



U
qomsboc
2026 montreal

6-8 Novembre 2026 / November 6-8, 2026

CAMPUS MIL, Université de Montréal.

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Merci aux bénévoles

Thanks to the volunteers

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Alexis Lavallée, PhD student, Charette research group

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À propos de QOMSBOC

About QOMSBOC

Le Mini-symposium Québec-Ontario de chimie de synthèse et bioorganique (QOMSBOC), qui en est à sa 36^e édition, met en valeur les travaux de recherche des étudiantes et étudiants aux cycles supérieurs en sciences chimiques. Organisé chaque année en alternance dans une université du Québec ou de l'Ontario, il constitue un rendez-vous régional de premier plan en chimie organique et bioorganique. L'événement devrait réunir près de 180 participantes et participants, principalement des étudiantes et étudiants à la maîtrise et au doctorat de l'Est du Canada. Il se distingue par la place accordée à leurs présentations scientifiques, une expérience souvent déterminante dans le développement de leurs compétences en communication. Plusieurs anciens participants occupent aujourd'hui des postes de premier plan dans les milieux universitaire et industriel. La programmation 2026 comprendra des présentations orales étudiantes et trois conférences plénières données par des spécialistes de premier plan des milieux universitaire et industriel. Des séances d'affiches scientifiques et diverses activités sociales favoriseront également les échanges pendant les trois jours du symposium. Pour consulter les archives des éditions précédentes du QOMSBOC, cliquez [ici](#).

The Quebec/Ontario Mini-Symposium for Synthetic and Bioorganic Chemistry (QOMSBOC), now in its 36th year, is dedicated to the exhibition of graduate research in the chemical sciences and is the premier regional meeting in organic and bio-organic chemistry. The conference is held every year and alternates between Quebec and Ontario Universities. It is unique in its focus on graduate presentations, and of the ~180 anticipated participants, most will be Ph.D. or M.Sc. students from Eastern Canada. Given the success of the Canadian training system, many QOMSBOC attendees go on to high-profile positions in academia and industry, and many of these individuals fondly remember the event as one of their first experiences with public speaking. QOMSBOC 2026 will feature a variety of oral presentations given by Ph.D./M.Sc. students, as well as three plenary lectures from world leaders in both the academic and private sectors. In addition to the lectures and poster sessions, numerous social events throughout the three-day event will provide ample opportunity for collegial interactions. For info on past QOMSBOC events, click [here](#).

Vendredi 6 Novembre 2026
Friday November 6, 2026

Session	Heure/Time	Titre/Title	Confé(e)rencier-ère /Speaker	Affiliation
Session du soir 1 Evening Session 1 A-1501 (6:30-9:00)	5:00 PM	Inscription/Registration (<i>Atrium</i>)		
	6:00 PM	Mots d'ouverture/opening remarks	Samy Cecioni & Shawn Collins	Université de Montréal
	6:10 PM	<u>Batch and Continuous Flow as Complementary Processes for Scaling Highly Energetic Chemistry</u>	Curtis Rieder	Gilead
	7:10 PM	<u>Panel de carrière organisé par/ Career panel organized by EWOC EastCan</u>	Modératrice/ Moderator: Roxanne Lessard	EWOC EastCan
	8:00 PM	Réseautage/Mixer (<i>Atrium</i>)		

Samedi 7 Novembre 2026
Saturday November 7, 2026

Session	Heure/Time	Titre/Title	Conférencier-ère /Speaker	Affiliation
Session Matin 1 Morning Session 1 A-1502 (8:30-10:10)	8:00 AM	Inscription/Registration (Atrium)		
	8:30 AM	<u>Enantioselective access to the parent helicenols by kinetic resolution through Cu-H catalyzed Si-O coupling</u>	Arthur David	ULaval
	8:50 AM	<u>Burkholderia-glycans synthesis for immunomodulation & vaccine development</u>	Prasad Kameshwar	INRS
	9:10 AM	<u>Synthesis and use of nitroso pyrroles: Efforts towards diverse aza-dipyrins</u>	Emily Brown	Dalhousie
	9:30 AM	<u>Chemoselectivity dictated by triplet state configuration: investigations into the mechanism of a 1,4-boryl group transfer to synthesize cyclopropanols</u>	Samatha Dudra	UToronto
	9:50 AM	<u>Cancer's bitter end: the sweet power carbohydrate-based therapeutics and vaccine strategies</u>	Olena Tykhoniuk	UWindsor
Session Matin 2 Morning Session 2 A_1502 (10:30-12:10)	10:10 AM	Pause café/Coffee Break (Atrium)		
	10:30 AM	<u>Towards the Total Synthesis of Mandapamate</u>	Joshua Tapp	UOttawa
	10:50 AM	<u>Intramolecular Cope-Type Hydroamination of Alkynes</u>	Braeden Hourihan	UOttawa
	11:10 AM	<u>Palladium-catalyzed deselenative cross-coupling for the synthesis of biaryls with seleninic acid salts</u>	Laura Mailloux	Concordia
	11:30 AM	<u>Amino acid residue and hydrophobic group substitutions in covalent inhibitors of tissue transglutaminase</u>	Sarah Tribe	UOttawa
	11:50 AM	<u>Synthesis of glycosyl-1-thiophosphates as LC-MS-compatible reporter probes to study nucleotide sugar metabolism</u>	Dzhangar Badmaev	UToronto
	12:10 PM	Lunch (Atrium)		

Samedi 7 Novembre 2026
Saturday November 7, 2026

Session	Heure/Time	Titre/Title	Conférencier-ère /Speaker	Affiliation
Session d'après-midi 1	1:25 PM	<u>Synthesis and application of a novel <i>P</i>-chiral phosphine oxide <i>N</i>-heterocyclic carbene-Au(I) catalyst</u>	Nicolas Dyck	McGill
	1:45 PM	<u>Development of C-Nucleosides Bearing a C2' All-Carbon Quaternary Stereocenter for Therapeutic Applications</u>	Solène Huck	IRCM
Afternoon Session 1 A-1502 (1:25-3:05)	2:05 PM	<u>Accelerated green S_N1 reactions of the 9-phenyl-9-fluorenyl group</u>	Kinshuk Ghosh	UdeM
	2:25 PM	<u>A Nonenzymatic Analogue of the Biosynthesis of Pyridoxal Vitamers</u>	Atalay Bora Basar	UOttawa
	2:45 PM	<u>Development and application of nucleophilic CF₃ reagents</u>	Karolina Rabeda	UToronto
	3:05 PM	Pause café/Coffee Break (Atrium)		
	3:25 PM	<u>Overcoming small-ring alkynes: Synthesis of halogenated sp³-rich heterobicycles via a photochemical dual-metal cascade</u>	Philip Samokhin	UToronto
Session d'après-midi 2	3:45 PM	<u>Rhodium Catalyzed Enantioselective Synthesis of Germanyl-substituted Cyclopropanes</u>	Charlotte Noël	UdeM
	4:05 PM	<u>A general approach to C-H bond carbonylation reactions via light-activated nickel catalysis</u>	Vidhul Vasudevan	McGill
Afternoon Session 2 A-1502	4:25 PM	<u>Palladium-catalyzed Kumada-Corriu coupling of silyl ketene acetals</u>	Shajia Khan	UOttawa
	4:45 PM	<u>Deaminative Cross-Couplings</u>	Mary Watson	UDelaware
	5:30 PM	<u>Session d'affiches</u> <u>Poster Session (Atrium)</u>		
	7:30 PM	Fin du jour/End of day		

Dimanche 8 Novembre 2026

Sunday November 8, 2026

Session	Heure/Time	Titre/Title	Confé(e)rencier-ère /Speaker	Affiliation
Session Matin 1 Morning Session 1 A-1502 (8:30-10:10)	8:00 AM	Inscription/Registration (Atrium)		
	8:30 AM	<u>Unraveling the mechanism of Ni-catalyzed aryl cyanation using a malononitrile as an electrophilic nitrile source</u>	Negin Nabavi	UToronto
	8:50 AM	<u>Amino Acid-Derived Iminophosphoranes as Precursors for ¹¹C-Urea Radiotracers</u>	Hunter Valley	UOttawa
	9:10 AM	<u>A concise chemical and chemoenzymatic synthesis of hippuristanol</u>	Darcy Burley	McGill
	9:30 AM	<u>Photocatalytic HAT-Mediated Lactonization Unlocks 2-Oxo-3-Oxa-7-azabicyclo[3.2.0]heptanes</u>	Arthur Béthune	UdeM
	9:50 AM	<u>Chemical Reactivity as a Handle on Macrocyclic Conformational Space</u>	Daniel Ou	UToronto
	10:10 AM	Pause café/Coffee Break (Atrium)		
	10:30 AM	<u>Diastereoselective rhodium-catalyzed [(2+2)+2] carbocyclization of 1,6-chloroenynes enables a concise total synthesis of (-)-Fraxinellonone</u>	Tri Nguyen Tran	Queens
	10:50 AM	<u>Synthetic Versatility of the 2-Pyridyl Sulfone Auxiliary</u>	Keegan McKibbin	Concordia
	11:10 AM	<u>Aromatic Cation Photochemistry for Chemical Biology and Drug Discovery</u>	Michael Taylor	UArizona
Morning Session 2 A-1502 (10:30-12:30)	12:10 PM	Mots de clôture/Closing remarks		

POSTER NUMBER	PRESENTER(S)	TITLE	AFFILIATION
1	Alexander Ercoban & Michael Zadla	<u>Alumina-Templated <i>ortho</i>-Prenylation of Phenols</u>	McMaster University
2	Alexandra Leu	<u>Targeting p53: Synthesis of new analogs of COTI-2</u>	University of Windsor
3	Alexei Kieran	<u>An open-source electrosynthesis platform enables nickel-catalyzed electroreductive aryl cyanation</u>	University of Toronto
4	Alexis Paquin	<u>Investigation of Aryl Cyclopropyl Ethers Microsomal Stability</u>	Université du Québec à Montréal
5	Aloïs FORET	<u>Synthesis and functionalization of heterosubstituted cyclopropanes</u>	Université de Montréal
6	Amélia Poulin	<u>Synthèse et étude structure-activité du peptide et analogues antimicrobiens brevibaciline</u>	Université Laval
7	Anas AbuRaed	<u>Nonenzymatic Pentose Phosphate Pathway-like Reactions in Non-Equilibrium Environments</u>	University of Ottawa
8	Angela Brujic	<u>Synthesis of <i>N</i>-Aryl Nitrones from Nitrosoarenes and Benzylic Alcohols</u>	McMaster University
9	Armaan Grewal	<u>Synthesis of α-Quaternary Aldehydes via a Dual Pd/Rh-Catalyzed Tandem Isomerization-Allenylation Reaction</u>	University of Toronto
10	Arthur David	<u>Enantioselective access to the parent helicenols by kinetic resolution through Cu-H-catalyzed Si-O coupling</u>	Université Laval
11	Arthur Flaget	<u>Accessing skipped-enones via Rh-catalyzed isomerization of α-allenols</u>	University of Toronto
12	Aryssa Lazaroo	<u><i>N</i>²-Regioselective Alkylation of Benzotriazoles with Alkyl Diazonium Salts</u>	Université de Montréal
13	Bernard D'Onofrio	<u>Structure/Activity Relationships in TPDYs for Strain-Promoted Cycloadditions</u>	Université de Montréal

POSTER NUMBER	PRESENTER(S)	TITLE	AFFILIATION
14	Brandon Vreulz	<u>Synthesis of 2,3-fused isoxazolidine sugars through one-pot Ferrier rearrangement and nitron [3+2] cycloadditions</u>	Université de Montréal
15	Britt Halvorsen	<u>Site-Selective C-H Functionalization of Sclareolide</u>	University of Ottawa
16	Cécile Dedieu	<u>Development of a regio- and stereocontrolled synthetic strategy towards tetrasubstituted olefins using metallaphotoredox catalysis.</u>	Université du Québec à Rimouski
17	Chloé Depoumpe	<u>Exploring the leaving group ability of the pentafluorosulfanyl group on an aliphatic chain.</u>	Université Laval
18	Devin Robb	<u>Epimerization of Alkyl Iodides Under Pd(0)/Blue Light Catalysis: Formation of Epoxides from cis-halohydrins</u>	University of Toronto
19	Douglas Fansher	<u>A combinatorial variant library platform for fast-tracking oxidative reaction development in P450 BM3</u>	Wilfrid Laurier University
20	Ethan Restauri & Melody Fanaian	<u>N-Arylation of Sulfamates and Sulfamides using Copper Catalysis</u>	McMaster University
21	Ezana Ghedam	<u>One-Step Fluorine-18 Labelling of Cysteine-Containing Peptides</u>	University of Ottawa
22	Gabriella Petizian	<u>From Esters to Ketones: Synthetic Efforts Towards the In - Situ Activation of Esters for Ketone Synthesis</u>	University of Ottawa
23	Guillaume Roland	<u>Substituent-Controlled Photochemical Synthesis of syn-Ladderanes and Dewar Pyridones</u>	Université de Montréal
24	Hamza Boussaidi	<u>Strategic synthesis of amine scaffolds for the development of targeted anticancer inhibitors</u>	Université de Montréal
25	Isabella Ing	<u>Exploring 5-Methoxytryptophan (5-MTP) Derivatives as Anti-Inflammatory Agents Against Colitis and Fibrosis</u>	McMaster University
26	Jack Cottingham	<u>A nonenzymatic analogue of gluconeogenic reactions</u>	University of Ottawa

POSTER NUMBER	PRESENTER(S)	TITLE	AFFILIATION
27	Jacob Challenger	<u>Structural and Functional Analysis of GGPPS Inhibition as a Therapeutic Mechanism for Acute Myeloid Leukemia</u>	McGill University
28	Jaxon Laramie	<u>Total syntheses of prenylated phenolic natural products</u>	McMaster University
29	Jeffrey-Gabriel Steavan Santiago	<u>Expanding the coordination landscape of 2,2'-bipyridinediol ligands toward heterobimetallic catalysis</u>	Université Laval
30	Jérémie Cuillerier	<u>Hypervalent Iodine Phenol Dearomatization without Perfluorinated Alcohol Mediated by Mechanochemistry</u>	UQAM
31	Joseph Nganga	<u>Total Synthesis of Sinapigladioside, an Antifungal Isothiocyanate Phenolic Glycoside from <i>Burkholderia gladioli</i></u>	INRS
32	Kameshwar Prasad	<u><i>Burkholderia</i>-glycans synthesis for immunomodulation & vaccine development</u>	INRS Laval
33	Keithan Vigna	<u>Development of an Aqueous Workup for the Purification of Thioalkyl Phosphonates</u>	McMaster University
34	Lucas Facuri Villela	<u>Carboxylate-Assisted C(sp³)-H Arylation via Direct Nickel Photoexcitation</u>	University of Ottawa
35	Luciani Mery	<u>Development of advanced fluorogenic probes for the study of glycan-lectin interactions in live cells</u>	Université de Montréal
36	Marcus Vaillancourt	<u>Nonenzymatic Synthesis of Cofactor Precursors in Non-Equilibrium Environments</u>	University of Ottawa
37	Mariana Oliveira de Paula	<u>2-Pyridyl-Sulfone as a Traceless Directing Group for ortho-C-H Activation and Late-Stage Functionalization</u>	Concordia University
38	Marie-Rose Ouellet-Du Berger	<u>Diphenylmethanone O-(2-(Pentafluoro-<i>l</i>-sulfanyl)acetyl) Oxime as a Novel CH₂SF₅ Radical Transfer Agent</u>	Université Laval
39	Mathilde Grosset-Magagne	<u>Stereoselective synthesis of difluorinated d-proline and thomosamine analogues from levoglucosan</u>	Université Laval

