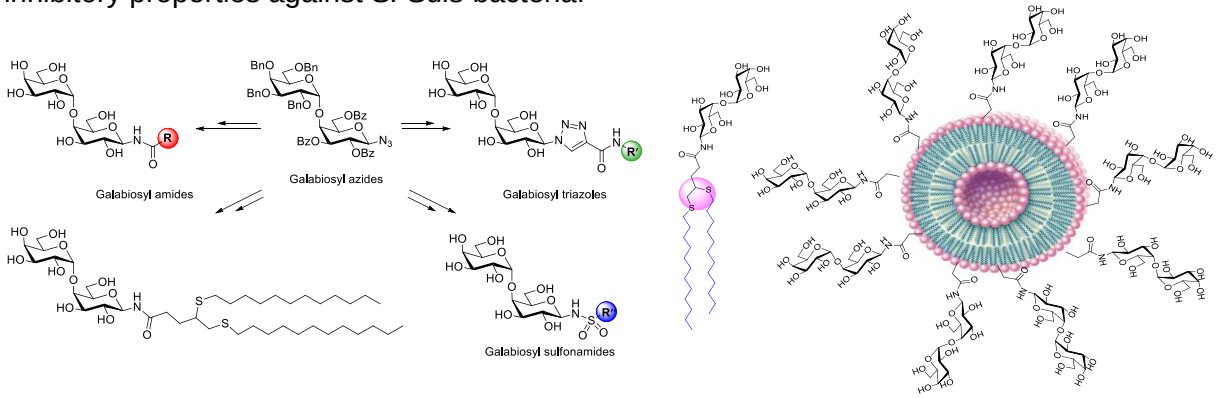


1. a) Matthews, P.M., *et all*, *Br J Clin Pharmacol*, **2012**. 73, 175. b) Henriksen, G. *et all. Brain*, **2008**,131,1171.

P34 Synthesis of Carbohydrate Nanoparticles and Analogs as Anti-Adhesins Against *Streptococcus suis* Infections

Elham Akbariromani , David *Goyard* and René ROY*, Département de chimie, UQÀM, Montréal, QC, H3C 3P8. roy.rene@uqam.ca

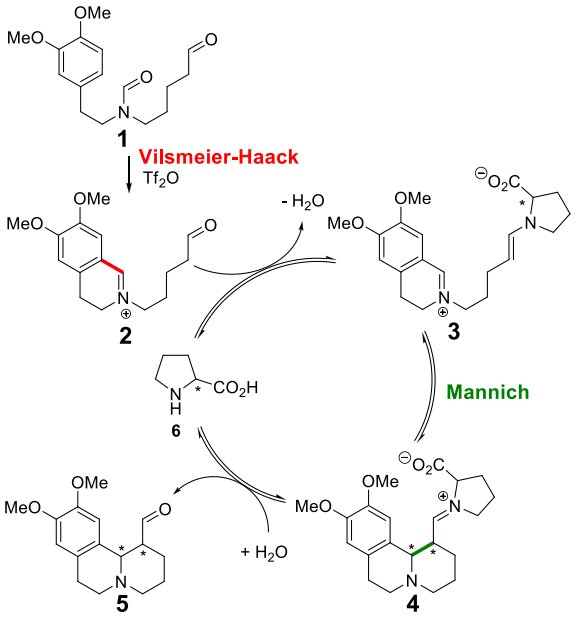
Three new collections of galabioside derivatives were synthesized as inhibitors of protein adhesions of *Streptococcus suis* strains. These collections of compounds such as galabiosyl -amides, -sulfonamides and -triazoles were prepared using galabiosyl azide as a starting precursor. We also have developed the methodology for the synthesis of biosensors for detecting *S. suis* bacteria. Furthermore, the preparation of new scaffolds for building hetero-glycodendrimers will be illustrated. These dendrimers will be also evaluated for their relative inhibitory properties against *S. Suis* bacteria.



P35 Study Towards a Stereoselective Synthesis of Quinolizidines by Sequential Intramolecular Vilsmeier-Haack and Asymmetric Organocatalyzed Mannich Reactions

Johanne Outin and Guillaume Bélanger*, Département de chimie, Université de Sherbrooke, Sherbrooke, QC, J1K 2R1, Guillaume.Belanger@USherbrooke.ca

Asymmetric organocatalysis has been extensively studied over the last decade and become one of the most promising fields in organic chemistry. We recently developed one pot sequential Vilsmeier-Haack and Mannich cyclization reactions with the aim to build quinolizidines as the core of several alkaloids. Although we demonstrated that the Vilsmeier-Haack reaction works nicely with a series of carbon nucleophiles, the ensuing Mannich cyclization is often of limited scope and with no stereoinduction. In order to overcome both of these limitations, this work combines the Vilsmeier-Haack reaction, run in the presence of an aldehyde, and organocatalysis with (chiral) secondary amines. So far, the reaction proved successful with achiral secondary amines. Mechanistic insights as well as recent development will be presented.

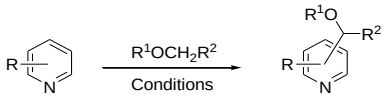


P36 Metal-free Minisci reaction: C–H alkylation of heteroarenes from unactivated ethers

Laurie-Anne Jouanno, Terry McCallum, Alexandre Cannillo, Louis Barriault*, Centre for Catalysis and Innovation, University of Ottawa, ON, K1N 6N5, Louis.Barriault@uottawa.ca

The Minisci reaction[1] is a well-known reaction that allows the C-H functionalization of heterocycles through the formation of a radical generated *in situ* in the presence of metal salts (Ag, Ir, [2]...). Due to the high interest of this reaction (easy preparation of complex molecule from simple commercial synthons), our group is interested in developing a metal-free Minisci reaction by generating the radical either thermally or photochemically.

In this context, new conditions to derivatize heterocycles have been developed. The activation of alkyl ethers through the formation of the corresponding radical was easily realized using potassium persulfate under thermal conditions without any photoredox catalysts. This method was successfully applied to prepare several substituted heterocyclic aromatic compounds.



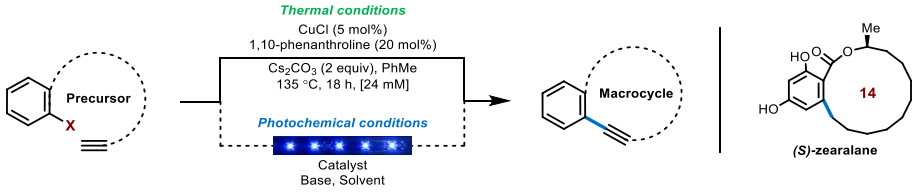
C-H functionalization of heterocycles with unactivated alkyl ethers

1. For reviews: (a) Tauber, J.; Imbri, D.; Opatz, T. *Molecules* **2014**, *19,* 16190-16222; (b) Duncton, M. A. J. Med. *Chem. Commun*. **2011**, *2*, 1135-1161.
2. Jin, J., Mac Millan, D. W. C*. Angew. Chem. Int. Ed.* **2015**, *54*, 1565-1569.

P37 Advances in Thermal and Photochemical Cu(I)-Catalyzed Macrocyclic Sonogashira-Type Cross-Couplings

Jeffrey Santandrea, Anne-Catherine Bédard, Clémentine Minozzi and Shawn K. Collins*, Département de Chimie, Centre in Green Chemistry and Catalysis, Université de Montréal, Montréal, Québec, Canada, 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 the 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 thermal and photochemical copper-catalyzed Sonogashira protocols performed at high-concentrations are described as alternatives to Pd-catalyzed methods to access a wider range of compounds and pharmaceutically relevant motifs such as polyketide-derived resorcylic acid lactones.[1]

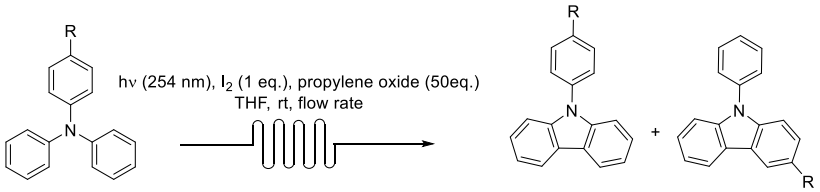


1. Santandrea, J.; Bédard, A.-C.; Collins, S. K. *Org. Lett*. **2014**, *16*, 3892-3895.

P38 A U.V Light Mediated Synthesis of Carbazoles Via Flow Chemistry

Antoine Caron, Augusto César Hernandez Perez, Shawn Collins*, Département de Chimie, Université de Montréal, Mtl, QC, H3T 1J4, shawn.collins@umontreal.ca

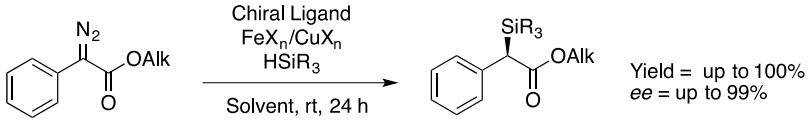
An evaluation of a UV-light mediated synthesis of carbazoles from various electronically different triaryl amines under continuous flow conditions has been conducted. In general, triaryl amines bearing electron-rich groups tend to produce higher yields than triaryl amines possessing electron-withdrawing groups. The incorporation of nitrogen-based heterocycles, as well as halogen-containing arenes in carbazole skeletons was well tolerated, and often synthetically useful complementarity was observed between the UV-light and visible-light (photoredox) methods.



P39 Iron and Copper Catalyzed Highly Enantioselective Carbenoid Insertion into Si–H Bonds

Hoda Keipour and Thierry Ollevier* Département de chimie, Pavillon Alexandre-Vachon, Université Laval, 1045 avenue de la Médecine, Québec (Québec), G1V 0A6. thierry.ollevier@chm.ulaval.ca

Chiral silanes are versatile intermediates for stereoselective transformations in organic synthesis. Transition metal catalyzed carbenoid insertion into Si–H bonds provides a direct and efficient method for the synthesis of chiral silane containing compounds. The reaction of alkyl α-diazophenylacetate with various silanes was performed in the presence of iron and copper salts together with a chiral ligand. In order to find the optimal the reaction conditions, a screening of a series of C_2 symmetrical chiral ligands was performed in the presence of various iron and copper salts.[1] These salts proved to be very efficient, when used with a selection of chiral ligands, leading to the corresponding α-silylesters with excellent yields and excellent enantioselectivities.



1. a) Ollevier, T.; Plancq, B. *Chem. Commun.* **2012**, *48*, 2289–2291. b) Plancq, B.; Ollevier, T. *Chem. Commun.* **2012**, *48*, 3806–3808. c) Lafantaisie, M.; Mirabaud, A.; Plancq, B.; Ollevier, T. *ChemCatChem* **2014**, *6*, 2244–2247. d) Ollevier, T.; Keipour, H. in *Topics in Organometallic Chemistry* (Ed.: E. Bauer), Springer, Heidelberg, 2015.

P40 Chemical Probe Development Projects at Structural Genomics Consortium in Collaboration with Canadian Academic Groups

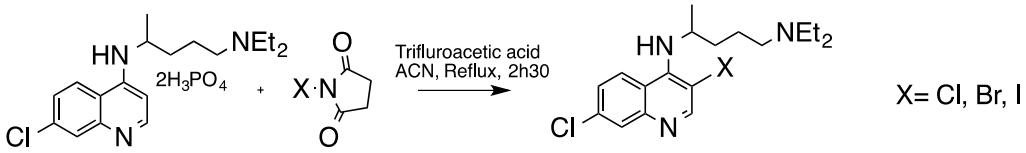
Santha Santhakumar*, Aled Edwards, Cheryl Arrowsmith, Peter Brown, Raymond Hui, Matthieu Schapira and Masoud Vedadi, Structural Genomics Consortium, University of Toronto, Toronto, ON, M5G 1L7, santha.santhakumar@uoronto.ca

The Structural Genomics Consortium (SGC) is an international public-private partnership that supports the discovery of new medicines through open-access research. Expanding from its initial to scope to determine the 3D structures targeting human proteins of biomedical importance and proteins from human parasites that represent potential drug targets, SGC is involved in developing chemical probes in collaboration with pharma partners and academic groups. ChemNet is a NSERC / CREATE funded medicinal chemistry training program for Canadian chemistry graduate students and post-doctoral fellows, and involved in chemical probe identification projects in collaboration with SGC and pharma partners. Overview of chemical probe identification projects at SGC, and overview of chemical probe identification projects, in the ChemNet program, in collaboration with Canadian academic chemistry laboratories will be presented.

P41 Restoring Chloroquines Efficacy: Synthesis and Characterization of 3-Iodo-Chloroquine as Potent Antimalarial and Inhibitor of Chloroquine Resistance in *P.falciparum*

Benita Kapuku[§], Dagobert Tazoo[§], Sonia Edaye[¥], Elias Georges[¥], Prof Scott Bohle[§*], [§]Chemistry Dept, [¥]Inst. Of Parasitology, McGill University, Montreal, QC, H3A 0G4, Scott.Bohle@McGill.ca

Malaria is a protozoan disease caused by the parasite Plasmodium, which is transmitted to humans by infected female mosquitoes. The parasite invades the red blood cells and breaks down hemoglobin to its end-product heme. Chloroquine (CQ), which was a highly effective antimalarial, in use since World War II, has now been rendered ineffective due to the build up of resistance. Mutations in Plasmodium falciparum chloroquine resistance transporter (PfCRT) are believed to be responsible for the rise of resistance to chloroquine. Our group has developed new synthesis to 3-halo-CQ derivatives (3-Chloro-CQ, 3-Bromo-CQ and 3-Iodo-CQ), which were evaluated against CQ-susceptible and -resistant *P. falciparum*. All three 3-halo-CQ derivatives were toxic to different strains of *P. falciparum,* with 3-Iodo-CQ (3ICQ) being more effective. At low nano-molar concentrations 3ICQ was found to be more effective than verapamil at sensitizing CQ-resistant parasites to chloroquine.

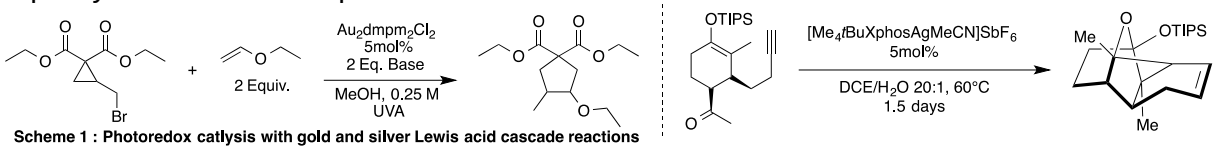


1) Ecker, A., et al., *PfCRT and its role in antimalarial drug resistance.* Trends Parasitol, 2012. **28**(11): p. 504-14.
2) Dagobert Tazoo, Sonia Edaye, Elias Georges, Prof Scott Bohle- Submitted

P42 Cascade Reactions Involving Gold Photoredox and Silver Catalysis

Julie Brousseau, Francis Barabé, Louis Barriault*, Centre for Catalysis Research and Innovation, University of Ottawa, Ottawa, ON, K1N 6N5, Louis.Barriault@uottawa.ca

Recently, our group has been interested in the potential of dimeric gold complexes for photoredox catalysis.[1] The use of gold allows for activation of non-activated carbon-halogen bonds. Presented here are the results of the investigation of a radical cascade that involves an intermolecular formal [3+2] cyclization, starting from 3 membered-ring substrates.
Our group has also investigated phosphine ligated silver complexes for their lewis acid properties. The reactivity of this transition metal enables interesting reaction cascades. Among others, we have studied a 6-endo *dig* / Prins / Prins cyclization cascade, which leads to the formation of 3 new covalent bonds.
These methodologies could be applied to the formation of subsequent cycles, allowing the rapid synthesis of natural product cores.



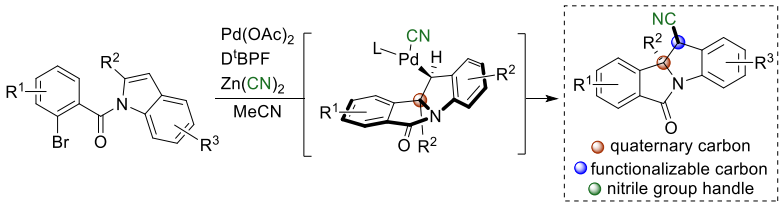
Scheme 1 : Photoredox catlysis with gold and silver Lewis acid cascade reactions

[1] Revol, G.; McCallum, T.; Morin, M.; Gagosz, F.; Barriault, Angew. Chem. Int. Ed. 2013 , 52 , 13342.

P43 Dearomative Indole Bisfunctionalization via a Diastereoselective Palladium-Catalyzed Arylcyanation

David A. Petrone, Andy Yen, Nicolas Zeidan, and Mark Lautens*, Davenport Research Laboratories, Department of Chemistry, University of Toronto, Toronto, Canada, M5S 3H6, mlautens@chem.utoronto.ca

The indoline core represents a ubiquitous structural motif found in a wide array of bioactive alkaloids that offer therapeutic potential.[1] Considerable efforts have been made towards accessing complex derivatives containing this heterocyclic core in an efficient and stereoselective manner.[2] In particular, the metal catalyzed dearomatization of (hetero)arenes has emerged as an attractive approach towards various privileged heterocyclic scaffolds. Our group has recently developed a dearomative indole bisfunctionalization strategy via a Pd-catalyzed domino arylation/anion capture sequence for the formation of diverse indoline scaffolds.[3] This methodology yields indolines bearing densely functionalized C2 and C3 centers in good to excellent yields with high levels of diastereoselectivity and demonstrates scalability as well as broad functional group tolerance. In this presentation, we will discuss the key findings in our development and application of this methodology.