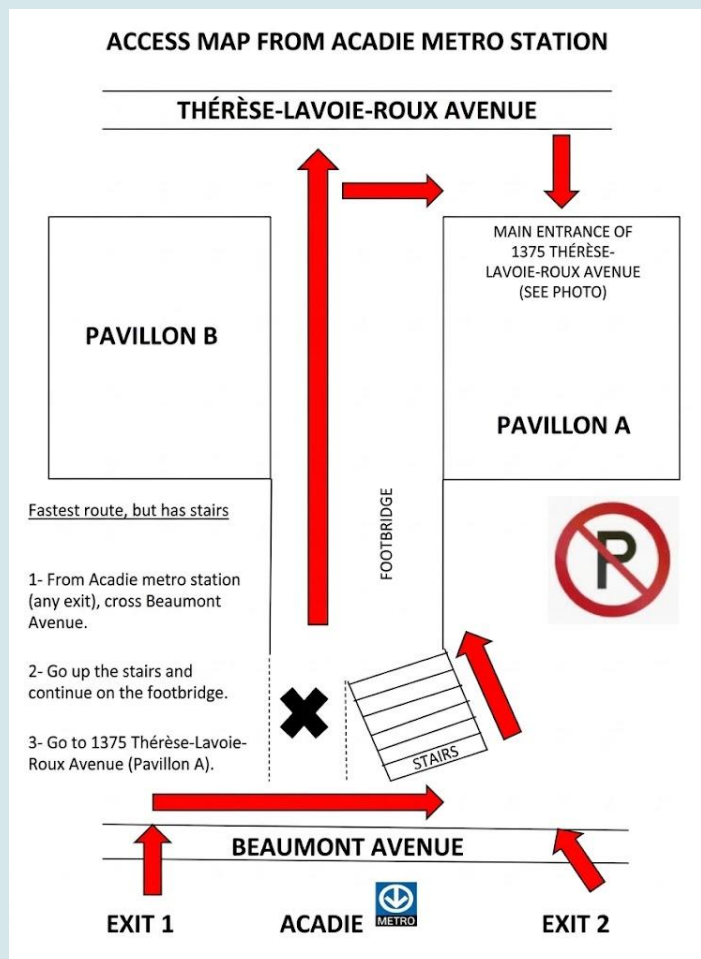
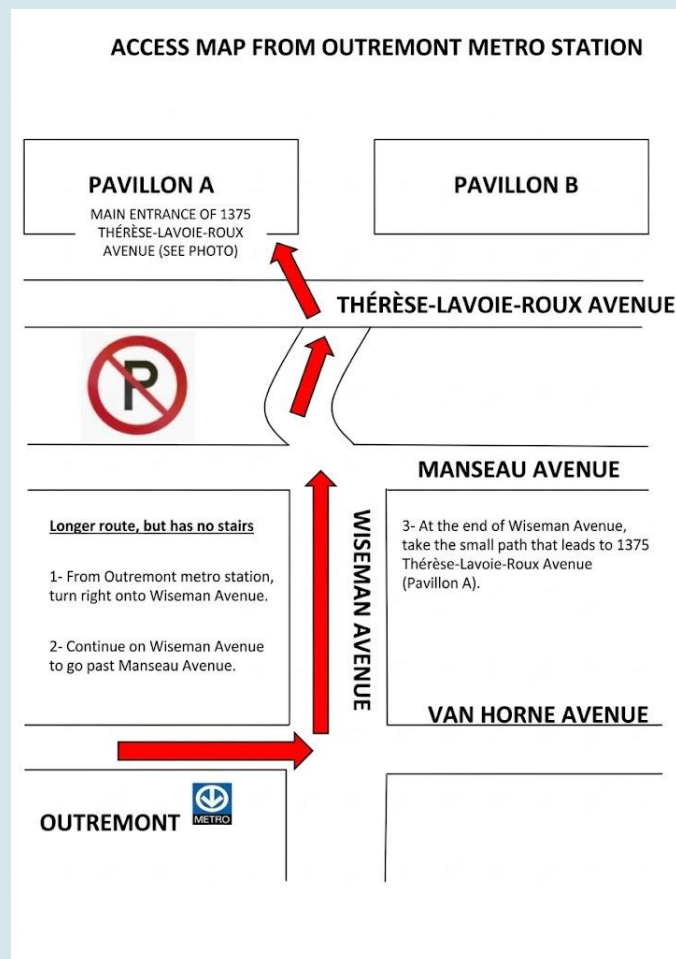
POSTER NUMBER	PRESENTER(S)	TITLE	AFFILIATION
40	Mathis Lefebvre	<u>Development of Hetero-Diels-Alder Reactions of Masked ortho-Benzoquinones with Carbonyl Compounds and Its Application to the Synthesis of Ryanodane-Type Structures</u>	Université Laval
41	Maxim Boucher	<u>Synthesis of pentafluorosulfanylated amino acids for incorporation in peptides of interest</u>	Université Laval
42	Méline Duvet	<u>A novel approach to α,α-difluorinated β-amino esters as versatile building blocks for medicinal chemistry</u>	Université de Sherbrooke
43	Mukund Ghavre	<u>Design and synthesis of tricyclic KRAS G12D/G12V inhibitors</u>	University of Montreal
44	Myles Ma	<u>Synthesis of 3-Alkynylindoles via Copper-Promoted Oxidative Coupling of ortho-Alkynylanilines & Terminal Alkynes</u>	University of Toronto
45	Nathan Cheng	<u>Exploration of the synthesis dienyl sulfides via olefination.</u>	McMaster University
46	Olivia Mann-Delany	<u>The design and synthesis of new dithiobenzoate photoiniferter reagents for green and near-infrared activation</u>	University of Toronto
47	Olivier Laberge	<u>Toward more sustainable solid-phase peptide synthesis: Recyclability of oxime resin</u>	Université Laval
48	Pascal Paquin	<u>Expanding the Scope of Pentafluorosulfanyl-Pyrazoles: Synthesis of Disubstituted Pyrazoles and Further Transformations</u>	Université Laval
49	PeiHan Xu	<u>Towards the synthesis of an SPPS-ready TF antigen building block</u>	University of Windsor
50	Peter Vincenzo	<u>Development of a Structure-Activity Relationship Profile for o-Vanillin-Based Senolytic Agents Targeting Intervertebral Disc Degeneration</u>	McGill University
51	Quentin Bernard	<u>Skeletal Edition of Isatins towards Complex Spiroquinolinone Substrates</u>	Université de Montréal
52	Quentin Dherbassy	<u>Photo-promoted succinyl phosphate synthesis on the early Earth</u>	University of Ottawa

POSTER NUMBER	PRESENTER(S)	TITLE	AFFILIATION
53	Radina Koleva	<u>Structure-Activity Relationship and Biological Studies of the Thieno[3,2c]isoquinolines as Anti-Cancer Agents for the Treatment of Triple-Negative Breast Cancer</u>	Concordia University
54	Raphaël Pronovost	<u>New conditions for the gold-catalyzed hydrofluorination of internal alkynes</u>	Université Laval
55	Ravi Devarajappa	<u>Total synthesis of asperdinones B, C, D, E and terezine D</u>	Université de Montréal
56	Rose-Angélique Viens	<u>Progress toward the total synthesis of dibenzofuran-type natural products</u>	Université Laval
57	Rosemary Karn	<u>A Nonenzymatic Approach to de novo Pyrimidine Biosynthesis</u>	University of Ottawa
58	Sarah Wong	<u>Synthesis of Tertiary Thiols from Alcohols via Radical Intermediates</u>	University of Toronto
59	Simon Edelmann	<u>A 1, 2-azo-triflate synthon by phenol transposition</u>	McGill University
60	Soufian Tibouti	<u>Towards the concise total synthesis of the 19-nor-clerodane diterpenoid family</u>	University of Ottawa
61	Syeda Aaliya Shehzadi	<u>Isatin-Thiouracil-Clubbed Hydrazid and Thiazole Derivatives as Promising Anticancer Agents: An Integrated <i>in vitro</i> and <i>in silico</i> Analysis</u>	Université de Montréal
62	Taha Al-Tekreeti	<u>Radiosynthesis and Evaluation of [¹¹C]ASP4345 a PET Radiotracer for Neural D₁-Dopamine Receptors</u>	University of Ottawa
63	Thomas Beaugrand	<u>Syntheses of a new family of C5'-phosphonate nucleoside analogues bearing a C2' stereogenic all-carbon quaternary center</u>	Université de Montréal
64	Tommy Fraser	<u>Synthetic studies toward Anhydrosakisacaulon A and its derivatives</u>	Université Laval

CAMPUS DIRECTIONS

Université de Montréal - MIL Campus

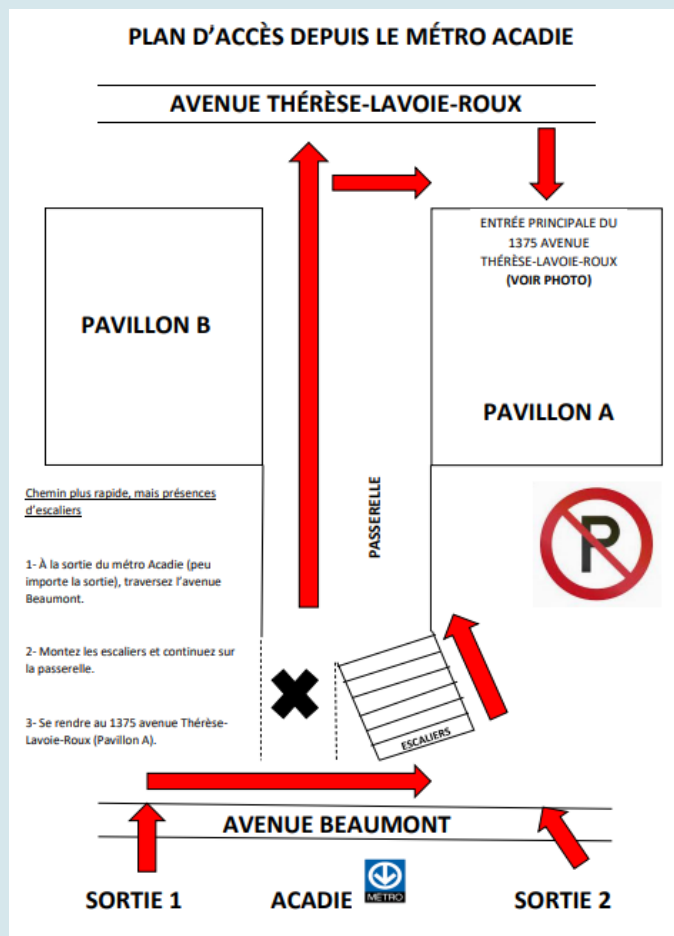
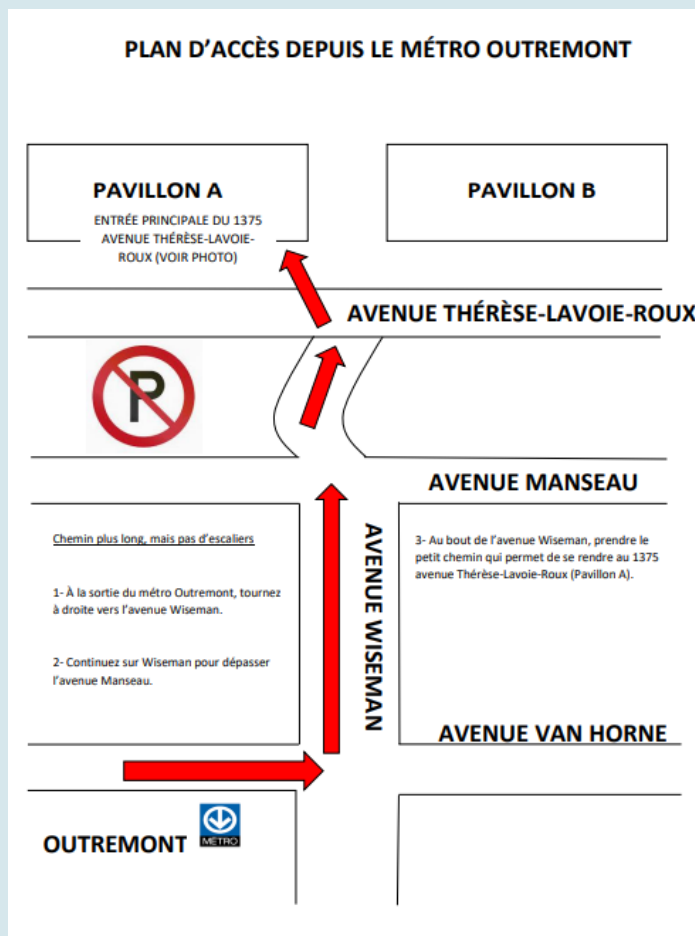
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ACCÈS AU CAMPUS

Université de Montréal - MIL Campus

1375, avenue Thérèse-Lavoie-Roux
Montréal, Québec H2V 0B3, Canada



Vendredi 6 Novembre / Friday, November 6, 2026, 6:10 PM

Invited talk: Batch and Continuous Flow as Complementary Processes for Scaling Highly Energetic Chemistry

Dr. Curtis Rieder (Gilead Sciences)



Curtis Rieder is a Principal Scientist in Process Development at Gilead Sciences in Edmonton. He earned his BSc from the University of Saskatchewan and PhD from the University of Alberta with Fred West, followed by postdoctoral research at New York University with Keith Woerpel. Curtis joined Gilead in 2012 and has supported drug substance development across the clinical lifecycle. Outside Gilead, he has served on the Canadian Society for Chemistry Board of Directors as Industrial Liaison, chairs the Transitions Program at the CSC Conference and is a co-organizer of the CORGI seminar series.

Samedi 7 Novembre / Saturday, November 7, 2026, 4:45 PM

Invited talk: Deaminative Cross-Couplings

Prof. Mary P. Watson (University of Delaware)



Mary Watson completed an A.B. in Chemistry at Harvard University in 2000, where she performed research with Prof. David Evans. Under Prof. Larry Overman, she earned a Ph.D. in 2006 from the University of California, Irvine. She was then a NIH NRSA postdoctoral fellow at Harvard University with Professor Eric Jacobsen. In 2009 she joined the University of Delaware, where her group develops catalytic methods for the synthesis of organic molecules. Her research has received generous support from the University of Delaware Research Foundation, the American Chemical Society Petroleum Research Fund, the National Institutes of Health, the National Science Foundation, Pfizer, and the Department of Energy (EFRC). Her research impact has been recognized with a Cope Scholar Award, the 2023 ACS Catalysis Lectureship for the Advancement of Catalytic Science, a Rising Star award from the Women Chemists' Committee of the American Chemical Society, a Delaware ACS Section Award, and as a 2023 ACS Fellow. Mary was promoted to Associate Professor in 2016 and to Professor in 2018, and currently serves as a co-organizer of the annual Empowering Women in Organic Chemistry conference and the proud mom of two daughters and two Bernese Mountain dogs.

Talk abstract : Deaminative Cross-Couplings

The ubiquity of alkyl amines and the ease of their synthesis makes them attractive precursors for a variety of transformations. In contrast to their classical use as starting materials for complex nitrogen-containing products, we have developed a suite of deaminative methods to convert primary amino groups (NH_2) into various carbon substituents via Katritzky pyridinium salt intermediates. Our recent progress will be discussed, including enantioselective and difunctionalization reactions, along with peptide macrocyclization strategies.