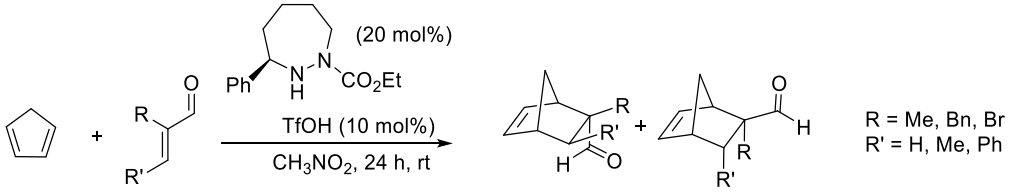
1. Ruiz-Sanchis, P.; Savina, S. A.; Albericio, F.; Álvarez, M. *Chem. Eur. J.*, **2011**, *17*, 1388. 2. Liu, D.; Zhao, G.; Xiang, L. *Eur. J. Org. Chem.*, **2010**, 3975. 3. a) Grigg, R.; Sridharan, V. *J. Organomet. Chem.*, **1999**, *576*, 65. b) Zhuo, C.-X.; Zheng, C.; You, S.-L. *Acc. Chem. Res.*, **2014**, *47*, 2558. c) Petrone, D. A.; Yen, A.; Zeidan, N.; Lautens, M. *Org. Lett.* **2015**, ASAP.

P44 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, due to A-1,3 interactions which hinder iminium formation.

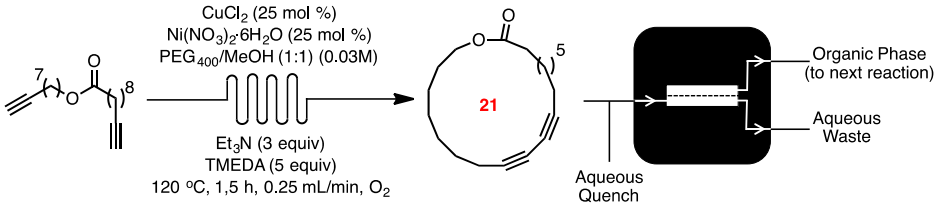
We have developed a 1,2-diazepane-carboxylate catalyst which together with an acid co-catalyst efficiently catalyzes the cycloaddition of sterically encumbered aldehydes. Use of this catalytic method provides high yields, *exo*-selectivity and a wide substrate scope, exemplified by its ability to perform novel Diels-Alder reactions, such as *α*-methylcinnamaldehyde with cyclopentadiene. Investigation involving asymmetric derivatives of these diazepane catalyst have yielded products with moderate enantioselectivity.



P45 In-Line Extraction and Purification of PEG Co-Solvents During Macrocyclizations Employing a "Phase Separation" Strategy

Émilie Morin, Anne-Catherine Bédard, Shawn K. Collins*, Département de Chimie, Université de Montréal, Montréal, Qc, H3T 1J4, shawn.collins@umontreal.ca

Macrocyclization is a fundamentally important transformation in organic synthetic chemistry. Our group has reported the development of a novel approach aimed at improving the efficiency of macrocyclization reactions through the control of dilution effects. The "phase separation" strategy exploits the aggregation properties of PEG co-solvents, and the macrocyclization can be used in continuous flow at high concentrations. Removal of PEG co-solvents is essential to developing sequential in-line transformations of macrocycles. We report the optimization of a first in-line extraction protocol of PEG using a membrane-based liquid-liquid separator.

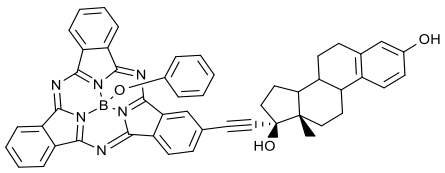


1. Bédard, A.-C.; Collins, S. K. *J. Am. Chem. Soc.* **2011**, *133* 19976.

P46 Synthesis of Estradiol-Subphthalocyanine Conjugate by Sonogashira Cross-Coupling Reaction

Samira Osati, Hasrat Ali, Johan E. van Lier*, Department of Nuclear Medicine and Radiobiology, Université de Sherbrooke, 3001, 12th Avenue North, Sherbrooke, QC J1H 5N4, Canadajohan.e.vanlier@usherbrooke.ca

Estrogen receptor (ER) imaging has received a great deal of attention as a potential tool to stage breast cancer and to guide treatment protocols. Many techniques have been developed to detect ligand–ER interaction including fluorescence imaging. Among available fluorescent probes subphthalocyanines (SubPc λ_{em} =570 nm), which are 14-π electron aromatic macrocycles, have not been widely used for biomedical application. We developed a strategy of attaching the fluorescent SubPc derivatives to an ER ligand to create fluorescent ER ligands. The synthesis involves attachment of a SubPc to the C17α-position of estradiol using Sonogashira cross coupling reaction of Iodo-SubPc and 17α-ethynyl estradiol.[1] The synthesis of a number of different Estradiol-SubPc conjugates, using a combination of various estradiol and SubPc moieties, is in progress.

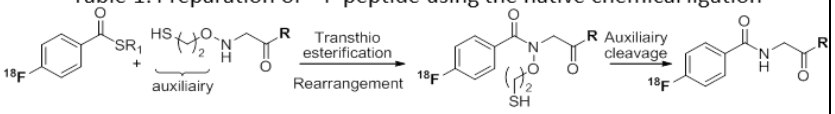


a) Anstead GM. *et al. Steroids* **1997**; 62:268. b) Bernhard Y. *et al. Chem. Commun.,* **2014**, 50, 13975.

P47 Novel synthetic approach for one-pot F-18 labeling of unprotected peptides for PET imaging

G Tremblay, S Aït-Mohand, R Ouellet and B Guérin*, Département de médecine nucléaire et radiobiologie, U Sherbrooke, Sherbrooke, Qc, J1H 5N4, brigitte.guerin2@usherbrooke.ca

Table 1. Preparation of ^{18}F-peptide using the native chemical ligation



R		Reaction time (min)	Yield (%)
–OCH_2Ph (model compound)	^{19}F	31	90[a]
	^{18}F	55	36[a,b]
–Gly-Gln-Phe-Ala-NH_2	^{19}F	26	>90[c]
	^{18}F	55	36[b]

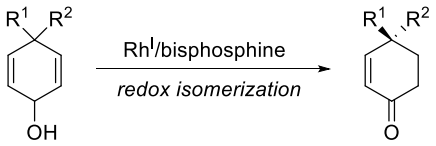
[a] Benzyl group was cleaved using Microwave; [b] Non-decay corrected yield by radio-UPLC; [c] HPLC estimated yield.

Although many methods have been developed for peptide labeling with F-18, new approaches, versatile and fast, involving the use of unprotected peptides, are needed. The aim of this study focuses on the development of cleavable thiol auxiliaries to radiolabel unprotected peptides with F-18. The proposed synthetic pathway starts with the preparation of the *N*-succinimidyl 4-[^{18}F]fluorobenzoate (FSB) and its thioester moiety. It is followed by its conjugation to the unprotected peptide through a highly selective chemical ligation reaction using a cleavable hydroxylamine auxiliary leading to a very stable amide bond formation. The ^{18}F-thioester was readily prepared, with a non-decay corrected radiolabeling yield of 40%. The preliminary results for the optimization of the chemical ligation reaction afforded a fast reaction through a one-pot process, yielding the radiolabeled peptides in good yields (Table 1). This process is currently under study with peptides of biological interest.

P48 Rhodium-catalyzed desymmetrative redox isomerization of cyclohexa-2,5-dienols

Thomas Johnson, Steffen Kress, Mark Lautens*, Department of Chemistry, University of Toronto, Ontario, M5S 3H6, mlautens@chem.utoronto.ca

The catalytic redox isomerization of allylic alcohols into saturated carbonyl compounds is one of the earliest metal-catalyzed reaction to have been studied. Despite notable advances over the years, little attention has been paid to this reaction in the field of complex molecule synthesis. In fact, the vast majority of reported examples are for the synthesis of non-functionalized linear allylic alcohols. In this context, we have developed a new redox isomerization for the synthesis of γ,ν-disubstituted cyclohexenones, which are useful intermediates in synthesis. The functional group tolerance of the reaction compares favorably with that of classical redox isomerizations. The synthetic and mechanistic aspects of the reaction as well as the characteristics of the enantioselective version will be discussed.



15 examples
up to 95% yield

R^1, R^2 contains ester, amide, ether, carbamate, etc.

P49 Large scale and flow processes for the synthesis of *N*-mesyloxy-carbamates: Application to the synthesis of trichloromethylcarbinols

Johan Bartholoméüs, Henri Piras, Samuel Blais, Hélène Lebel*, Département de chimie, Université de Montréal, QC, H3T 1J4.

Trichloromethylcarbinols are important intermediates with a multitude of uses.[1] They can be used as intermediates in the Jocic reaction (Reeve, W and al. *Can. J. Chem*. **1980**, 485) or in the preparation of a nitrene precursor developed in our group, *N*-mesyloxycarbamates.[2]
This poster presents our effort to synthesize *N*-mesyloxycarbamates in a large scale process using batch and continuous flow methodologies. The optimization of the reaction conditions in both batch and flow systems will be presented. New methods for the synthesis of racemic or enantioenriched trichloromethylcarbinols using continuous flow chemistry will also be discussed.

[1] Snowden and al. *Org. Lett.*, **2006**, 5881
[2] a) Lebel, H. and al. *Chem. Commun.,* **2012**, 7799. b) Lebel, H. and al. *J. Org. Chem*., **2015**, 3572.

P50 Identification of inhibitors of HIF-2a as modulators of the hypoxia response for the treatment of cancer

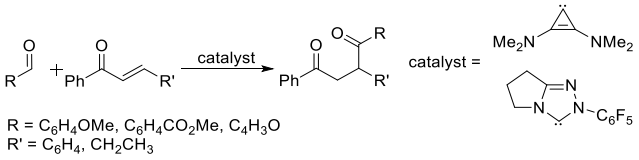
Brian Masek;[1] Lei Wang;[1] Steve Bourgault,[2] Martin Coupal;[3] Eric Grazinni;[3] Shawn Johnstone;[3] Shaun Brothers;[4] and Jeffrey S. Albert[3]. [1]Certera, 350-210 North Tucker, St. Louis; UQAM, 2101 Jeanne-Mance, Montreal, [3]IntelliSyn Pharma, 7171 Frederick-Banting, Montreal, [4]Miami Miller School of Medicine, 1501 NW 10th Ave, Miami.

Solid tumors typically contain regions that are hypoxic (reduced oxygen concentration) where cancer cells proliferate. They do this by up-regulating certain genes via specific transcriptional regulators, including HIF2a. Under normoxic conditions (normal oxygen concentration), HIF2a is oxidatively deactivated. An emerging class of potential drugs functions by inhibiting HIF2a, thereby stopping cancer cells from proliferating. Such drugs offer the potential to affect only hypoxic cancer cells while having no effect on normoxic cells. To strengthen validation of this target, we demonstrate by siRNA knockdown that disruption of the regulatory complex leads to halting of protein expression in hypoxic cells without affecting normoxic cells. For lead generation, we developed a computational screening model and validated its ability to correctly discriminate between leads and decoys, computationally screened a virtual library of 5 million commercial compounds, and employed Muse's genetic algorithm to score ligand-receptor interactions, synthetic feasibility, and physicochemical properties in an iterative fashion. The most drug-like hits were evolved through computational analysis and synthetic optimization. Through these efforts, we have identified novel families of inhibitors across 6 different chemotypes. Binding of these compounds has been demonstrated in an alpha-screen based assay and functional activity has been demonstrated in a VEGF suppression assay. We show that selected representatives from the 6 leading chemotypes are among the most potent inhibitors yet described for this target.

P51 DFT study of the Reactivity of Bis(amino)cyclopropenylidenes as Organocatalysts in the Intermolecular Stetter Reaction

Odile Moutounet, Michel Gravel, Claude Legault*, Département de chimie, Université de Sherbrooke, Sherbrooke, Québec, J1K 2R1, Claude.Legault@USherbrooke.ca

Bis(amino)cyclopropenylidenes (BAC), derived from the bis(amino)cyclopropenium motif, received renewed attention in 2006. Recently, derivatives have been synthesized and studied as organocatalysts by the group of M. Gravel.[1] They were used in the intermolecular Stetter reaction between various aldehydes and *trans*-chalcone. They provided far better yields than the *N*-heterocyclic carbenes (NHCs) along with a different selectivity profile in an aldehyde competition reaction. We report here our progress in the theoretical study of this system, using Density Functional Theory calculations (DFT), to understand and explain these differences. The calculations are in good agreement with the experimental data. We will describe a comparison of a NHC and a model for the BAC, for four reactions. We will also discuss the rationalization of the observed reactivity profile.

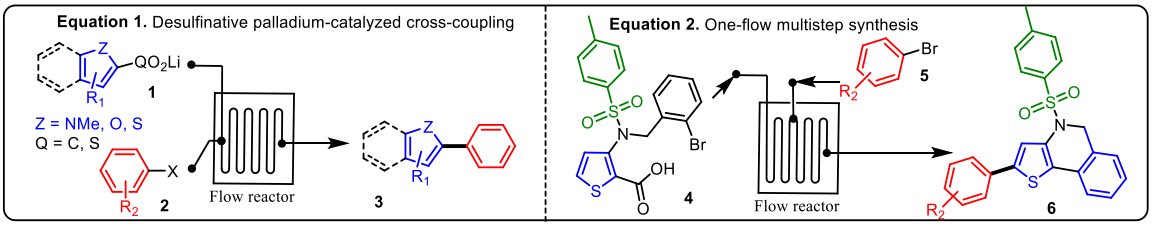


1. Wilde M. and Gravel M. *Angew. Chem. Int. Ed.* **2013**, *52*, 12651-12654

P52 Decarboxylative and Desulfinative Palladium-Catalyzed Cross-Coupling Reactions using Continuous-Flow Process

Cindy Buonomano, Michael Holtz-Mulholland, Sydney Sullivan and Pat Forgione*, Department of Chemistry & Biochemistry, Concordia University, Montréal, QC, H4B 1R6; pat.forgione@concordia.ca

Heteroaromatics are a key motif present in biologically interesting compounds. Their synthesis can be achieved via palladium-catalyzed reactions. Decarboxylative and desulfinative cross-couplings have emerged as an alternative to classical cross-couplings.[1] To increase the attractiveness of our methodologies for industry, it is crucial to adapt them to new synthetic technologies, such as continuous-flow process that offers advantages such as control of heat transfer and mixing. Flow chemistry can provide facile automation, improved safety and reproducibility. The purpose of this research project is to apply the flow chemistry to the methodologies developed by our group, and make them more efficient and versatile. The final objective will lead to the continuous-flow multi-step synthesis of isoquinoline derivatives[2].

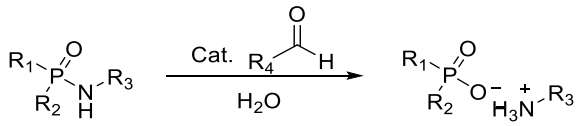


(1)(a) Bilodeau, F.; Brochu, M.-C.; Guimond, N.; Thesen, K. H.; Forgione, P. *J. Org. Chem.,* 2010, **75**, 1550; (b) Ortgies, D. H.; Forgione, P. *Synlett,* 2013, **24**, 1715; (c) Sévigny, S.; Forgione, P. *N. J. Chem.,* 2013, **37**, 589; (2) Chen, F.; Wong, N. W. Y.; Forgione, P. *Adv. Synth. Catal.,* 2014, **356**, 1725.

P53 Electrophilic Catalysis: Hydrolysis of Phosphonic Amides and Related Derivatives

Binjie Li, Ryan Simard and André M. Beauchemin*, Department of Chemistry and Biomolecular Sciences, CCRI, University of Ottawa, Ottawa, ON, K1N 6N5

For decades, organophosphorous compounds have attracted widespread interest from a variety of research areas. In particular, phosphoramidates and related derivatives are widely used in pharmaceuticals, agrochemicals and in bio-organic chemistry. Recently, we were drawn to the concept of electrophilic activation, documented over 50 years ago by Jencks[1] using formaldehyde as catalyst for mild hydrolysis of phosphoramidates. This reactivity was aligned with our research interests, since we showed that simple aldehydes acted as tethering organocatalysts for difficult hydroamination reactions,[2] and are interested in developing other reaction types. In this presentation, we will discuss our progress in the development of aldehyde-catalyzed hydrolysis reaction at pentavalent organophosphorus derivatives.



1. Jencks, W. P.; Gilchrist, M. *J. Am. Chem. Soc.* **1964**, *86*, 1410.
2. a) Beauchemin, A. M. *et al*. *Chem. Eur. J.* **2013,** *19*, 2597. b) Beauchemin, A. M. *et al*. *J. Am. Chem. Soc*. **2012**, *134*, 16571. c) Beauchemin, A. M. *et al*. *J. Am. Chem. Soc*. **2011**, *133*, 20100.