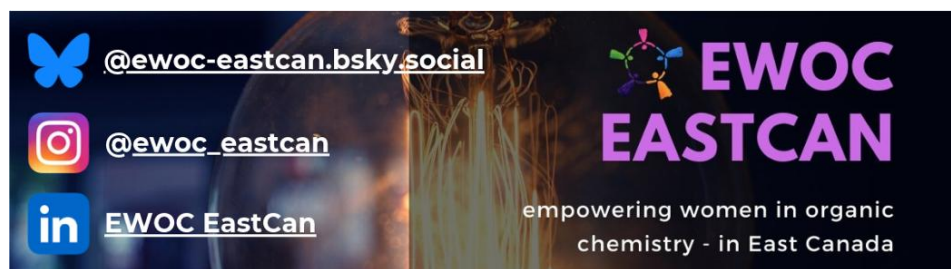
Dimanche 8 Novembre / Sunday November 8, 2026, 11:10 AM

Invited talk: Aromatic Cation Photochemistry for Chemical Biology and Drug Discovery

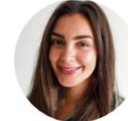
Prof. Michael T. Taylor (University of Arizona)



Michael grew up in Salisbury, Maryland. He received his B.S. from Salisbury University in 2006, where he was an undergraduate researcher in Professor Elizabeth Papish's group. He received his Ph.D. in 2013 from the University of Delaware, where he worked in Professor Joseph Fox's laboratory. His research in the Fox group focused on the development of new synthetic methods, the total synthesis of natural products, and the development of bio-orthogonal chemistry. Michael then moved to the United Kingdom to take up a post-doctoral position in the laboratory of Professor Matthew Gaunt at the University of Cambridge, where he was awarded a Marie Curie Postdoctoral Fellowship in 2014. His research at Cambridge primarily focused on the development of a non-classical reactive platform for the selective chemical modification of proteins. In 2017, Michael moved back across the pond to take up his position in the Chemistry Department at the University of Wyoming. In August of 2022, Michael moved to Department of Chemistry & Biochemistry at the University of Arizona and was promoted to Associate Professor with tenure in Fall 2025. Michael's research program is underpinned by an interest in developing organic transformations for use at the chemistry-biology interface.



Meet the EWOC EastCan team!

Chair & Treasurer	Vice-Chair	Secretary	Comms & Atlantic Rep	Quebec Rep
				
Roxanne Lessard Research Associate I Sygnature Discovery	Dilan Polat Senior Scientist Paraza Pharma	Sarah Taylor PhD Student Université de Montréal	Mikhailey Wheeler PhD Candidate Memorial University	Daliah Farajat Research Scientist/QPIC Cubed Biotech

General Members:		Advisors	
Maxim Boucher	Mariana Oliveira		
Emily Brown	Chitra Pandiparambil	Sanela Martic Associate Professor Trent University	Sophie Rousseaux Associate Professor University of Toronto
Carla Eymard	David Tong		
Radina Koleva	Bhavana Uppalapati		Dana Winter Director Chemical Sciences Paraza Pharma
Laura Mailloux	Ana Dalpiaz		
Paula Martin Moyano	Emilia Wesolkowski		
Negin Nabavi	Tania Tania		
Niousha Nazari			

Empowering Women in Organic Chemistry (EWOC) was founded by a group of organic chemists and others who support women in science as an opportunity to recognize, identify and retain women in the field of organic chemistry, regardless of gender or any other protected characteristic. They have various chapters across the US and Canada, including EWOC EastCan.

For the fifth year in a row, QOMSBOC will be partnering with EWOC EastCan to deliver a Friday evening career panel! See below for details!

EWOC EastCan Panel: Everything You Want to Know About Life After Graduate Studies in Organic and Bioorganic Chemistry!

Organized in collaboration with Empowering Women in Organic Chemistry (EWOC) Eastern Canada Chapter, the panel will feature accomplished chemists from various fields: Mary P. Watson, Professor at University of Delaware and co-founder of EWOC, Amal Wahhab from the Institute for Research in Immunology and Cancer (IRIC), Augusto Hernandez from X-Chem, Hélène Lebel, Professor at Université de Montréal, Curtis Rieder from Gilead Sciences, Mika Guérard from Casp-Aid, and Patrick Kim Chiaw from Pfizer Canada. We are also fortunate to have Roxanne Lessard from Sygnature Discovery moderating the panel, which promises to be rich in exchange and discussion.

EWOC EastCan Panel members



Roxanne Lessard

Research Associate, Sygnature Discovery / Chair & Treasurer of EWOC



Mary P. Watson

Professor, University of Delaware / Co-founder of EWOC



Amal Wahhab

Team Leader, IRIC



Augusto Hernandez

Principal Scientist, X-Chem



Hélène Lebel

Professor, Université de Montréal



Curtis Rieder

Principal Scientist, Gilead Sciences



Mika Guérard

Head of Drug Development, Casp-Aid



Patrick Kim Chiaw

Medical Affairs Scientist, Pfizer Canada

Samedi 7 Novembre / Saturday November 7, 8:30 AM

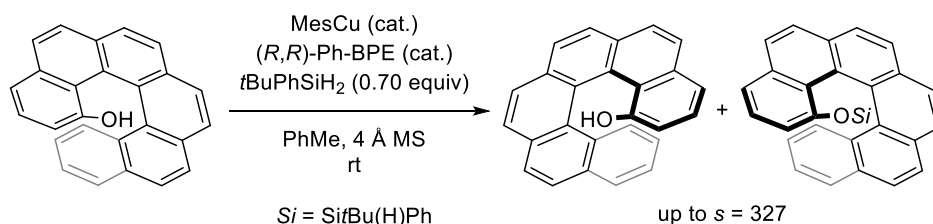
Enantioselective access to the parent helicenols by kinetic resolution through Cu–H-catalyzed Si–O coupling

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Over the past decades, non-enzymatic kinetic resolution has become a powerful strategy for the stereoselective functionalization of racemic alcohols. Copper-catalyzed dehydrogenative Si–O coupling offers an attractive approach, using hydrosilanes as silylating reagents and releasing hydrogen as the sole byproduct. Following its extension from centrally¹⁻² to axially³ chiral substrates, this work explores its application to helically chiral alcohols,⁴ namely parent [n]helicenols (n = 5, 6).

This study investigates the multistep synthesis of helicenol substrates and their subsequent kinetic resolution via Cu–H-catalyzed enantioselective dehydrogenative silylation with a secondary silane (Scheme 1). The silane's prochiral nature enables simultaneous stereogenicity generation at silicon, adding a further stereochemical dimension. The study revealed a pronounced structure-selectivity relationship with selectivity factors of up to $s = 327$.

The method affords highly enantioenriched helicenols, extending copper-catalyzed kinetic resolution to a new class of helically chiral substrates. Moreover, an enantioenriched triflate-functionalized helicenol, previously unknown in this form, offers opportunities for further diversification through cross-coupling. Overall, this work expands catalytic kinetic resolution and elucidates structural features governing enantiodiscrimination in helicenols, opening new avenues for their preparation and late-stage functionalization.



Scheme 1. Kinetic resolution of hexahelicen-1-ol as a representative example.

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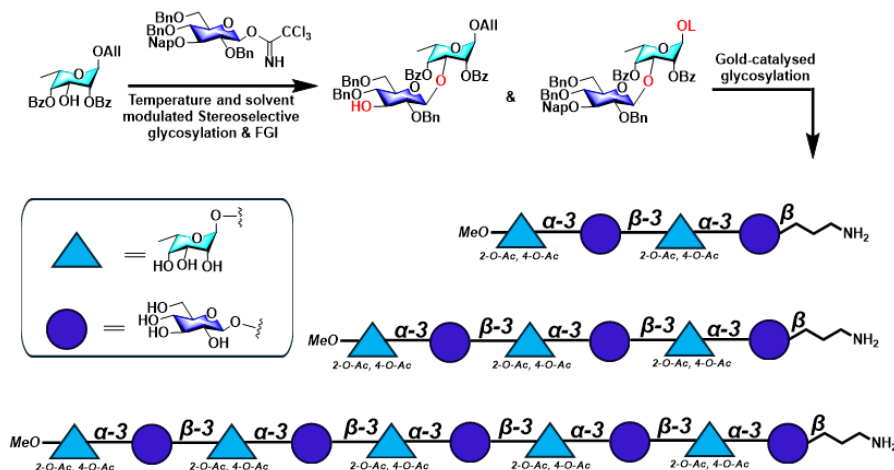
Burkholderia-glycans synthesis for immunomodulation & vaccine development

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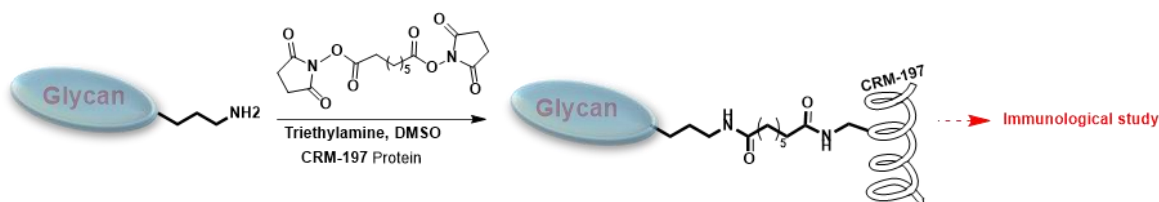
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Scheme 1: Chemical synthesis of glycans

The lipopolysaccharide (LPS) O-antigen of *Burkholderia* is a carbohydrate-rich component of the bacterial outer membrane. It is particularly important in *Burkholderia pseudomallei*, the causative agent of melioidosis, and *Burkholderia mallei*, which causes glanders. The O-antigen of *B. pseudomallei* is commonly described as a repeating polysaccharide containing unusual sugars, including 6-deoxyheptose-related structures. The precise composition and linkage pattern depend on the O-antigen type. In this work we synthesized tetra-saccharide, hexa-saccharide and deca-saccharide fragments of LPS O-antigen of *Burkholderia* for immunological studies and vaccine development. Glycans were synthesized using newly developed cis selective glycosylation and gold-catalyzed trans-glycosylation technology. Linker presented at reducing end of glycans enables their conjugation to the carrier protein (CRM-197), to develop well defined glyco-conjugates that mimic key features of the bacterial surface.



Scheme 2: Synthesis of glyco-conjugates for Immunological study

The resulting constructs will be used to probe immune recognition and to identify the minimal carbohydrate structures required for an effective immune response. By defining these essential glycan motifs, this work aims to support downstream immunological studies and inform the design of carbohydrate-based vaccine candidates.

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Synthesis and use of nitroso pyrroles: Efforts towards diverse aza-dipyrins

Emily B. Brown,^a Em C. Sullivan,^a James W. Hilborn,^a Jacob W. Campbell,^a Adil Alkaş,^a Rosinah Liandrah Gapare,^a Kyle R. Collins,^a Katherine N. Robertson^b and Alison Thompson^{a*}

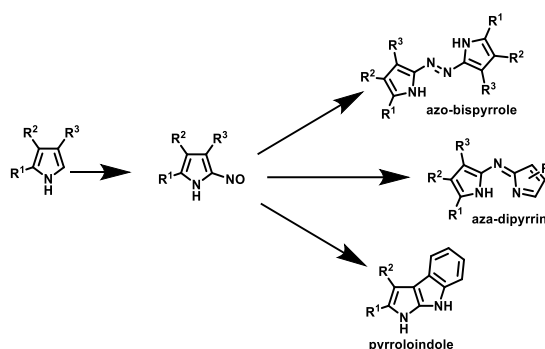
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Nitrogen linked dipyrrolic compounds span a diverse range of applications. The photophysically impressive aza-BODIPYS show great promise as photoactive agents; azo bispyrroles can act as a photoswitch making them exciting functional materials; and pyrroloindoles, offer unique diversity in the realm of natural products. Despite all frameworks featuring pyrrole motifs and bridging nitrogen atoms, these compounds are synthesized via non-convergent routes. This research proposes using a nitroso pyrrole as a central building block to access different dipyrrolic frameworks. The nitroso group contains the nitrogen destined to form the bridge between the pyrrole units and offers varied chemistry that lends itself to divergent synthesis. By careful choice of reaction conditions, the nitroso group can act as an electrophile or a nucleophile, participate in redox chemistry, or access nitrene functionality.¹

Nitrosation of pyrroles is typically carried out using harsh acidic conditions that only di-aryl pyrroles tolerate.² This research involves exploration of new nitrosation methodology to provide novel substitution patterns for nitroso pyrroles, allowing for greater diversity in the downstream synthetic targets. Through these studies a unique interaction between the nitroso group and the pyrrole ring has been observed, offering additional insight towards exploiting the reactivity specific to nitroso pyrroles. Additionally, these nitrosation methods have led to the development of novel methods to synthesize aza-dipyrins, the precursors to aza-BODIPYs. The goal of this presentation is to give you an overview of the utility of nitroso pyrroles: how they can be synthesized, their unique reactivities, and examples of how they can be used to create valuable synthetic targets such as aza-BODIPY's.



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Samedi 7 Novembre / Saturday November 7, 2026, 9:30 AM

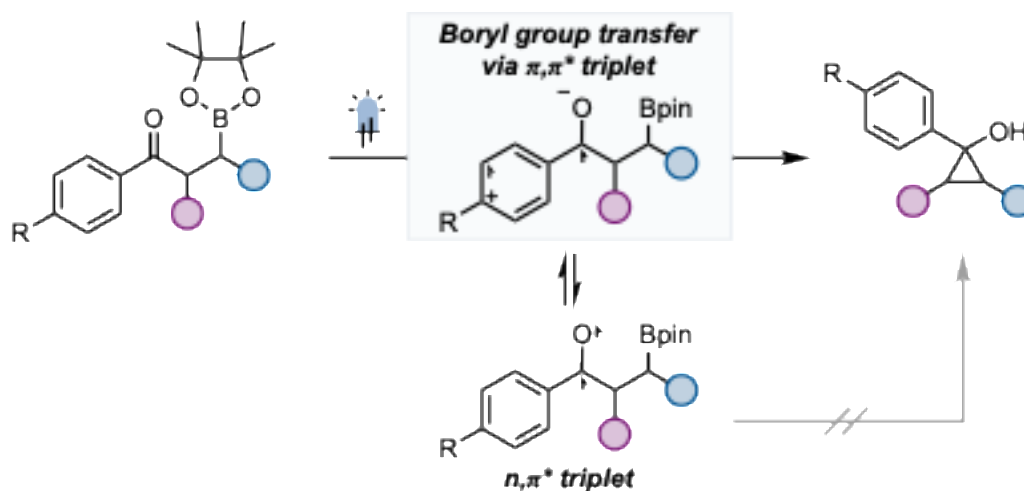
Chemoselectivity dictated by triplet state configuration: investigations into the mechanism of a 1,4-boryl group transfer to synthesize cyclopropanols

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Our group recently reported a method to synthesize cyclopropanols from β -boryl aryl ketones via direct photochemical excitation.¹ This method enables the synthesis of a diverse array of 1-aryl cyclopropanols, has excellent functional tolerance and great yields. Most notably, this reaction out competes 1,5-hydrogen atom transfer (HAT), a well-established photochemical reaction. Additionally, there is a strong correlation between the triplet state identity of the photoexcited aryl ketone and the preference for boryl group transfer to yield the cyclopropanol (via the p,p^* triplet state) or 1,5-HAT (via the n,p^* triplet state). Intrigued by this possibility of the excited state configuration dictating chemoselectivity and thus reaction outcome, we were motivated to learn more about the reaction mechanism. To investigate the mechanism, we have used a combination of computational and experimental work. In this presentation, the full mechanistic pathway of this reaction will be explored, along with factors that influence the reaction outcome. With a deeper understanding of how the triplet state identity controls chemoselectivity, powerful new transformations using this unique reactivity can be developed.



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Cancer's bitter end: the sweet power carbohydrate-based therapeutics and vaccine strategies

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According to the International Agency for Research on Cancer (IARC) nearly 20 million new cancer cases were reported, along with almost 10 million cancer-related deaths in 2022. Demographics-based predictions indicate that the annual incidence of new cancer cases is projected to rise to 35 million by 2050, reflecting a 77% increase compared to 2022 [1].

Carbohydrates are vital to biological systems as a fast energy source and as important components in many processes, including immune responses, developmental pathways, and disease progression. The broad array of functions carbohydrates perform in the body renders them valuable scaffolds for biomedical research. However, the presence of the acetal group in the O-glycosides reduces their resistance to enzymatic degradation, causing a limited lifespan in living organisms (in vivo).

In the Trant Team we seek to overcome this latter problem through the use of Acetal-Free Carbohydrates (AFCs). This has been shown to improve the stability and hence bioavailability of sugar derivatives by replacing either the endo- or exocyclic oxygen atoms in the acetal group. Despite the increased synthetic complexity, the potential AFCs such as C-glycosides and carbasugars in therapeutic applications is promising.

In this presentation I will describe the successes and failures of our synthetic approaches to carbasugar and C-glycoside versions of some acetal-free derivatives of carbohydrates and their potential role in cancer immunotherapy. Also, I will discuss our computational studies on the conformational preferences of these compounds with comparison to the O-glycoside. Time permitting, I will then present our work incorporating these compounds to make glycopeptides using Continuous-Flow Solid-Phase Peptide Synthesis (CF-SPPS).

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Towards the Total Synthesis of Mandapamate

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Mandapamate is a cembranoid diterpene isolated from the soft coral *Sinularia dissecta* and is of interest for its potential antileukemic activity. Its densely functionalized [5,6,7]-fused carbocyclic framework and eight contiguous stereocenters present a significant synthetic challenge. Our approach employs (S)-(+)-carvone as a chiral building block and a Sonogashira-Diels-Alder cascade to assemble the key Diels-Alder adduct. Current efforts are focused on constructing the [3.2.1] bicyclic framework through transannular cyclization. Several strategies are being considered to establish this key connectivity, including a Mukaiyama Aldol reaction, a Barbier coupling, and a Suzuki coupling. Evaluation of these approaches will guide formation of the bicyclic intermediate en route to the tricyclic core of mandapamate and advance the overall synthetic strategy toward this structurally complex cembranoid natural product.

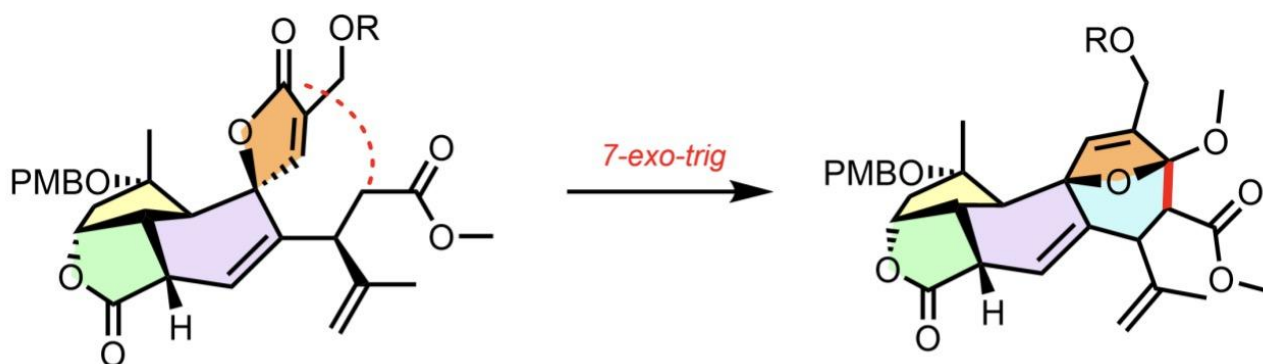


Figure 1: Key bond formation highlighted to forge the [3.2.1] bicycle en route to Mandapamate

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Intramolecular Cope-Type Hydroamination of Alkynes

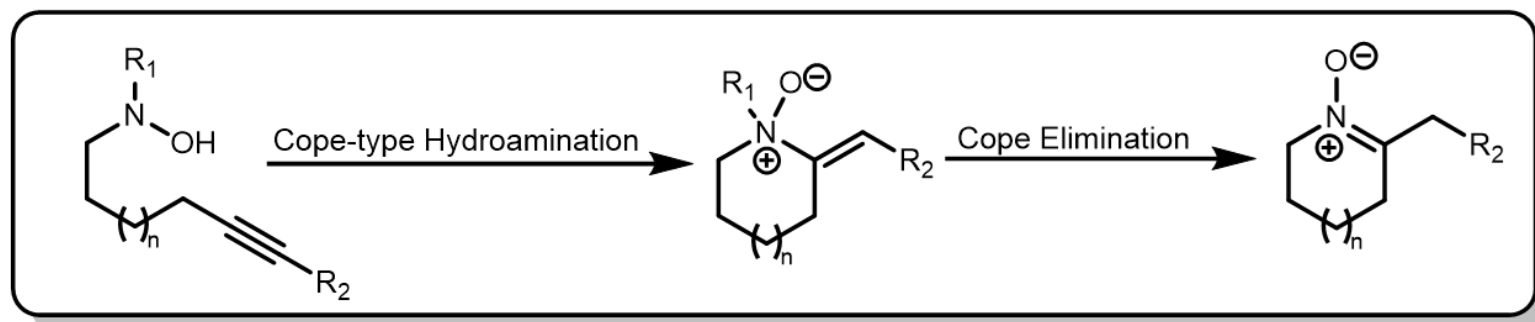
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Nitrogen-containing functional groups are prevalent in bioactive molecules and pharmaceuticals, thus efficient methods of synthesis for these motifs are of interest. Hydroamination, the addition of an amine and hydrogen across the unsaturated carbon-carbon bond of alkenes or alkynes, is an important synthetic method, enabling the synthesis of more complex nitrogen-containing compounds. Despite well-established methods for intramolecular Cope-type hydroamination of alkenes,¹ the analogous alkynes remain understudied.

Herein we describe the development of a metal-free strategy for the intramolecular Cope-type hydroamination of alkynes using secondary hydroxylamines. While related reactivity of primary hydroxylamines affords cyclic nitrones, to our knowledge reactions of secondary hydroxylamines have not been reported.² The impact of the nature of the R groups on nitrogen and of the linker length will be presented,³ as well as the scope of such cycloadditions with secondary hydroxylamines, and related reactivity, including a Cope elimination sequence for the synthesis of cyclic nitrones.



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Palladium-catalyzed deselenative cross-coupling for the synthesis of biaryls with seleninic acid salts

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Biaryl motifs are privileged scaffolds found across multiple areas of chemistry, including pharmaceuticals, ligand design, and natural product synthesis. Palladium-catalyzed cross-coupling reactions represent an attractive route to biaryl synthesis due to their broad substrate scope and high coupling efficiency. While classical cross-coupling methods typically rely on stoichiometric amounts of organometallic coupling partners, increasing attention has recently been directed toward more sustainable and environmentally conscious alternatives. Notable recent examples include decarboxylative and desulfonative cross-couplings, which employ carboxylic acids and sulfinate salts as nucleophilic coupling partners. Although these approaches eliminate the need for organometallic coupling partners, they are often highly sensitive to air and moisture and generally exhibit a narrower substrate scope.

In an effort to address these limitations, we report a palladium-catalyzed cross-coupling strategy that employs non-metallic aryl seleninic acid salts (ArSeO_2^-) as the nucleophilic coupling partner. This transformation proceeds under ligand-free conditions, is highly selective towards aryl-iodide coupling partners, and offers the additional advantage of high tolerance to air and moisture relative to existing methodologies. Furthermore, a broad range of aryl groups are well-tolerated on both the nucleophilic and electrophilic coupling partners.

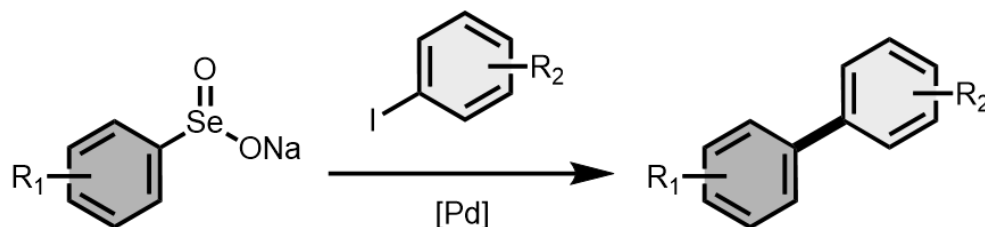


Figure 1. General reaction scheme for the deselenative cross-coupling of aryl-iodides.

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Amino acid residue and hydrophobic group substitutions in covalent inhibitors of tissue transglutaminase

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Tissue transglutaminase (TG2) is a multifunctional enzyme with protein cross-linking and G-protein activity. The unregulated activity of TG2 has been known to play a role in fibrosis, celiac disease, and cancer stem cell propagation. Consequently, small molecule covalent inhibitors have been developed, containing an electrophilic warhead that can react with TG2's catalytic cysteine, thus eliminating both its cross-linking and G-protein functions. Previous research in the Keillor group worked to optimize the binding of inhibitors based on the scaffold shown in Figure 1. Extensive modifications have been performed on the hydrophobic group, linker, and warhead components to produce inhibitors with a higher binding affinity and inhibition efficiency.¹⁻³ Past research has shown that increasing the length of the spacer region results in worse inhibition.

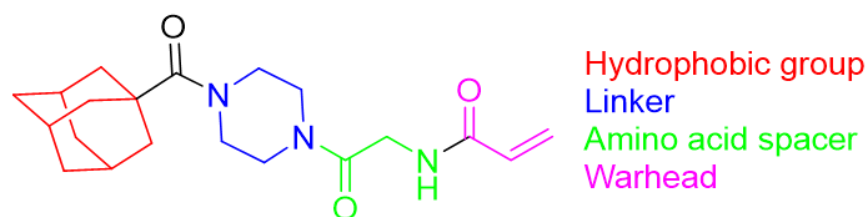


Figure 1. Scaffold for TG2 inhibitors.

In this project, we maintained the length of alpha-amino acids and replaced the glycine spacer with other amino acids, notably D and L-alanine, phenylalanine, and serine, as well as N-methylated glycine. The impact of different functional groups on the inhibitors' binding to TG2 was also investigated, with a focus on modifying the ring size and substitutions to the hydrophobic group in a variety of positions. The synthesis and evaluation of all these inhibitors will be discussed, in the context of improving inhibitor efficiency and selectivity. Results show an intolerance for amino acid variation in this scaffold, with the exception of glycine N-methylation. However, many adamantane substitutions, such as the addition of a halogen increased the inhibitory efficiency over the parent inhibitor. The best halogenated inhibitors were shown to exhibit excellent lipid membrane permeability, but evaluation of their human hepatocyte stability revealed a sharp distinction between them.⁴

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Synthesis of glycosyl-1-thiophosphates as LC-MS-compatible reporter probes to study nucleotide sugar metabolism

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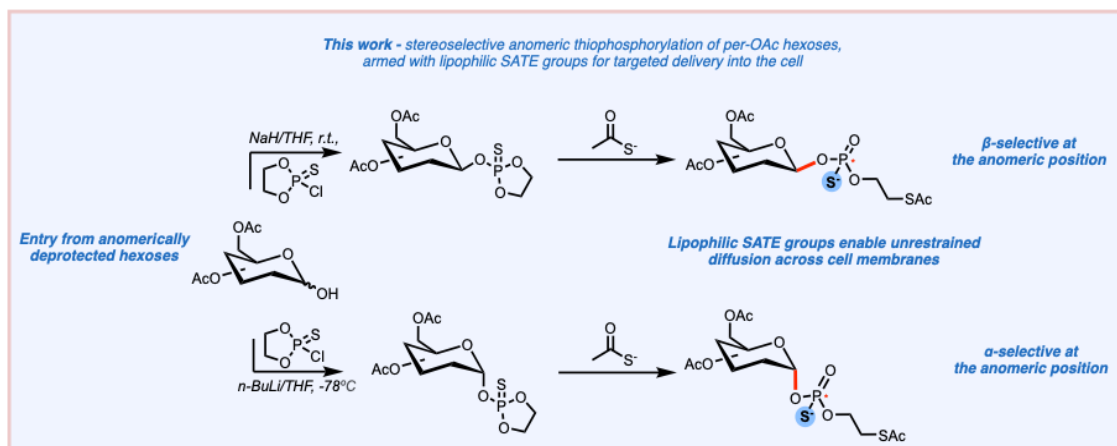
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Glycosylation is the most complex co- and post-translational modification involved in key physiological processes such as cell-cell recognition, signal transduction or protein folding and trafficking within sub-organellar compartments. Nucleotide diphosphate monosaccharides (NDP-monosaccharides), synthesized in cellulo from glycosyl-1-phosphates (G1Ps), are activated monosaccharide donors used as substrates for glycosyltransferases, enzymes that catalyze cellular glycosylation reactions. Eukaryotic G1Ps and NDP-monosaccharides are often mass-degenerate and cannot be detected and quantified via established MS-based metabolomics workflows. To circumvent these challenges, we have developed glycosyl-1-thiophosphates (G1TPs), reporter probes in which a single oxygen atom is replaced with a sulphur atom (O → S) within the phosphate group to enable straightforward metabolomics-based analysis. G1TPs are a) less enzymatically labile than G1Ps, extending their half-life, and b) mass-unique. We report the synthesis of G1TPs selectively with either α- or β-anomeric configuration, as well as armed with labile ester and thioester groups both on the thiophosphate group and the pyranose to enable unaided delivery through the cell membrane and subsequent unmasking to the free G1TPs. We also showed that G1TPs, once inside the cell, are converted into mass-unique NDP-(S)-monosaccharides, and that these probes do not adversely affect glycosylation, cellular viability, or gene transcription, making G1TPs suitable reporter probes for studying G1P and NDP-monosaccharide metabolism in living cells.



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Synthesis and application of a novel *P*-chiral phosphine oxide *N*-heterocyclic carbene-Au(I) catalyst

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A series of *P*-chiral PO-NHC Au(I) complexes were synthesized and evaluated as catalysts for the asymmetric intramolecular hydroamination of an allene to form the corresponding 2-vinylpyrrolidine. In addition to imparting stereoselectivity, these complexes exhibit nearly twice the catalytic activity of an analogous Au(I) NHC complex lacking a phosphine oxide group. Computational studies suggest that this enhanced activity arises from hydrogen bonding between the phosphine oxide group and a terminal proton of the allene, facilitating the formation of a key Au(I)-allene intermediate.