P54 Studies of synthetic membrane perturbing peptides incorporating crown-ethers by oriented circular dichroism

Pierre-Alexandre Paquet-Côté, François Otis, Jochen Bürk, Anne S. Ulrich, Normand Voyer*, Département de chimie, Université Laval, Québec, Qc., G1V 0A6, normand.voyer@chm.ulaval.ca

Lately, we see an important increase in antibiotic resistant bacteria. Such threat requires the development of new antimicrobial agents. One promising family of compounds is the amphiphilic cationic peptides.[1] Unfortunately, natural cationic peptides also target eukaryotic cells. To get a better understanding of the molecular determinants governing the biological activity of cationic peptides, a model peptide **1** was developed in our group to have a similar membrane perturbing activity. A library of analogs of **1** was synthesized incorporating cationic amino acids and compounds with good antimicrobial activity with no hemolysis were identified. However, their action mechanism are not fully elucidate. To achieve this, the biophysical method of oriented circular dichroism spectroscopy[2] is used to study the model peptide **1** and two of its analogs. This method allow to determine the orientation of peptide in lipid bilayer. Three peptides were studied with different phospholipids bilayers having different charge and thickness.

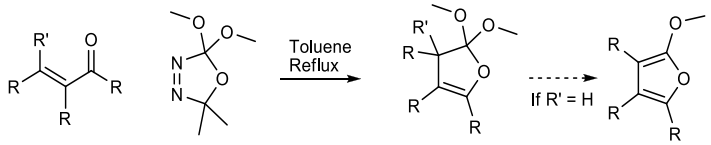
1 L-CE-L-L-L-CE-L-L-CE-L-L-L-CE-L
CE = (21-crown-7)-L-phenylalanine

1- Brogden, K. A. *Nat. Rev. Microbiol.* **2005**, *3*, 238-250.
2- Buerck, J.; Roth, S.; Wadhwani, P.; Afonin, S.; Kanithasen, N.; Strandberg, E.; Ulrich, A. S. *Biophys. J.* **2008**, *95*, 3872-3881.

P55 Formal Cycloaddition (4+1) of Dimethoxycarbene with Enones and Synthesis of 1-Methoxy Furan from the Resulting Orthoester

Jean-Philippe Croisetière et Claude Spino*, Départment de chimie, Université de Sherbrooke, Sherbrooke, QC, J1K 2R1

Dimethoxy carbenes have been studied for many years by different chemists. With John Warkentin's precursor oxadiazoline[a], they have now become easily accessible to synthetize. In our previous work we focused on the formal cycloaddition of these carbene with different electron-deficient dienes. Our group is now working with dimethoxycarbene to effect a formal intermolecular cycloaddition on enones and enals. These cycloaddition gives an access to orthoesters that allow an easy access to all kinds of furans in good yields. While enals are more reactive than enones, they often give trouble because of polymerisation. We are currently working to reduce this problem with different strategies. In this presentation we will discuss the results and the potential of the method.

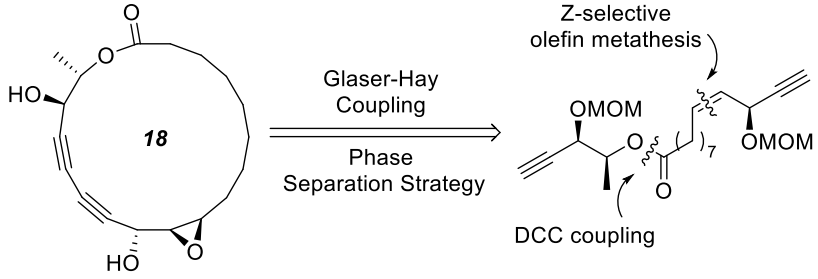


1. Warkentin, J. et al. Org. Lett. **2005**, 7, 3. 2. a) Spino, C. et al. Org. Lett. **2007**, 9, 5361. b) Spino, C. et al. *Can. J. Chem.* **2006**, *84*, 1290.

P56 Progress toward the total synthesis of Ivorenolide A

Mylène de Léséleuc, Éric Godin, Shawn Parisien-Collette, Shawn K. Collins*, Département de chimie, Université de Montréal, Montréal, Québec, H3T 1J4, shawn.collins@umontreal.ca

Macrolactones are one of the most common cyclic motifs in chemistry, but their synthesis is often difficult due to the competitive intermolecular reactions during the macrocyclization step. The common strategy to overcome potential oligomerization involves the use of slow addition and high dilution conditions. Our group has developed a macrocyclic Glaser-Hay coupling of terminal alkynes via a phase separation strategy which allows macrocyclization at high concentrations without the need for slow addition. Herein, we present the application of the method towards complex molecule synthesis. Progress towards the synthesis of Ivorenolide A, an 18-membered ring macrolactone which possesses a rare conjugated diyne and immunosuppressive properties, will be discussed. Key steps include the Glaser-Hay macrocyclization in continuous flow and a Z-selective olefin metathesis reaction.

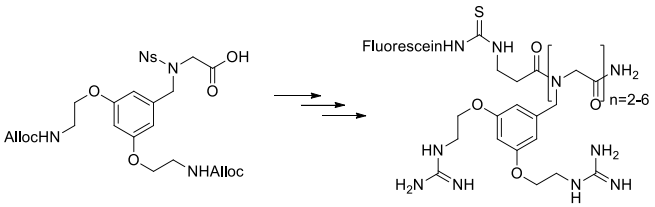


Ivorenolide A

P57 Synthesis and biological evaluation of constrained guanidinium-rich transporters

Etienne Marouseau, Albane Neckebroeck, Heidi Larkin, Antoine Le Roux, Leonid Volkov, Christine Lavoie, Eric Marsault, Université de Sherbrooke, Sherbrooke, QC, J1E 1L9, Eric.Marsault@usherbrooke.ca

Since the discovery of the HIV-1 Tat protein which led to guanidinium-rich transporters, and despite the great pharmaceutical interest of the latter as vectors, few studies have investigated the mechanism of entry of those transporters through the plasma membrane. Since it was recently shown that those transporters need to interact with glycosaminoglycans (GAGs) to enter cells, we decided to investigate in this direction and synthesize conformationally restrained scaffolds which can be functionnalized with guanidine groups in a modular fashion. By having a determined distance and orientation between the guanidine functions, we aim to create synthetic transporters able to interact preferentially with specific sulfate and carboxylate motives on GAGs, which could potentially lead to selective drug delivery. The synthesis of the first scaffolds and their assembly to create synthetic peptoids will be discussed in this presentation as well as the first biological results obtained.



Wender *et al., Proc Natl Acad Sci U S A,* **2000**, 97, 13003. 13., Wexselblatt *et al.*, *J. Org. Chem.*, **2014**, *79*, 6766–6774.

P58 Proteins and oligopeptides as green catalyst for chiral epoxidations

Christopher Bérubé, Corinne Bouchard, Normand Voyer*, Département de chimie et PROTEO, Université Laval, Québec, QC, G1V 0A6, normand.voyer@chm.ulaval.ca

Enzymes are the most efficient class of catalyst in terms of reactivity and selectivity, particularly in living cells where all reactions occur in aqueous media. Inspired by such features, different biomimetic approaches have been developed to mimick enzymatic acitivity.

Inspired by those works, our objective is to developed a novel ecofriendly way for the chiral epoxidation of α,β-unsaturated ketones in water without any co-solvent. Our hypothesis is based on the use of oligopeptides or proteins as solubilizing agents and chiral catalysts for the substrates. Indeed, performing efficiently the reactions in water in absence of co-solvent is highly favourable for economic and environmental reasons.

We will report the results of our initial investigation on the enantioselective epoxidation of enones using bovine serum albumin and poly-L-leucine in pure water. Results demonstrated that no organic co-solvent is necessary for the Juliá-Colonna epoxidation of a wide variety of electron deficient enones with high enantioselectivities.

P59 The application of oligonucleotide-templated chemical Reactions to DNA aptamers

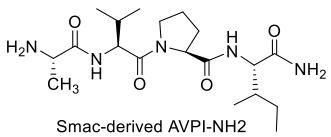
Christopher M.C. Mattice, Jeffrey M. Manthorpe, Maria C. DeRosa*, Department of Chemistry, Carleton University, Ottawa, ON, K1S 5B6, maria_derosa@carleton.ca

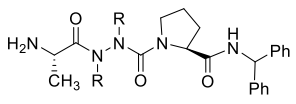
The ability of an aptamer to catalyze an organic reaction under selective conditions presents a novel avenue for the exploration of biosensors and molecular payload delivery. To date, limited research exists for pairing oligonucleotide-templated chemical reactions with the selective nature of aptamers. A system can be designed wherein the binding of the aptamer to its target induces a conformational change, bringing two previously spatially isolated reactants into close proximity and thereby catalyzing a reaction through an increase in their effective molarity. A rationally designed aptamer-mediated S_N2 displacement of a sulfonyl-based fluorescence-quencher resulted in an effective increase in fluorescence upon mixing of the aptamer with two appropriately modified complementary oligonucleotides. This increased fluorescence could be slowed by the presence of the aptamer target, permitting the development of an aptamer-based sensor for ochratoxin A, a potent wheat mycotoxin. Direct incorporation of reactive functionalities into an aptamer through chemical synthesis constitutes a step toward aptamer-based catalysis.

P60 Design and synthesis of azo-peptides to obtain conformationally constrained Smac mimetics

Ramesh M. Chingle and William D. Lubell*, Department of Chemistry, Université de Montréal, P.O. Box 6128, Succursal Centre-ville, Montréal, QC H3C 3J7, Canada

Aza-analogs of amino acids possess a nitrogen atom in place of CHα, resulting in conformational restrictions, due to their planar urea and lone pair repulsion between adjacent hydrazine nitrogen, which rigidify the backbone dihedral angle geometry.[1] As illustrated by computational, spectroscopic and crystallographic studies, semicarbazide constraints tend to favor turn geometry within the aza-peptide, which may facilitate interactions with a protein receptor. In spite significant research on aza-peptides, their unsaturated “azo” counterparts have not been previously described. Exploring the potential of azo-amino acid residues, their synthesis and reactivity in pericyclic chemistry will be preseted.[2] Moreover, their application in the synthesis of second mitochondria-derived activator of caspases (Smac) mimics will be described in efforts to develop potential agents to treat cancer.[3]



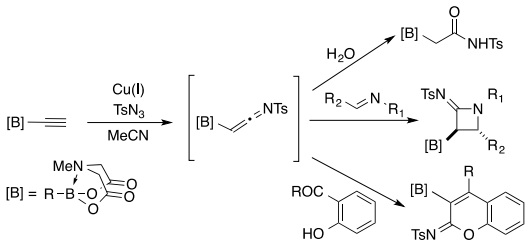


[1] Proulx, C. *et al. Future medicinal chemistry*, **2011**, *3*, 1139. [2] Chingle, R.; Lubell, W. D. *Submitted*. [3] Bourguet, C. B.; Boulay, P.-L.; Claing, A.; Lubell, W. D. *Bioorg. Med. Chem. Lett.*, **2014**, *24*, 3361.

P61 Synthesis and Trapping of Amphoteric Borylated Ketenimines using Cu(I) Catalysis

Sherif James Kaldas, Prof. Andrei Yudin, Department of Chemistry, University of Toronto, Toronto, Ontario, M5S 3H6, ayudin@chem.utoronto.ca

In transition metal catalysis sp^2- hybridized organoboranes have obtained a privileged status; however, the same cannot be said about sp^3-hybridized organoboranes. This is mainly due to difficulty installing sp^3-hybridized carbon-boron bonds in heteroatom rich environments. Using copper catalysis, our group has developed a mild and efficient method to generate (N-methyliminodiacetyl (MIDA) protected borylated ketenimines in situ, which can be trapped with various reaction partners. This method allows access to α-boryl amides, borylated azetidimines and borylated coumarins. The applications of these compounds in downstream functionalization will be discussed.

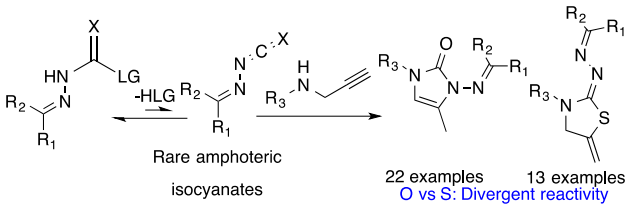


(1) He, Z.; Zajdlik, A.; Yudin, A. K. *Acc. of Chem. Res*. **2014**, 47, 1029-1040.
(2) He, Z.; Yudin, A. K. *J. Am. Chem. Soc.* **2011**, 133, 13770-13773.
(3) St Denis, J. D.; He, Z.; Yudin, A. K. *ACS. Catal.* **2015**, 5, 5373-5379.

P62 Diversity-oriented heterocyclic synthesis using divergent reactivity of N-substituted iso(thio)cyanates

Joshua Derasp, Jean-Francois Vincent-Rocan, André M. Beauchemin*, Dept of Chemistry and Biomolecular Sciences, CCRI, University of Ottawa, Ottawa, ON, K1N 6N5

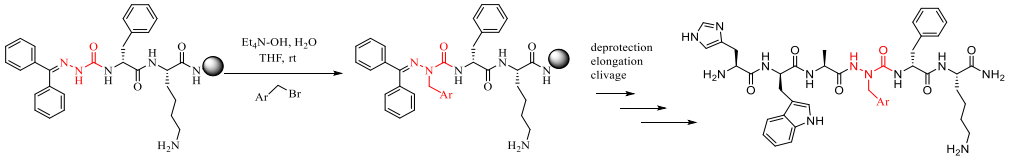
Carbon-substituted isocyanates (*C*-isocyanates) and isothiocyanates are thoroughly studied building blocks: their importance in organic synthesis and polymer chemistry (e.g. polyurethanes) cannot be overstated. In stark contrast, nitrogen-substituted isocyanates and isothiocyanates have been seldom used in synthetic transformations and remain mostly scientific curiosities. In this work we compare the reactivity of *N*-isocyanates and *N*-isothiocyanates in cascade reactions, and highlight their differences in reactivity. Efficient new syntheses of imidazolones and thiazolidines were achieved using masked *N*-iso(thio)cyanate precursors with readily available propargylic amines. Using allylic amines, a novel method for *in situ* formation of complex azomethine amines was also developed and exploited for [3+2] cycloadditions.



P63 Synthesis of [azaTyr^4]-GHRP-6 analogues as potential CD36 modulators

Kelvine Chignen Possi, Yesica Garcia-Ramos, William D. Lubell, Département de Chimie, Université de Montréal, QC H3C 3J7, Canada.

Targeting the cluster of differentiation 36 receptor (CD36), our lab has developed azapeptide analogs of growth hormone-releasing peptide-6 (GHRP-6) that exhibit anti-atherosclerotic activity in a CD36 dependent manner. In addition, introduction of aza-amino acid residues at the 4-position, such as in [azaTyr^4]-GHRP-6 has provided analogs with CD36 receptor affinity that reduce neovascularization in a mouse laser burn assay. Studying structure-activity relationships of [azaTyr^4]-GHRP-6, we are pursuing analogs in which the *p*-hydroxybenzyl side chain has been replaced by other aromatic residues, by employing a solid phase approach featuring alkylation of a hydrazone-protected aza-glycine residue using substituted arylbromides. Our report will present the synthesis and preliminary activity of the novel analogs.

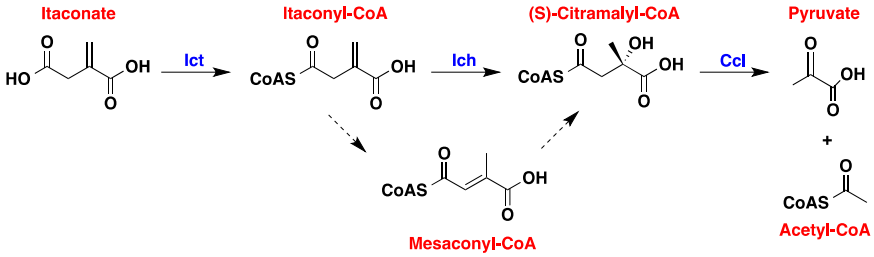


a) Picard, E.; Houssier, M.; Bujold, K.; Sapieha, P.; Lubell, W.; Dorfman, A.; Racine, J.; Hardy, P.; Febbraio, M.; Lachapelle, P.; Ong, H.; Sennlaub, F.; Chemtob, S. *Aging,* **2010***, 2, 981-991* b) Sabatino, D.; Proulx, C.; Pohankova, P.; Ong, H.; Lubell, W. D.*J. Am. Chem. Soc.* **2011***, 133, 12493-12506* c) Proulx, C.; Picard, E.; Boeglin, D.; Pohankova, P.; Chemtob, S.; Ong, H.; Lubell, W. D. *Journal of Medicinal Chemistry,* **2012**, 55, 6502-6511 *Journal of Medicinal mistry,* **2012**, 55, 6502.

P64 Design and synthesis of inhibitors of itaconyl-CoA hydratase as potential agents to resensitize bacteria to the host's defenses

Justin Chang, Fabien Hammerer, Karine Auclair*, Department of Chemistry, McGill University, Montreal, Qc, H3A 0B8, karine.auclair@mcgill.ca

Resistance to itaconate, a molecule involved in the innate immune response against bacteria, has been observed and is attributed to the metabolism of itaconate by a triad of enzymes.[1] The goal of this project is to synthesize potential inhibitors of itaconyl-CoA hydratase (Ich), the second enzyme of the triad. It is proposed that Ich acts as an isomerase, then as a hydratase.[1] As no solved crystal structure of Ich has been published, the first iteration of molecules were inspired from the substrate and or from the putative mechanism. The design also takes advantage of a prodrug strategy developed in the Auclair lab, where a CoA moiety is assembled *in vivo* by the CoA biosynthetic enzymes.[2] The molecules synthesized are next assayed for their ability to re-sensitize bacteria to itaconate.