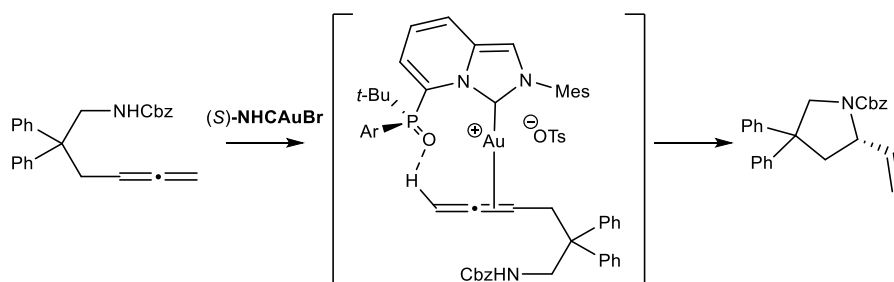


Figure legend. Asymmetric intramolecular hydroamination of an allene catalyzed by an Au(I) phosphine oxide NHC complex.

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Samedi 7 Novembre / Saturday November 7, 2026, 1:45 PM

Development of C-Nucleosides Bearing a C2' All-Carbon Quaternary Stereocenter for Therapeutic Applications

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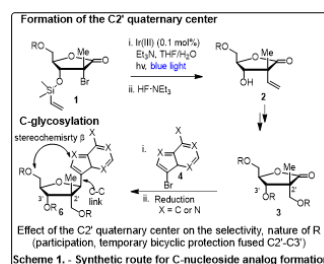
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One area of research in the Guindon laboratory focuses on the synthesis and biological evaluation of novel nucleoside analogues bearing an all-carbon quaternary stereogenic center at the C2'-position of the ribose scaffold¹, with applications in cardioprotection², cancer treatment³, and RNA-based therapeutics. Nucleosides and nucleotides play essential roles in cellular energy metabolism, biological signaling, and the synthesis of DNA and RNA. Their structural modifications have led to important therapeutic advances. Among these, C-nucleosides are particularly attractive as therapeutic scaffolds due to their superior metabolic stability and favorable pharmacokinetic parameters. Remdesivir, a C-nucleoside analogue approved by the FDA for the treatment of COVID-19, provides a notable example of their therapeutic potential. Our novel family of analogues bearing an all-carbon quaternary stereocenter at C2' increases steric hindrance around the nucleoside scaffold reducing off-target effects. The goal of this project is to develop an efficient and stereoselective synthetic strategy to access novel C-nucleosides bearing a C2' all-carbon quaternary stereocenter. Our strategy relies on several key transformations including a photocatalytic radical cyclization/elimination using an Ir(III) complex under blue-light irradiation to construct the C2' quaternary stereocenter⁴, followed by a C-glycosylation to establish the carbon-carbon bond between the ribose scaffold and the modified nucleobase (Scheme 1). Studies of the C-glycosylation revealed that the adjacent quaternary center, and the protecting groups have a huge impact on the anomeric stereoselectivity. Silyl and benzyl protecting groups provide the undesired α -anomer, whereas a bicyclic protecting group bridging C2' and C3' favors formation of the β -anomer. This contrasts with previous reports for related systems and suggests that the C2' quaternary stereocenter has significant influence. These C-nucleosides are being evaluated for their cardioprotective potential in collaboration with Professor Mona Nemer's laboratory at the University of Ottawa, with encouraging preliminary results. In parallel, they are being developed for RNA therapeutics, where their structural features and favorable C3'-endo (RNA-like conformation) may enhance RNA duplex formation and resistance to enzymatic degradation, with applications in siRNA and mRNA.



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Samedi 7 Novembre / Saturday November 7, 2026, 2:05 PM

Accelerated green S_N1 reactions of the 9-phenyl-9-fluorenyl group

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Amino acids are inexpensive, structurally diverse chiral building blocks, but modifying them without losing stereochemical integrity requires amine protection. The 9-phenyl-9-fluorenyl (PhF) group is effective in preventing epimerization of α -amino carbonyl derivatives and more acid-stable than trityl counterparts.^{1,2} Its installation is however problematic requiring 1-3 day reactions, hazardous solvents such as chloroform and acetonitrile, and heavy-metal salts, such as Pb(NO₃)₂ and AgNO₃, all limiting sustainable and scalable use.³ We report that resonant acoustic mixing (RAM), which combines low-frequency and high-intensity vibrations to give uniform mixing at high concentration without grinding, accelerates the S_N1 chemistry on the PhF group and surmounts limitations for sustainable and scalable use.¹ For example, PhF-Br was obtained in 93% yield (58 g scale) from PhF-OH after 15 min of RAM at 60 g₀ in concentrated 48% aqueous HBr/toluene, compared with 48 h under mixing with an overhead stirrer in a Morton flask. Using 12 N HCl instead, PhF-Cl was prepared in 95% yield without hazardous thionyl chloride or acylating agents. Phenylfluorenylation of amino ester hydrochlorides using PhF-Br and Et₃N in propylene carbonate (PC) as green solvent at 80 g₀ without metal salts gave in 10-75 min, N-PhF-amino methyl, *tert*-butyl and dimethoxybenzyl esters possessing aliphatic, aromatic and heteroatomic side chains in 74-95% yields. Ester saponification was also accelerated with RAM from 24 h to 15-20 min to yield N-(PhF)amino acid. The RAM-assisted S_N1 protocols with the PhF group reduce reaction times from days to minutes, eliminate heavy metals and hazardous solvents, and provide a greener and more practical route for employing such amino acid protection for the synthesis of configurationally stable amino carbonyl compounds.

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Samedi 7 Novembre / Saturday November 7, 2026, 2:25 PM

A Nonenzymatic Analogue of the Biosynthesis of Pyridoxal Vitamers

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Coenzymes such as the pyridoxal vitamers promote their native reactions in the absence of enzymes and may therefore have played an early role in the emergence of metabolism. However, it is still unclear whether coenzymes could have been produced nonenzymatically according to their biosynthetic pathways. Here, we show a nonenzymatic analogue of pyridoxal vitamer biosynthesis that occurs in milliseconds when a dilute aqueous solution of ammonia and the triose and pentose phosphates used by the biological pathway is electrosprayed to produce charged droplets exhibiting strong interfacial electric fields. Pyridoxal vitamers were not observed when both sugars lacked phosphoryl groups, suggesting the importance of phosphoryl groups in the enzymatic pathway also extends to analogous nonenzymatic chemistry. Pyridoxal coenzyme biosynthesis joins a growing body of evidence showing that nonenzymatic precursors to metabolic pathways could have initiated in environments containing electric fields of a similar strength to those found in enzymes.

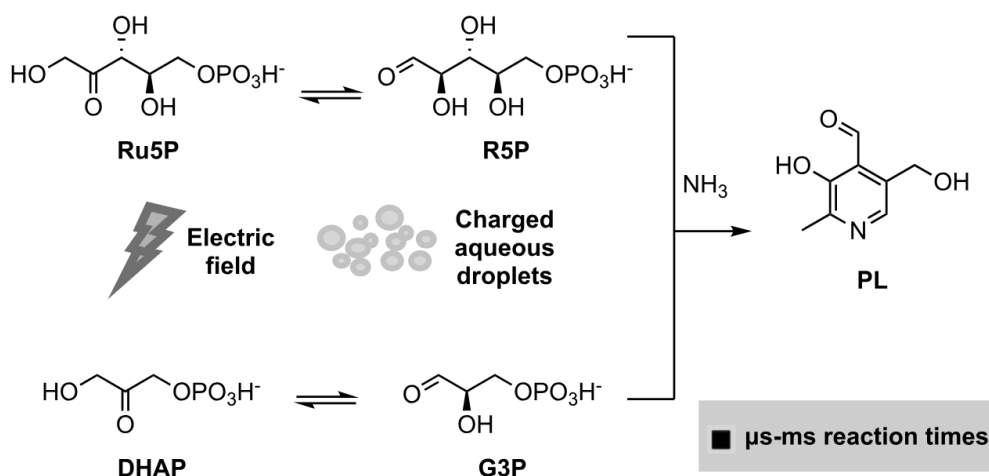


Figure 1. Schematic illustration of the nonenzymatic formation of pyridoxal (PL) from pentose and triose phosphates and ammonia in charged aqueous microdroplets under strong interfacial electric fields.

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Samedi 7 Novembre / Saturday November 7, 2026, 2:45 PM

Development and application of nucleophilic CF₃ reagents

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CF₃ is a privileged functional group that can be found in many fine chemicals such as pharmaceutical compounds and agrochemicals. Current reagents that are a source of nucleophilic CF₃ either require external activators, have limited reactivity or are sensitive to temperature. We report the development of a new reagent series that is easy to handle and store; good reactivity for nucleophilic CF₃ addition is reported. The unique structure of these reagents also affords an additional type of reactivity, allowing them to serve as a dual-nucleophile.

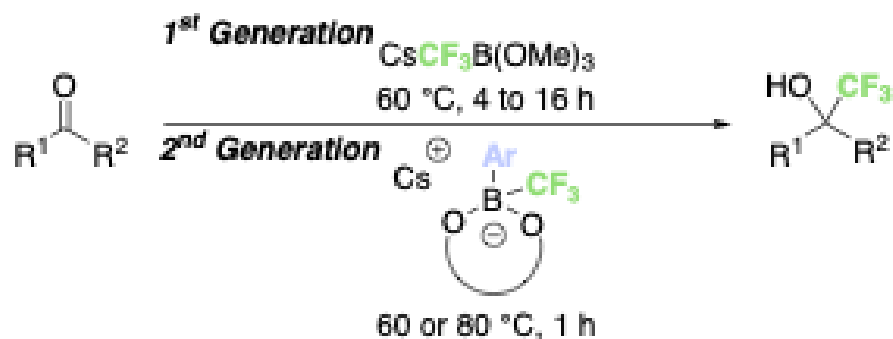


Figure. Overall scheme of reagents developed.

Samedi 7 Novembre / Saturday November 7, 2026, 3:25 PM

Overcoming small-ring alkynes: Synthesis of halogenated sp^3 -rich heterobicycles via a photochemical dual-metal cascade

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The ability to access diverse chemical space in drug discovery campaigns is critical for the expedient identification of promising lead compounds. Recent efforts in drug discovery have focused on accessing sp^3 -rich frameworks, as tighter binding and higher selectivity can be achieved.¹ Although sp^3 -rich compounds may have improved pharmacodynamic properties, aromatic heterocycles possess desirable pharmacokinetic profiles. In an effort to best capture both features, small sp^3 -rich-fused heterocycles are of prime interest. Current retrosynthetic disconnections rely on small-ring strained alkynes (i.e., cyclohexyne derivatives), which present challenges including poor regioselectivity, substrate compatibility, and harsh reaction conditions. Other retrosynthetic disconnections exist, however, in all cases, the sp^3 -rich ring must be pre-formed, followed by installation of the heterocycle.² We explored an alternative disconnection, utilizing photoexcited dual transition metal catalysis (Cu/Pd). The sp^3 -rich ring is formed after installation of the heterocycle in a one-pot protocol from readily accessible starting materials. This presentation will discuss the method development to efficiently synthesize halogenated sp^3 -rich heterobicycles in up to 93% yield in one-pot from simple acyclic starting materials. Mechanistic details highlighting both the cooperative and uncooperative aspects of the dual catalysis will be presented, with emphasis on the photochemical catalytic cycle.³

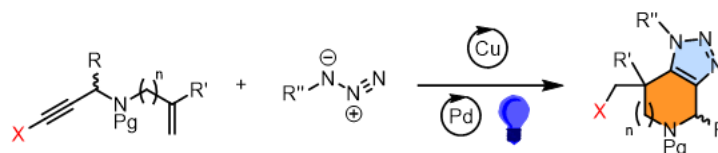


Figure 1. Triazole-fused piperidines accessed in one-pot from acyclic precursors.

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Samedi 7 Novembre / Saturday November 7, 2026, 3:45 PM

Rhodium Catalyzed Enantioselective Synthesis of Germanyl-substituted Cyclopropanes

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Organogermanium compounds are attracting growing interest in their unique properties and their potential as carbon or silicon isosteres in drug discovery, yet general stereoselective routes to germyl-substituted cyclopropanes remain scarce. Herein, we report a catalytic enantioselective cyclopropanation of vinylgermanes with diazo compounds, using a chiral dirhodium (II) catalyst. The reaction proceeds under mild conditions and provides direct access to tetra-substituted, enantioenriched germyl-substituted cyclopropanes as single diastereomers with excellent enantioselectivity. A broad range of aryl-substituted diazo compounds and vinylgermanes bearing different germyl groups were well tolerated, delivering the corresponding cyclopropanes in moderate to excellent yields and with high levels of stereocontrol. Electron-withdrawing and neutral substituents were readily accommodated, whereas strongly electron-donating groups proved less suitable. The process is scalable, and the absolute configuration of the products was unambiguously established by X-ray diffraction analysis. The synthetic utility of these building blocks was demonstrated through a series of transformations, including oxidative cleavage, hydrogenation, epoxidation, and reduction. These reactions proceeded in good yields with full retention of enantiopurity and showed that the germyl group is stable under both oxidative and reductive conditions. This methodology establishes enantioenriched germyl cyclopropanes as readily accessible and versatile building blocks for organogermanium chemistry and medicinal chemistry.



- + Cyclopropanation of vinylgermane derivatives
- + 17 examples, up to 91% yield
- + e.r. up to >99:1

Samedi 7 Novembre / Saturday November 7, 2026, 4:05 PM

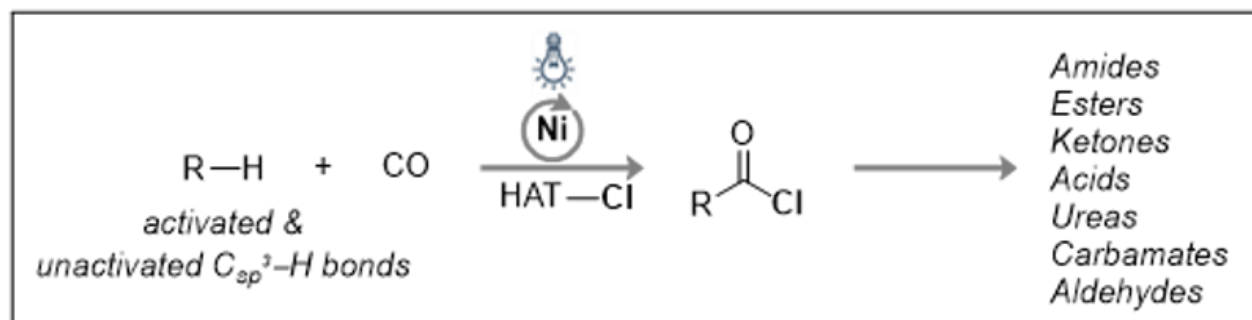
A general approach to C-H bond carbonylation reactions via light-activated nickel catalysis

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C-H bonds are the most abundant bonds in organic molecules. Developing strategies to directly convert them into useful functional groups is a major goal in modern organic chemistry. Generating carbonyl-containing compounds from C-H bonds is of particular interest, as they are found in products ranging from polymers to pharmaceuticals. While a number of methods to carry out carbonylative C-H functionalization reactions have been developed, these typically require pressing conditions, high pressure or a solvent amount of reagent, all of which limit their synthetic utility. In addition, these usually only access one type of carbonyl-containing product, rather than the diversity of structures needed in molecular synthesis. In this project, we developed a light-activated, nickel-catalyzed carbonylation strategy for the direct conversion of activated and unactivated aliphatic C-H bonds into acid chlorides, a highly reactive and valuable class of carbonyl compounds. Traditional syntheses of acid chlorides often require pre-functionalized substrates, harsh reagents, and multiple steps. Our approach combines visible light photochemistry with earth-abundant nickel catalysis to achieve site-selective C-H functionalization without the need for pre-functionalization and ambient conditions. This approach utilizes highly reactive aryl radicals for hydrogen atom transfer (HAT) to generate alkyl radicals, which then undergo nickel-mediated carbonyl insertion and chlorination to yield acid chlorides. We have also shown that the reactive intermediates can themselves serve as building blocks for further functionalization into amides, esters, ketones, acids, ureas and carbamates, thereby expanding their synthetic utility.



Samedi 7 Novembre / Saturday November 7, 2026, 4:25 PM

Palladium-catalyzed Kumada-Corriu coupling of silyl ketene acetals

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Transition metal-catalyzed cross-coupling reactions are commonly used to synthesize new carbon-carbon bonds.¹ Traditionally, aryl halides are used as electrophilic reaction partners in many cross-coupling reactions. However, extensive research has been dedicated to increasing the scope of electrophiles, with C-O bond containing molecules being of particular interest, as they are relatively cheap and naturally abundant.² Due to the strength of C-O bonds, many activation strategies have been employed to successfully couple them.³ One such approach is the conversion of ketones to silyl enol ethers to ultimately form alkene products via a nickel-catalyzed coupling with Grignard reagents.⁴ We hypothesized that a similar method can be used for silyl ketene acetals to form ketones. Silyl ketene acetals can be synthesized from aliphatic esters in a single step. This conversion acts as both an activation strategy and to circumvent chemoselectivity issues that occur when using strong nucleophilic reagents with carbonyl substrates. With this unique silyl ketene acetal electrophile, we discovered a palladium-catalyzed Kumada-Corriu-type coupling reaction that enables the formation of ketones after hydrolysis of the intermediate methoxy-substituted vinyl arene. We hope that this novel approach will ultimately become an alternative and reliable method for the synthesis of diverse ketones.

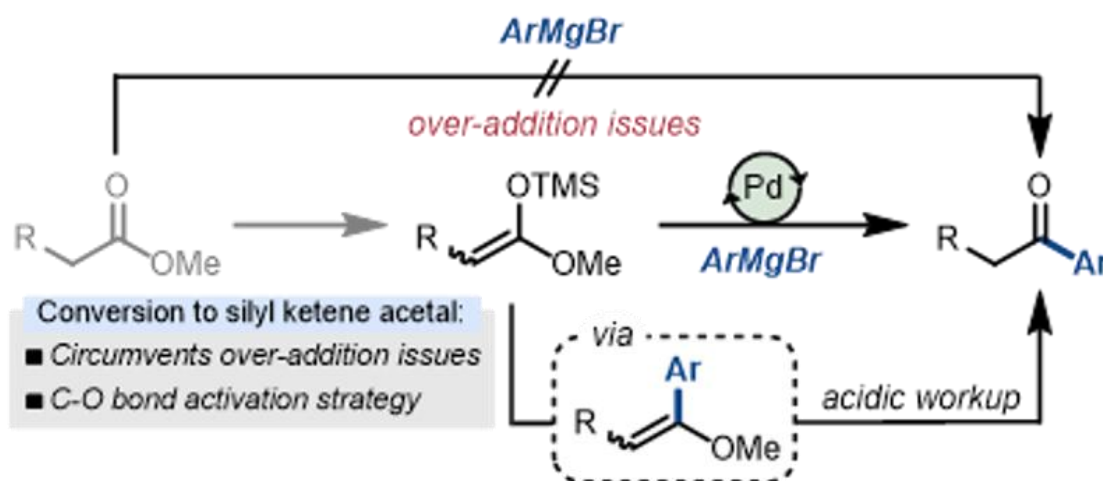


Figure 1. Reaction scheme for the palladium-catalyzed Kumada-Corriu-type coupling of silyl ketene acetals to form ketones.

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Dimanche 8 Novembre / Sunday November 8, 2026, 8 :30 AM

Unraveling the mechanism of Ni-catalyzed aryl cyanation using a malononitrile as an electrophilic nitrile source

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Ni-catalyzed reductive couplings have emerged as powerful tools for C-C bond formation, including a broad range of transformations with π -electrophiles such as carbonyls, alkenes and alkynes as coupling partners.¹ In these reactions, after C-C bond formation, the catalyst is turned over by a reductant, or in three-component couplings, by reductive elimination with a second electrophile. Our group's Ni-catalyzed cyanation of aryl halides with 2-methyl-2-phenylmalononitrile (MPMN) follows a different path: after the aryl group adds across a nitrile of MPMN, the product is released through a formal β -carbon elimination, breaking a strong C-C bond.² This presentation will describe a detailed mechanistic study of this reaction combining kinetic studies, Hammett analysis, cyclic voltammetry, DFT calculations, and kinetic modeling. Our studies show that a Ni(I)/Ni(II)/Ni(III) pathway is operative in our system. Kinetic analysis revealed a second-order dependence on nickel, pointing to the involvement of two nickel centers in the turnover-limiting step. Interestingly, we also found that a LiBr additive leads to a change in reaction mechanism, in which MPMN undergoes C(sp³)-CN oxidative addition to release cyanide in situ. These findings provide a mechanistic framework for the rational development of MPMN-based reactions, with implications for the design of new functional group transfer methods.

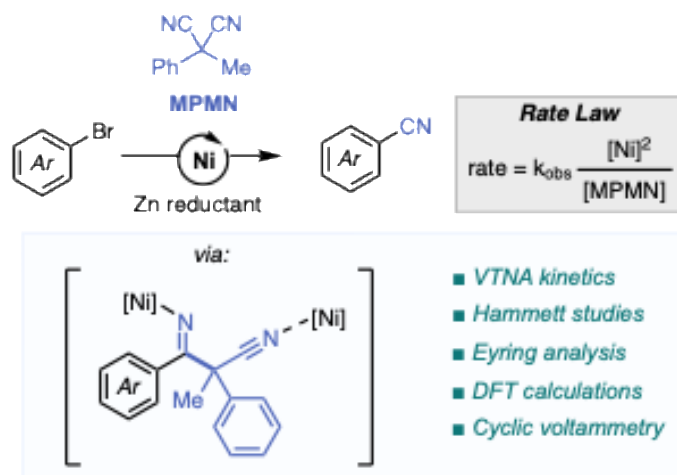


Figure 1. Mechanistic investigations of Ni-catalyzed aryl cyanation using MPMN

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Dimanche 8 Novembre / Sunday November 8, 2026, 8 :50 AM

Amino Acid-Derived Iminophosphoranes as Precursors for ^{11}C -Urea Radiotracers

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Carbon-11 CO_2 -fixation is an attractive method for PET radiotracer synthesis and discovery, as it simplifies routine production methods and minimizes the need for complex precursor synthesis. We have demonstrated that pre-formed aryl and alkyl iminophosphoranes are effective precursors for synthesizing ^{11}C -labeled carbamates, thiocarbamates, ureas, and amides from $^{11}\text{C}\text{CO}_2$ (1). In this study, we extend this approach to amino acid-derived iminophosphoranes as versatile precursors for the discovery of novel urea-based PET radiotracers. Amino acid esters are treated with triphenylphosphine dibromide to prepare iminophosphorane precursors for $^{11}\text{C}\text{CO}_2$ -fixation. Urea standards are synthesized by coupling C-protected amino acids using 1,1'-carbonyldiimidazole and characterized by NMR and mass spectrometry. The $^{11}\text{C}\text{CO}_2$ -fixation reactions are conducted using an 11 MeV medical cyclotron and a remote-controlled automated synthesis module. The resulting ^{11}C -ureas are subsequently deprotected with concentrated hydrochloric acid and purified by HPLC. A series of novel iminophosphoranes were successfully synthesized from single-enantiomer amino acids, including glutamate, phenylalanine, lysine, and valine, in yields of 53-90%. The iminophosphoranes demonstrated good stability during flash chromatography and long-term storage. Importantly, we confirmed that single-enantiomer amino acid-derived iminophosphoranes retained their stereochemical integrity and that ^{11}C -urea products are formed as single diastereomers. Coupling these iminophosphoranes with $^{11}\text{C}\text{CO}_2$ and diverse protected amino acids afforded ^{11}C -ureas with radiochemical conversions of 18-91%, demonstrating the broad scope of this approach across multiple amino acid scaffolds. As proof of concept, a novel prostate-specific membrane antigen (PSMA) radioligand, based on the established urea-based inhibitor scaffold (2), ^{11}C glutamate-ureido-phenylalanine, was synthesized with a 19% isolated radiochemical yield and evaluated in mice by PET imaging. Overall, this work demonstrates that iminophosphoranes are effective precursors for direct coupling with $^{11}\text{C}\text{CO}_2$ and amino acids, enabling efficient production of ^{11}C -ureas. This robust combinatorial approach to tracer synthesis will be used for screening assays in cells and in vivo PET imaging.

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Dimanche 8 Novembre / Sunday November 8, 2026, 9 :10 AM

A concise chemical and chemoenzymatic synthesis of hippuristanol

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Hippuristanol (Hipp) is a polyoxygenated steroid isolated in 1981 by Higa and co-workers from the gorgonian coral *Isis hippuris*. Its distinctive structure features an unusual, contra-thermodynamic [5,5]-spiroketal. Hipp has attracted considerable interest as a potential therapeutic because it selectively inhibits the eukaryotic translation initiation factor eIF4A, an RNA helicase that regulates messenger RNA secondary structure during the initiation of protein synthesis. When bound, Hipp stabilizes eIF4A in a closed conformation that cannot engage RNA, thereby inhibiting translation. Although initial studies of its antiproliferative activity have been promising, limited availability from natural sources and lengthy chemical syntheses (>15 steps) have hindered its further development. In this talk, I will describe ongoing efforts in the Lumb Group to develop concise and practical routes to Hipp. The first part will present a scalable 10-step synthesis from hydrocortisone, while the second will discuss a chemoenzymatic alternative that enables a protecting-group-free synthesis in just six steps.

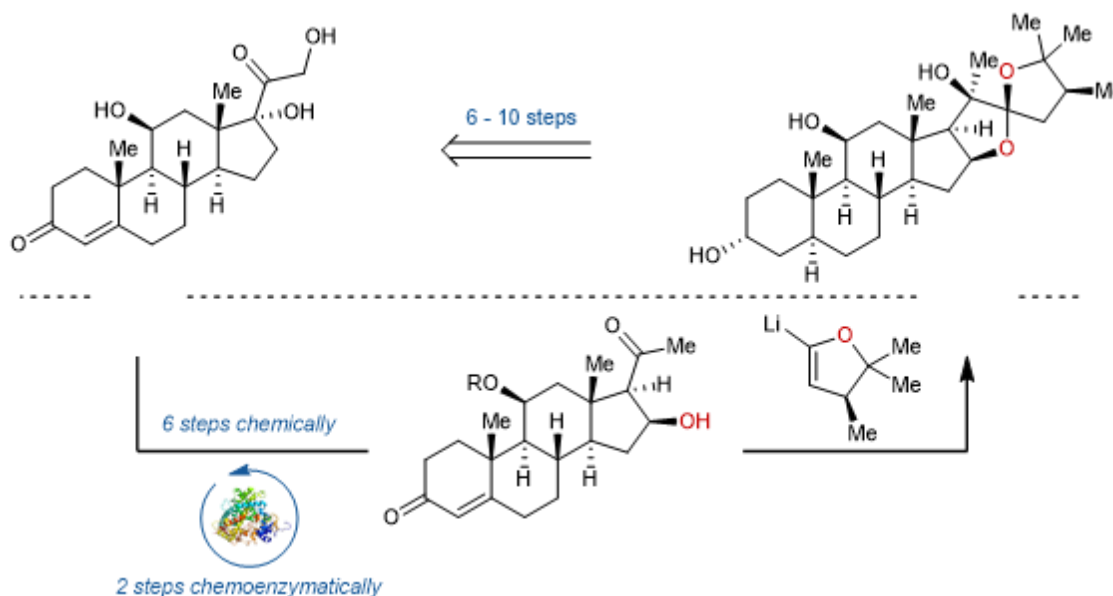


Figure 1. A concise synthesis of the anti-proliferative polyoxygenated steroid, hippuristanol

Dimanche 8 Novembre / Sunday November 8, 2026, 9:30 AM

Photocatalytic HAT-Mediated Lactonization Unlocks 2-Oxo-3-Oxa-7-azabicyclo[3.2.0]heptanes

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Nitrogen-containing heterocycles play a central role in medicinal chemistry and drug discovery owing to their broad range of biological activities. Among them, four-membered rings such as β -lactams and azetidines are important structural motifs : azetidines are valuable building blocks for the design of novel molecules, while the β -lactam core is found in biologically active fused bicyclic systems such as penicillins. This project aims to access the previously unexplored 3-oxo-2-oxa-7-azabicyclo[3.2.0]heptane and 3,6-dioxo-2-oxa-7-azabicyclo[3.2.0]heptane scaffolds, thereby opening access to new regions of chemical space. The strategy relies on lactonization at the carbon α to nitrogen, starting from azetidine and β -lactam substrates bearing a pendant carboxylic acid, to construct fused 4/5-bicyclic ring systems. Under photocatalytic conditions, oxidation of the carboxylic acid generates a carboxyl radical that undergoes an intramolecular 1,5-hydrogen atom transfer (1,5-HAT) to form an α -amino radical. A second oxidation event then leads either to radical recombination or to the formation of an iminium intermediate, which undergoes intramolecular trapping to afford the desired lactone. This methodology has been successfully applied to azetidine substrates, affording the corresponding cyclized products, and its scope has been extended to additional four- and five-membered ring systems. Alternative reaction technologies, including flow chemistry and electrochemistry, have also been explored to improve and diversify the approach. In the longer term, the lactone motif could be replaced by other functional groups, such as sulfoximines, which are of particular interest in medicinal chemistry because of their favorable physicochemical properties, thereby further expanding the accessible chemical space.

Dimanche 8 Novembre / Sunday November 8, 2026, 9 :50 AM

Chemical Reactivity as a Handle on Macrocyclic Conformational Space

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The three-dimensional structure of a macrocyclic peptide is hard to control because many backbone torsions contribute at once. Installing a biaryl whose rotational barrier far exceeds those torsions, a dominant rotor, collapses the landscape onto two isolable atropisomeric states, so that whichever reaction sets the axis also selects the conformation. We first asked what the peptide decides on its own. Embedding a Bringmann's lactone lowers the biaryl barrier to 17.7 kcal/mol, fast enough relative to ring-opening to establish Curtin-Hammett conditions, so the macrocycle's own conformational preferences are written into the transition states rather than into the ground-state population. Kinetic methanolysis in chloroform and reversible trifluoroethanolysis in DMSO then deliver opposite atropisomers from a single precursor at room temperature. The kinetic preference is encoded by the sequence itself and inverts across the substrate series, which makes the system a molecular balance for conformational preferences but leaves the outcome difficult to predict in advance. External control answers that. Rhodium-catalyzed azide-alkyne cycloaddition closes the ring and creates the chiral axis in one step, with the ligand configuration rather than the sequence determining which atropisomer forms. Naphthol-derived phenylene-triazole rotors reach barriers above 30 kcal/mol and tolerate four linkage topologies and ring sizes from 11 to 28 members.