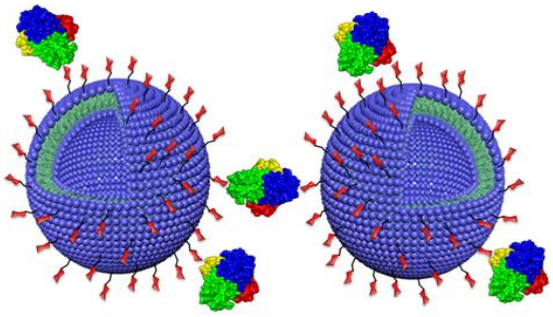


1. Sasikaran et al. *Nature Chem. Bio.* **2014**, *10*, 371.
2. Vong, K. et al. *ACS Chem. Biol.* **2012**, *7*, 470.

P65 Amphiphilic Janus glycodendrimers synthesis and their self-assembly into glycodendrimersomes : improved lectins binding properties

Yihong Cao, Tze Chieh Shiao and Rene Roy*, Department de Chimie, UQAM, Montréal, QC, Canada H3C 3P8. roy.rene@uqam.ca

The first examples of amphiliphilic Janus glycodendrimers was reported by Roy and Percec.[1] The modular synthesis of several libraries with various carbohydrate on surface, their hydrophilic part, like D-mannose, D-galactose, and the disaccharide D-lactose playe an important element for lectins. The multivalence of this self-assembling amphiphilic Janus glycodendrimers call glycodendrimersomes with different sizes and their ligand bioactivity were demonstrated by selective agglutination with a diversity of sugar-binding protein receptors including leguminous, bacterial, and mammalian lectins. Roy's team has successfully found 3 potential leading compounds that can inhibit galectin-1 activity, D-lactose in this case, 60 times more potently than that of galectin-3. Thoses compounds were prepare by simple injection of organic solution into water and by hydratation was analyzed by dynamic light scattering (DLS), confocal microscopy, cryogenic transmission electron microscopy (Cryo-TEM) and, theirs affinities to galectin-1 were testing by BIACORE-SPR (Surface Plasmon Resonance). In addition, a mixed hybrid synthesis with a non carbohydrate hydrophilic arm was also achieved to evaluate the effects of the relative sugar densities upon protein binding.[2] The potential specific for Galectin-1 compound will be modify further to obtain highly efficient and specific inhibitors for Galectin-1. This new candidacy glycodendrimersomes as new mimics of biological membranes with programmable glycan ligand, as supramolecular lectin blockers, vaccines, and targeted delivery devices.[3]

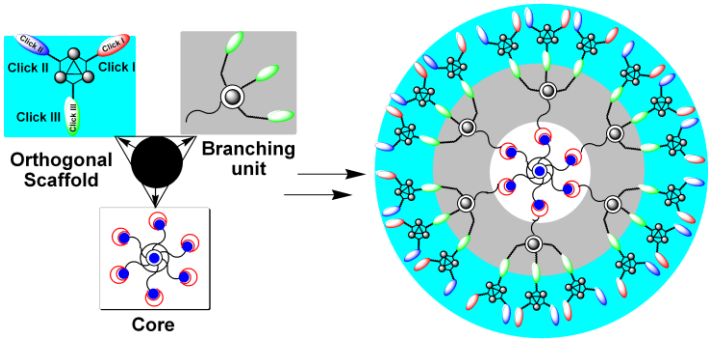


1. Percec, V.; Leowanawat, P.; Sun, H.-J.; Kulikov, O.; Nusbaum, C. D.; Tran, T. M.; Bertin, A.; Wilson, D. A.; Peterca, M.; Zhang, S.; Kamat, N. P.; Vargo, K.; Moock, D.; Johnston, E. D.; Hammer, D. A.; Pochan, D. J.; Chen, Y.; Chabre, Y. M.; Shiao,T. C.; Bergeron-Brlek, M.; André, S.; Roy, R.; Gabius, H.-J.; Heiney, P. A.; *J. Am. Chem. Soc.* **2013**, *135*, 9055-9077.
2. Zhang, S.; Moussodia, R.-O.; Sun, H.-J.; Leowanawat, P.; Muncan, A.; Nusbaum, C. D.; Chelling, K. M.; Heiney, P. A.; Klein, M. L.; André, S.; Roy, R.; Gabius, H.-J.; Percec, V. *Angew. Chem Int. Ed*., **2014**, *53*, 10899-10903.
3. Zhang, S.; Moussodia, R.-O.; Murzeau, C.; Sun, H.-J.; Klein, M. L.; Vértesy, S.; André, S.; Roy, R.; Gabius, H.-J.; Percec, V. *Angew. Chem. Int. ed.,* **2015**, 54, 4036-4040.

P66 Orthogonality as novel approach towards the synthesis of multifunctional hybrid dendrimers

Rahul S. Bagul, Rabindra Rej, Tze Chieh Shiao and Rene Roy*, Department de Chimie, UQAM, Montréal, QC, Canada H3C 3P8. roy.rene@uqam.ca

Dendritic macromolecules established their immense importance in studies across various disciplines since three decades.[1] Increasing applications of dendrimers in various disciplines warranted the development of efficient and quick synthetic strategies for the dendrimers which includes facile reactions and rationally designed building blocks.[2] Recently "onion peel strategy" was introduced for the fast track construction of dendritic macromolecules in the quest of efficient dendrimer synthesis.[3] Rapid synthetic protocol was adapted using highly efficient "click" reactions and chemo-selective orthogonal building blocks. Herein, we report an application of novel "onion peel strategy" towards the synthesis of multifunctional hetero-dendrimers. Differentially functionalized tri-substituted cyanuric acid was chosen as a model for orthogonality. Selective attachment of two structurally different chemical entities to the tri-substituted cyanuric acid was achieved using chemo-and regio-selective reactions. Chosen reactions were namely Cu (I) catalyzed azide-alkyne [1,3]-dipolar Huisgen cycloaddition (CuAAc) and photolytic thiol-ene reaction. Finally, orthogonal scaffold was grafted to various hypervalent branching units and hypercore using CuAAc to afford multifunctional hetero-dendrimers having 36 peripheral units.

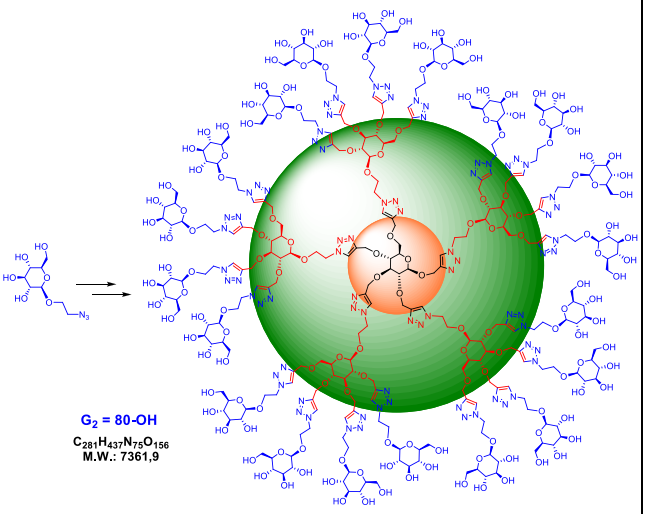


1. T. C. Shiao, R. Roy. *Chem. Soc. Rev*. **2015**, *44*, 3924-3941.
2. K. L. Wooley, C. J. Hawker, J. M. J. Frechet, *J. Am. Chem. Soc.,* **1991**, *113*, 4252–4261.
3. R. Sharma, K. Naresh, Y. M. Chabre, R. Rej, N. K. Saadeh, R. Roy, *Polym. Chem*., **2014**, *5*, 4321.