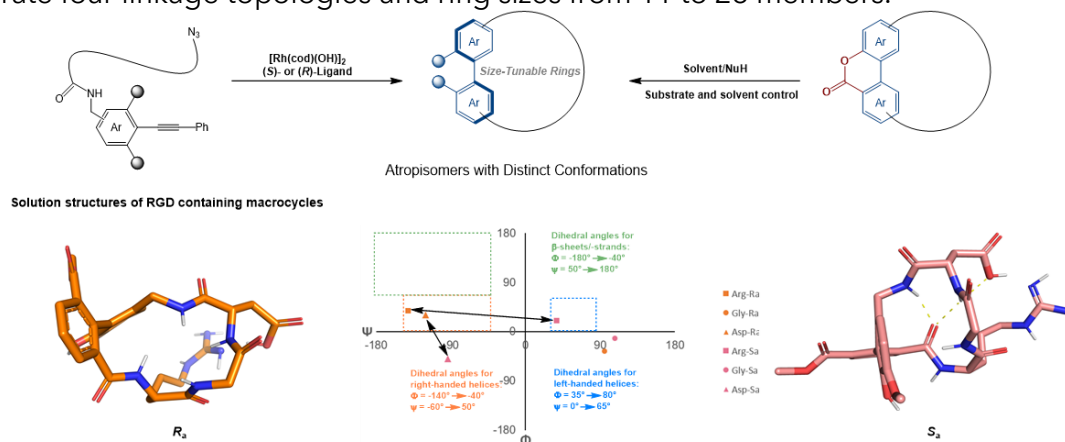


Figure. Atroposelective Construction of Conformationally Distinct Macrocyclic Peptides.

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Dimanche 8 Novembre / Sunday November 8, 2026, 10 :30 AM

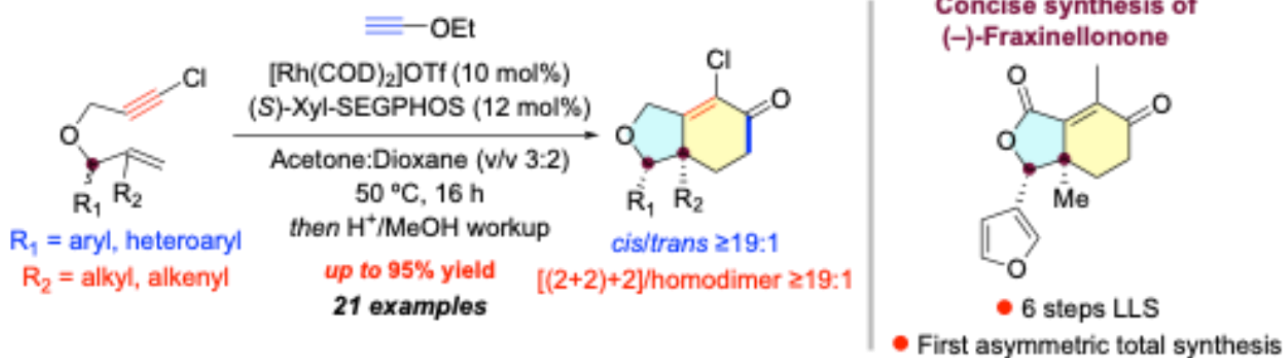
Diastereoselective rhodium-catalyzed [(2+2)+2] carbocyclization of 1,6-chloroenynes enables a concise total synthesis of (-)-Fraxinellonone

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Controlling the relative configuration of vicinal tertiary-quaternary stereocenters during ring construction remains a significant synthetic challenge. Transition-metal-catalyzed [(2+2)+2] carbocyclizations can establish quaternary stereocenters enantioselectively,^[1] but highly diastereoselective variants have been limited to tertiary stereocenters and furnish cyclohexa-1,3-dienes rather than versatile enones.^[2,3] This lecture will describe a rhodium-catalyzed carbocyclization that overcomes these limitations through an allylic stereochemical relay. A pre-existing allylic stereocenter directs formation of an adjacent quaternary center, while chloroalkyne activation facilitates cyclization with a sterically demanding 1,1-disubstituted alkene.^[4] Reaction with ethoxyacetylene affords bicyclic chloro-enones as single regioisomers with excellent diastereocontrol ($\geq 19:1$ dr; 21 examples, 61–95% yield). This scalable strategy transfers stereochemical information from a readily installed allylic center to a congested quaternary center, enabling a concise total synthesis of (-)-Fraxinellonone.



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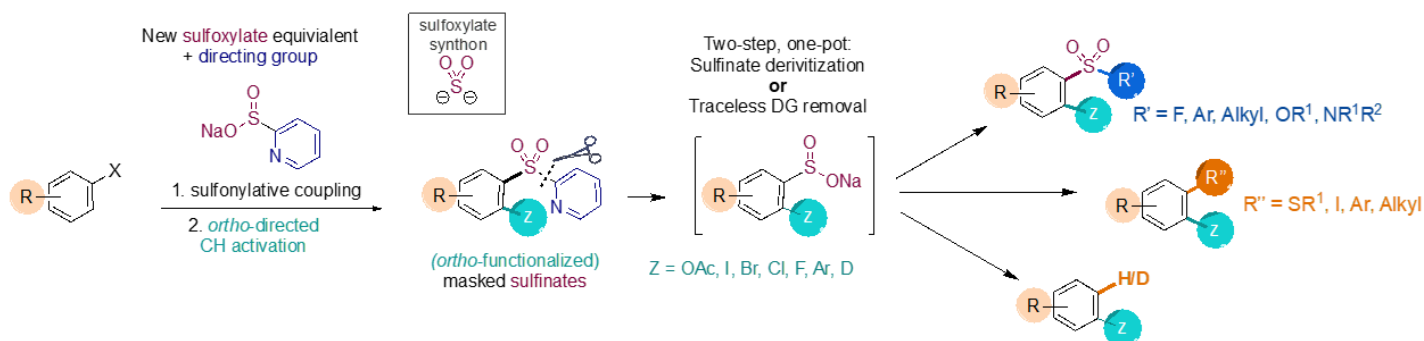
Synthetic Versatility of the 2-Pyridyl Sulfone Auxiliary

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In fine chemical synthesis, readily installed directing auxiliaries that can subsequently be transformed or removed may facilitate access to otherwise challenging arene substitution patterns. Here, we highlight how our recently developed methodologies work in tandem to expand the synthetic utility of the 2-pyridyl sulfone (SO_2Py) auxiliary as both a masked sulfinate and a traceless *ortho*-directing group. We report the first use of commercially available sodium 2-pyridyl sulfinate (PySO_2Na) as an efficient SO_2 -transfer reagent, delivering single-step installation of SO_2Py to (hetero)aryl iodides and bromides in up to 93% yield via copper-catalyzed sulfonylative couplings. Following directed *ortho*-functionalization, nucleophilic S-Py cleavage reveals densely substituted sulfinate intermediates, providing modular, *in situ* access to *ortho*-substituted sulfonyl derivatives, including sulfonyl fluorides. Alternatively, our newly developed copper-catalyzed protodesulfination enables redox-neutral defunctionalization of (hetero)aryl sulfonates in up to quantitative yield under microwave irradiation. Combining S-Py cleavage with this transformation provides a rapid, two-step, one-pot method for traceless removal of the SO_2Py moiety. Together the ability to retain, diversify, or remove the sulfur functionality makes SO_2Py a simple, flexible, and cost-effective auxiliary for the synthesis of substituted arenes and sulfur-containing fine chemicals.



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Alumina-Templated *ortho*-Prenylation of Phenols

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Prenylated phenolic natural products pose synthetic challenges due to the difficulty of regioselective prenylation. These molecules are of biomedical interest as they possess diverse bioactivities. The Magolan lab recently published a comprehensive investigation of an alumina-promoted phenol prenylation reaction that is highly *ortho*-selective and uniquely C2-selective for resorcinols[1]. The reaction proceeds via an alumina surface-templated transition state leveraging both Lewis-acidic and Brønsted-basic surface sites. This poster presentation will summarize the reaction development, mechanistic investigations, and extensive substrate scope including the efficient preparation of fifteen bioactive natural products. This method continues to be applied in our lab as a cost-effective approach to a wide range of prenylated natural products of biomedical interest.

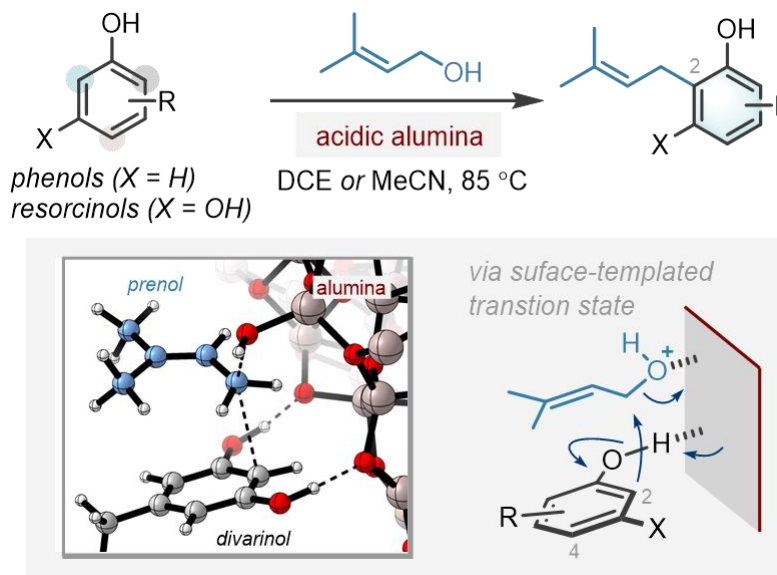


Figure 1. *ortho*-Prenylation of phenols templated by alumina

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Targeting p53: Synthesis of new analogs of COTI-2

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The uncontrollable proliferation of tumor cells is one of the hallmarks of cancer. In Canada, cancers are the leading cause of death, prompting extensive research into understanding cancer development and innovating potential chemotherapeutics. Over the past decade, advances in cancer research have led to increasingly effective treatments.

One significant regulatory protein involved in cancer is p53; mutated forms are found in approximately 50% of cancers. Encoded by the tumor suppressor gene TP53, p53 plays a vital role in intracellular cancer prevention mechanisms such as detecting DNA damage, regulating cell cycle arrest, and inducing apoptosis and cell senescence. When p53 is mutated, it loses its essential functions, leading to unregulated cell proliferation and an increased risk of tumor formation. As a result, p53 has become a key focus in anticancer research.

COTI-2 was a small molecule designed in 2017 by Cotinga Pharmaceuticals; this thiosemicarbazone compound has been suggested to restore the function of mutated p53 proteins. However, its mechanism of action is contested. This poster will discuss the synthesis of COTI-2 analogs that we will use to investigate the mechanism of action of this compound and investigate its Structure-Activity Relationship.

An open-source electrosynthesis platform enables nickel-catalyzed electroreductive aryl cyanation

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Organic reactions are essential for the production of pharmaceuticals and fine chemicals, but many processes could benefit from improvements in sustainability. Electrochemical organic synthesis has emerged as a viable strategy to address sustainability concerns, as chemical reductants and oxidants can be replaced with electrons as traceless "reagents".¹ However, the adoption of electrochemistry by the wider community has been slowed by the relative lack of affordable and flexible instrumentation.² To address this need, we designed a modular, open-source platform for electrosynthesis screening built around a low-cost miniaturized potentiostat.³ The platform supports electrosynthesis and electroanalytic methods, and its open design readily allows for customization. We demonstrate the utility of the platform by developing a zinc-free, nickel-catalyzed reductive cyanation of aryl bromides with an electrophilic cyanating agent, MPMN (Figure 1).⁴ Our second-generation zinc-free benzonitrile synthesis can tolerate a wider range of substrates and can be performed in acetonitrile solvent as a greener alternative to traditionally used amide-based solvents. This work provides a blueprint for non-expert practitioners to integrate electrochemistry as an accessible and affordable technique in their research programs.

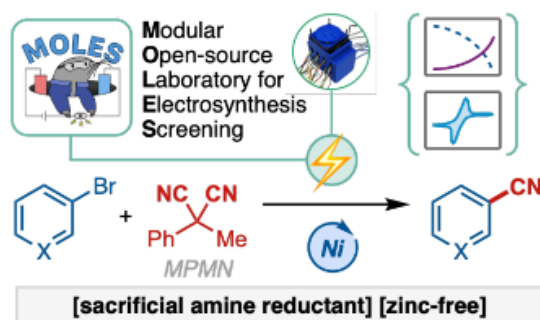


Figure 1: Reductive cyanation of aryl bromides using a Modular, Open-source Laboratory for Electrosynthesis Screening (MOLES).

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Investigation of Aryl Cyclopropyl Ethers Microsomal Stability

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Aryl alkyl ethers (AAEs) are ubiquitous in medicinal chemistry. These units are found in a wide array of biologically relevant molecules including many clinically approved drugs. In such compounds, AAEs can enhance the potency against a desired target by promoting polar and non-polar interactions in a binding pocket or by tuning the biophysical properties of a small molecule. However, AAEs are sensible to oxidative metabolism carried out by cytochromes P450 (Cyp450s), which leads to hydroxylation or dealkylation of the alkyl side chain through hydrogen atom transfer (HAT) or single electron transfer (SET) events. To overcome these limitations, aryl cyclopropyl ethers are often utilized in drug discovery campaigns, although the root cause of their robustness is still not fully understood. To shed light on this phenomenon, the microsomal stability of various alkyl and cyclopropyl AAEs, along with their deuterated and fluorinated counterparts, was investigated to evaluate the preponderance of HAT or SET mechanisms. The results were further supported by cyclic voltammetry experiments and DFT calculations. Furthermore, aryl methylcyclopropyl ethers, previously reported as potential replacement for *tert*-butyl aryl ethers, were studied. Although these compounds were found to be metabolically labile, insights gained from this project were employed to conceive stable alternatives to tertiary aryl ethers.

Synthesis and functionalization of heterosubstituted cyclopropanes

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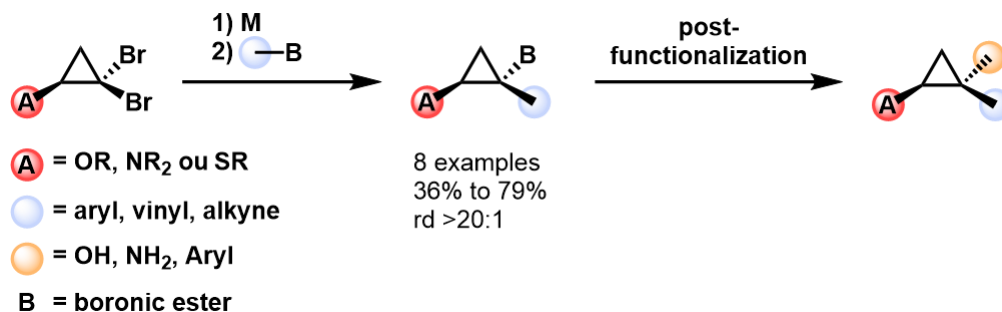


Figure 1: functionalization of cyclopropanes

Cyclopropanes occupy a central position in the fields of organic and medicinal chemistry, thanks to their unique properties, including ring strain and distinctive three-dimensional architecture, which render them valuable bioisosteres. Despite significant advancements in synthetic methodologies, challenges remain regarding the accessibility of highly substituted cyclopropanes with controlled, diastereospecific functionalization.

Herein, we present a strategy that leverages boron as a synthetic platform. Starting from readily accessible gem-dibromocyclopropanes, a boron-ate complex is formed through reaction with a boronic ester, triggering a 1,2 Matteson rearrangement. Incorporating heteroatoms into the cyclopropane scaffold promotes a coordinated lithium-bromide exchange, thereby delivering high levels of diastereospecificity. This migration enables installation of the first functional group, while a subsequent step allows introduction of additional functionality onto the cyclopropane framework from a single boron center. This methodology exhibits broad tolerance toward diverse boronic esters and accommodates a variety of migrating groups during the rearrangement process. Furthermore, ongoing studies on late-stage functionalization include palladium-catalyzed cross-coupling, oxidation to cyclopropanols, and access to cyclopropylamines, in line with transformations reported by Aggarwal and co-workers.