P67 Combined glyconanosynthons and onion peel approach : highly efficient synthesis of chiral dendrimers

Rabindra Rej, Tze Chieh Shiao, Mariecka Rose and Rene Roy*, Department de Chimie, UQAM, Montréal, QC, Canada H3C 3P8. roy.rene@uqam.ca

The syntheses of glycodendrimers have been mainly focused on using versatile multivalent building blocks for several years. Carbohydrates are clearly underexploited as building blocks towards the rapid construction of multifaceted, dense, and chiral dendrimers.[1] Our laboratory has recently developed an orthogonal coupling strategy by using carbohydrates as versatile and chiral scalffolds (''*glyconanosynthons*''). Dense dendrimers can be rapidly constructed with a very high number of surface groups within a low generation number by combining thiol-ene and thiol-yne click reactions.[2] In addition, an interesting and versatile ''onion peel '' strategy[3] has been added to the arsenal of sophisticated methods with both convergent and divergent methodologies towards dendrimer synthesis.[4] Herein, we report a facile and efficient route for dendrimer synthesis that can introduce a dense, chiral, and a large number of varied surface group at low generation. To this end, perpropargylated carbohydrate derivatives constituting dense A_5 core molecules were used as starting point. An orthogonal building block, representing an AB_4 layer for the next generation, was readily prepared. Combination of nanomaterial sciences with glycobiology has triggered an exponential growth of research activities for the design of novel functional bionanomaterials[5] and glyconanotechnologies.[6]

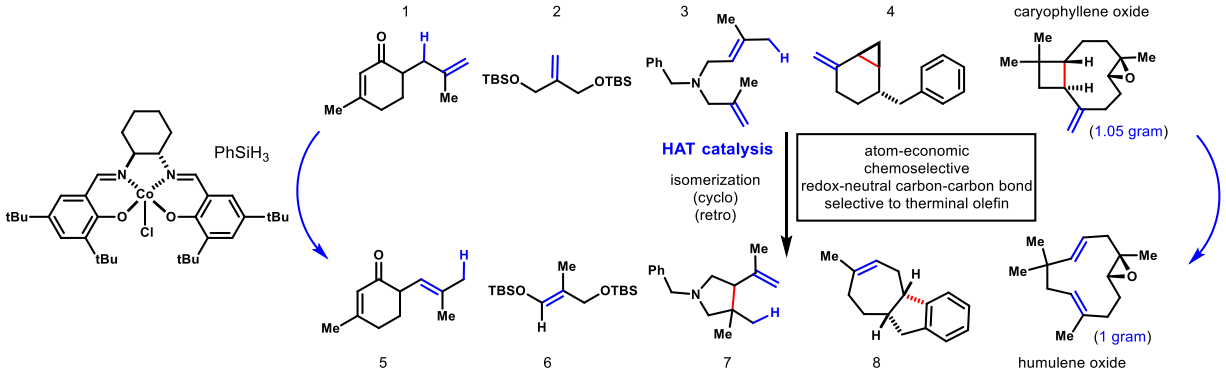


1. Roy, R.; Shiao, T. C. *Chem. Soc. Rev.* **2015**, *44*, 3924-3941.
2. Kottari, N.; Chabre, Y. M.; Shiao, T. C.; Rej, R.; Roy, R. *Chem. Commun,* **2014**, *50*, 1983-1985.
3. Sharma, R.; Kottari, N.; Chabre, Y. M.; Rej, R.; Saadeh, N. K.; Roy, R. *Polym. Chem.*, **2014**, *5*, 4321-4331.
4. Sharma, R.; Kottari, N.; Chabre, Y. M.; Abbassi, L.; Shiao, T. C.; Roy, R. *Chem. Commun,* **2014**, *50*, 13300-13303.
5. Gatard, S.; Liang, L.; Salmon, L.; Ruiz, J.; Astruc, D.; Bouquillon, S. *Tetrahedron Lett.*, **2011**, *52*, 1842-1846.
6. Kottari, N.; Chabre, Y. M.; Sharma, R.; Roy, R. *Adv. Polym. Sci.*, **2013**, *254*, 297-342.

P68 Simple, Chemoselective, Catalytic Olefin Isomerization

Steven W. M. Crossley≠, Francis Barabé≠, and Ryan A. Shenvi*, The Scripps Research Institute, San Diego, California

Our research is directed to the study of hydrogen-atom-transfer (HAT) catalysis using cobalt(III)-salen complexes. We developed synthetically useful and chemoselective olefin isomerizations, diene cycloisomerizations and even olefin retro-cycloisomerizations.[1] To increase the scope of this catalytic system, we need to expand the alkene substitution patterns engaged by the catalyst and control the selectivity for linear versus cyclic isomerization products in multiply-unsaturated substrates. To this end, I have worked to understand the selectivity of the catalyst using a simple 6-exo-trig cyclization and to achieve selectivity for the linear isomer over the cycloisomer and vice-versa.

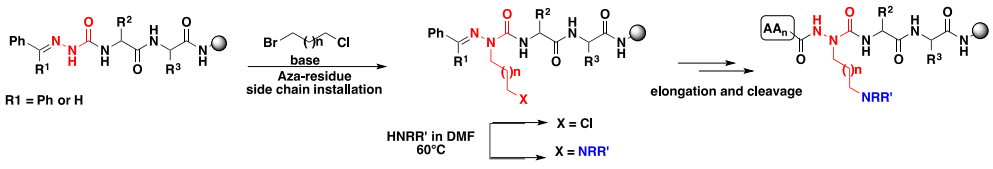


1) Crossley, W. S., Barabé, F. Shenvi, A. S. *J. Am. Chem. Soc.*. **2014**, 136, 16788.

P69 Aza-lysine and aza-arginine peptide substrate synthesis and reactivity in the presence of trypsin and thrombin.

Mariam Traoré, William D. Lubell, Departement of chimie, Université de Montréal, Montréal, Québec, H3T 1J4, traore-mariam@laposte.net

Amino acids with positively charged side chains such as lysine and arginine are involved in numerous biological processes including protein post-translational modification, enzymatic cleavage, and cell penetration. To study the structural requirements for such biology, azapeptides have been pursued, because their semicarbazide residues may favor turn geometry, enhance molecular recognition and prevent protease degradation.[1] Our general approach for making azapeptides with aza-Lys and aza-Arg residues will be presented with focus on its use to make modified substrates of trypsin and thrombin.[2] The influence of azapeptide structure on protease activity will also be reported.



1. Proulx, C.; Sabatino, D.; Hopewell, R.; Spiegel, J.; Garciia Ramos, Y.; Lubell, W. D. *Future Med. Chem*. **2011**, *3*, 1139–1164.

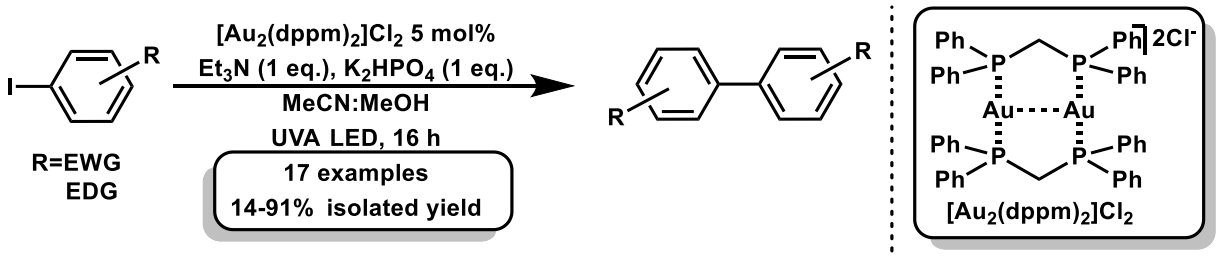
2. Traoré, M.; Doan, N-D.; Lubell, W. D. *Org. Lett*. **2014**, *16*, 3588−3591.

P70 The homocoupling of iodoarenes via photoredox gold catalysis.

Huy Tran, Terry McCallum, Mathieu Morin, Louis Barriault*. Department of Chemistry, University of Ottawa, Ottawa, ON, K1N 6N5, lbarriau@science.uottawa.ca

The synthesis of aromatic dimers has been of synthetic value, especially when considering Ullman type coupling reactions. These types of structures are found in nature as biosynthesis products. Recently, our group has been interested in generating reactive radical intermediates from unactivated haloalkanes and haloarenes using dimeric Au(I) photocatalysts such as $[Au_2(dppm)_2]Cl_2$[1]. Presented here is the development of a photoredox mediated homocoupling strategy using diverse iodoarenes. Upon photoexcitation of the dimeric Au(I) complex, generation of highly reactive aryl radicals is achieved, leading to homocoupled products.

[1] Barriault, L. *et al*. *Angew. Chem. Int. Ed*. **2013**, *52*, 13342.



P71 A Catalytic Aerobic Synthesis of Aromatic Carbon-Sulfur Bonds: Sulfur Addition to ortho-Quinones

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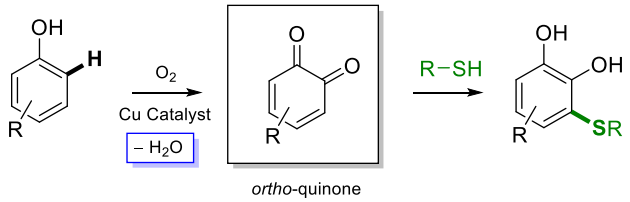
Aromatic carbon-sulfur bonds are fundamentally important as functional portions of a vast number of biologically active molecules, including heterocycles that include benzothiazepines, benzothiophenes, and aryl sulfones. Despite this importance, the installation of aromatic C-S bonds remains challenging. Current methods, reliant upon traditional cross-coupling, require precious metals, long reaction times and pre-functionalization of the starting material. As a result of their fundamental importance, methods for the increased efficiency of S-arylation are required. Sulfur addition to ortho-quinones is 1) a known process in literature, 2) a reaction shown to proceed rapidly, and 3) is accomplished without external catalysis. However, the potential for this reaction to be an efficient S-arylation process has yet to be recognized. Herein, we discuss the development and implementation of a facile method of C-S bond formation using sulfur addition to ortho-quinones.



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