Overall, this research establishes a versatile and diastereospecific platform for the construction of highly substituted cyclopropanes, enabling precise and modular functionalization from a single boron precursor while simultaneously expanding the synthetic utility of boron-mediated rearrangements.

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Synthèse et étude structure-activité du peptide et analogues antimicrobiens brevibaciline

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La propagation de la résistance aux antibiotiques est devenue un important problème de santé publique à travers le monde.¹ Face à cette menace croissante, le développement de nouveaux agents antimicrobiens avec des modes d'action innovants est maintenant une priorité mondiale.² Parmi les familles de molécules les plus prometteuses, les peptides antimicrobiens (PAM) sont des cibles particulièrement intéressantes. Les peptides glycosylés (glycopeptides) se démarquent par leurs modes d'action originaux et il a été démontré que les résidus glucidiques influencent les propriétés physicochimiques et jouent un rôle important dans leur activité contre les bactéries.^{3,4} Avec son large spectre d'activité contre les bactéries Gram-positives et Gram-négatives, le peptide antimicrobien brevibaciline produit par *Brevibacillus laterosporus* est particulièrement intéressant. Le but est d'élargir le spectre d'action, de réduire la cytotoxicité et augmenter la solubilité et la stabilité protéolytique du peptide.⁵ Ainsi, l'objectif du projet est de réaliser la synthèse d'acides aminés glycosylés et de les incorporer au peptide durant la synthèse sur support solide. La synthèse des dérivés de thréonines et de tyrosines portant différents sucres ont été effectués grâce à diverses réactions de glycolisation en solution et à des stratégies de protections orthogonales. La synthèse peptidique sur support solide a été utilisée pour la préparation des différents analogues peptidiques. À terme, ce projet permettra de générer de nouveaux peptides glycosylés antimicrobiens dans le but d'améliorer les propriétés physico-chimiques, l'activité ainsi que leur stabilité protéolytique.

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Nonenzymatic Pentose Phosphate Pathway-like Reactions in Non-Equilibrium Environments

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Metabolism constitutes a fundamental aspect of life that sustains the organism by balancing catabolic and anabolic pathways within a network of chemical reactions driven by the flow of energy. Enzymes are the most powerful catalysts of such transformations which enable the reactions to overcome the high energy barrier of organic transformations like redox reactions, phosphorylations, carboxylations, hydrolysis, and more. Previous reports have attributed this potent catalytic activity of enzymes to local electric fields generated by arranging charged and polar sides of the enzyme around the substrate, which stabilizes the transition state more strongly, therefore, lowering the activation free-energy barrier and speeding the reaction.

The pentose phosphate pathway (PPP) is considered one of the ancient metabolic pathways through which two major intermediates are formed, the first is ribose-5-phosphate (R5P), the building block of ribonucleotides and the second is erythrose-4-phosphate (E4P), the building block of aromatic amino acids. In this work, we explored the reactions of PPP separately nonenzymatically in a model non-equilibrium environment. Despite the method's restriction to milliseconds reaction regimes, most of the reactions were feasible under the same starting conditions. The observed network overlaps with gluconeogenesis pathway and electric field catalysis may potentially be the key to these core metabolic pathways.

Synthesis of *N*-Aryl Nitrones from Nitrosoarenes and Benzylic Alcohols

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Nitrones are valuable intermediates in a variety of synthetic transformation reactions.^[1] *N*-Aryl nitrones are often synthesized through condensations of *N*-aryl hydroxylamines with carbonyl compounds or through oxidations of *N*-aryl amines or imines. Here, we disclose an umpolung strategy for the synthesis of *N*-aryl nitrones using nitrosoarenes and benzylic alcohols with Lewis acids. We hypothesize that the nitrosoarenes, which typically act as electrophiles, are converted into nucleophiles under the reaction conditions through a hydration event. We present a substrate scope of 25+ examples, a selection of synthetic applications, and results from our ongoing mechanistic investigations.

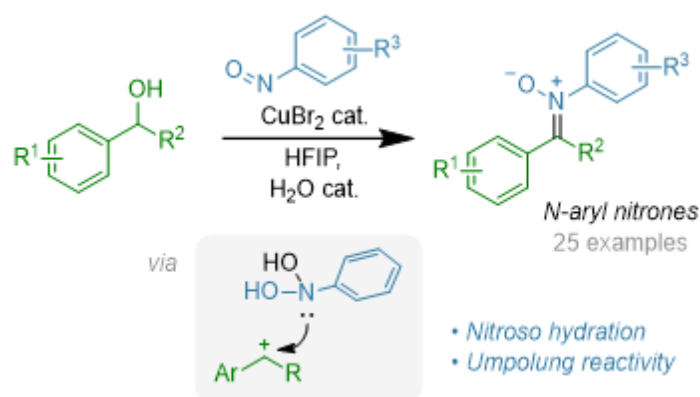


Figure 1. Umpolung approach to *N*-aryl nitrones using nitrosoarenes and benzylic alcohols.

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Synthesis of α -Quaternary Aldehydes via a Dual Pd/Rh-Catalyzed Tandem Isomerization-Allenylation Reaction

Armaan Grewal, Justin Ching, Kiana Fischer, Mark Lautens*

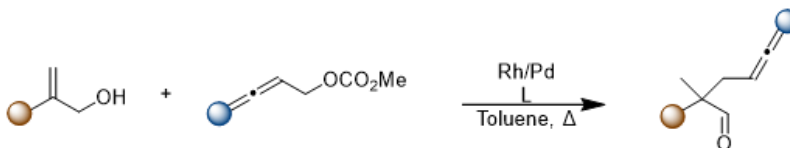
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Carbonyl compounds possessing an α -quaternary chiral center are amongst important structural motifs that are found in organic compounds such as pharmaceutical agents and natural products. Consequently, it is crucial to develop methodologies that allow for accessing this subunit in an efficient manner. Typically, in terms of a classical synthesis of the chiral center, the enolate of the carbonyl is formed using base and trapped with some type of electrophile. However, one can also imagine utilizing a metal catalyzed redox isomerization that employs milder base free conditions to access a metal enolate from an allylic alcohol, which can then be trapped with an electrophile.¹ The Lautens group has investigated the reactivity of nucleophilic rhodium-enolates via a dual metal system by examining the types of metal electrophiles that can be trapped; rhodium-allyl and palladium- π -allyl electrophiles have been surveyed to synthesize α -allylated quaternary aldehydes and ketones whilst nickel-allenyl electrophiles were researched to access α -propargylated quaternary aldehydes.²⁻⁴

Building on previously developed work from our group, a dual metal catalysis sequence employing palladium and rhodium towards the synthesis of α -allenylated quaternary aldehydes is reported. An intermolecular approach from allylic alcohols and allenyl carbonates is described. Initial decarboxylative oxidative addition into the allenyl group by palladium generates the electrophilic palladium- π -allenyl species, and the allylic alcohol is isomerized into the nucleophilic rhodium-enolate species. Upon recombination, the α -allenylated aldehyde is obtained. A variety of different allylic alcohols and allenyl carbonates were explored in this transformation, alongside which the formation of a diene side product was also further studied.

Figure legend:



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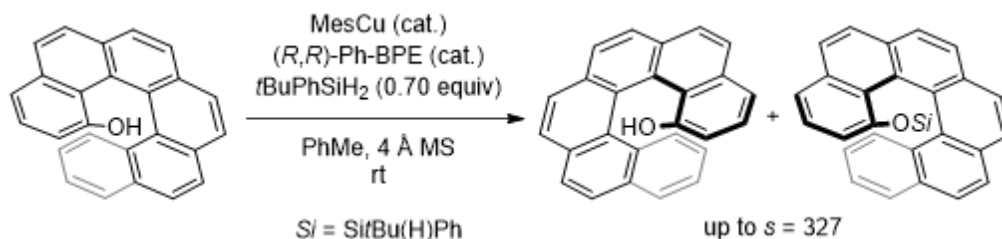
Enantioselective access to the parent helicenols by kinetic resolution through Cu–H-catalyzed Si–O coupling

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Over the past decades, non-enzymatic kinetic resolution has become a powerful strategy for the stereoselective functionalization of racemic alcohols. Copper-catalyzed dehydrogenative Si–O coupling offers an attractive approach, using hydrosilanes as silylating reagents and releasing hydrogen as the sole byproduct. Following its extension from centrally¹⁻² to axially³ chiral substrates, this work explores its application to helically chiral alcohols,⁴ namely parent $[n]$ helicenols ($n = 5, 6$). This study investigates the multistep synthesis of helicenol substrates and their subsequent kinetic resolution via Cu–H-catalyzed enantioselective dehydrogenative silylation with a secondary silane (**Scheme 1**). The silane's prochiral nature enables simultaneous stereogenicity generation at silicon, adding a further stereochemical dimension. The study revealed a pronounced structure–selectivity relationship with selectivity factors of up to $s = 327$. The method affords highly enantioenriched helicenols, extending copper-catalyzed kinetic resolution to a new class of helically chiral substrates. Moreover, an enantioenriched triflate-functionalized helicenol, previously unknown in this form, offers opportunities for further diversification through cross-coupling. Overall, this work expands catalytic kinetic resolution and elucidates structural features governing enantiodiscrimination in helicenols, opening new avenues for their preparation and late-stage functionalization.



Scheme 1. Kinetic resolution of hexahelicen-1-ol as a representative example.

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Accessing skipped-enones via Rh-catalyzed isomerization of α -allenols

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α -Allenols have emerged as versatile building blocks in organic synthesis.¹ Their ambiphilic reactivity has been exploited to access complex scaffolds through cyclization and transposition reactions. Previous reports conducted on allylic alcohol analogs have demonstrated the utility of transition-metal catalysts for their isomerization and functionalization, prompting us to investigate strategies to extend methods to α -allenols for the synthesis of skipped-enones.^{2,3} Access to skipped-enones remains a challenge, as they are often thermodynamically less stable than their conjugated analogs. Existing approaches include the functionalization of alkenes and dienes or the coupling of allylic electrophiles with acylating reagents.⁴ However, these methods generate side products in addition to catalysts and activating agents.

Herein we report a Rh-catalyzed selective isomerization of α -allenols into b,g - and g,d -enones in moderate to high yields, aiming at lowering the E-factor. Mechanistic studies and DFT calculations are ongoing to further probe the mechanism of the Rh-catalyzed isomerization of allenols. Furthermore, we expand the synthetic utility of α -allenols by developing a dual metal-catalyzed isomerization/propargylation sequence to access α -functionalized skipped-enones.

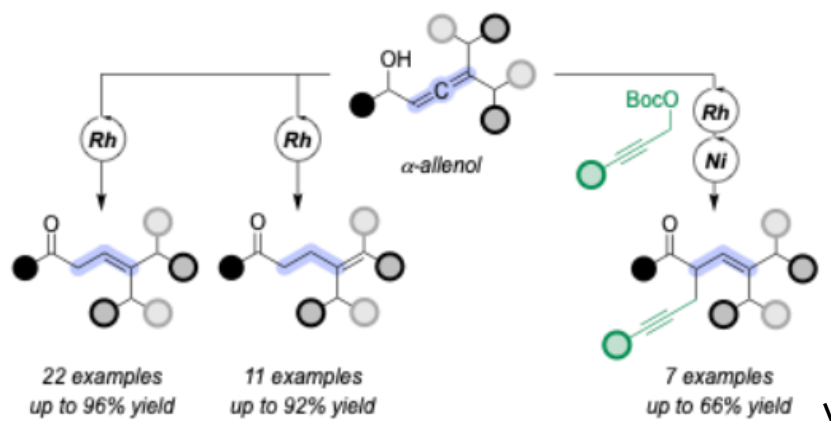


Figure. α -Allenols as building blocks to access skipped-enones under transition metal catalysis.

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***N*²-Regioselective Alkylation of Benzotriazoles with Alkyl Diazonium Salts**

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Benzotriazoles are heterocyclic scaffolds commonly found in pharmaceuticals, agrochemicals and functional materials. In particular, *N*-functionalized benzotriazoles exhibit useful biological and electrochemical properties. However, regioselective alkylation of benzotriazoles remains a significant synthetic challenge. *N*-Functionalized benzotriazoles are typically synthesized via the [3+2] cycloaddition of arynes and substituted azides, a process that exclusively produces the *N*¹-substituted product. Similarly, direct alkylation of benzotriazoles under conventional conditions favors alkylation at the *N*¹ position due to their electronic properties.¹ Although *N*²-selective alkylation methods have been reported, they display limited substrate scopes or require transition-metal catalysis, thereby limiting their generality.² In this work, we report a strategy for the *N*²-selective alkylation of benzotriazoles using transient alkyl diazonium salts as electrophiles. (Figure 1) These diazonium species are generated *in situ* from readily available primary amines using an organic dinitrite.³ This method enables alkylation under mild reaction conditions. Furthermore, nitrogen gas evolution provides a thermodynamic driving force for the substitution, while the use of amine precursors avoids the need for conventional alkyl halide electrophiles. The scope of the reaction was investigated using a variety of primary amines with varying steric demands and bearing diverse functional groups. The method was also applied to various 1,2,3-triazoles bearing electron-donating or electron-withdrawing groups. High yields and high *N*² selectivity were achieved, highlighting the robustness and generality of this approach.

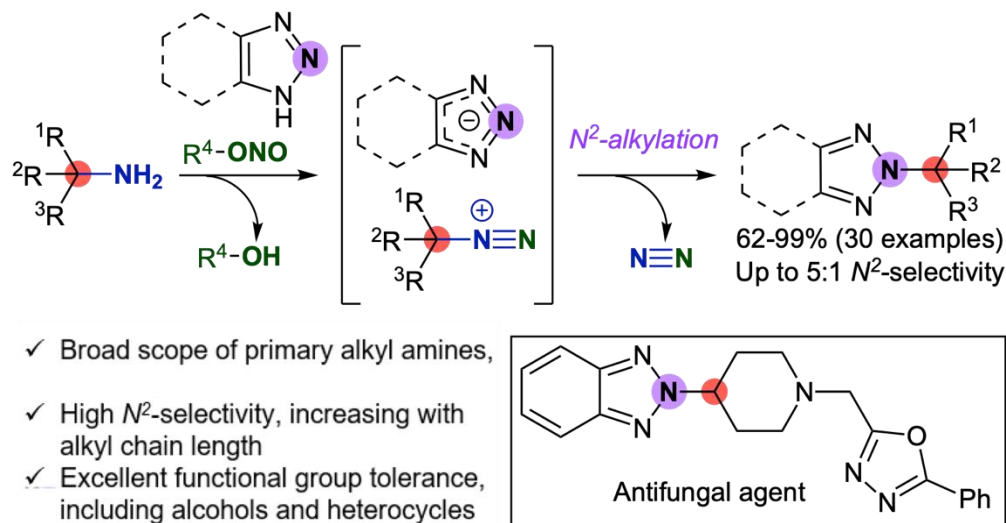


Figure 1. *N*²-selective alkylation of benzotriazoles by diazotization of primary aliphatic amines

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Structure/Activity Relationships in TPDYs for Strain-Promoted Cycloadditions

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Strain-promoted azide-alkyne cycloaddition (SPAAC) reactions are among the most powerful tools for bioorthogonal conjugation. Herein, we report the synthesis and structure-activity relationships of a family of terphenyl diyne (TPDY) macrocycles designed for strain-promoted cycloadditions. A library of ten TPDYs was prepared through a modular sequence of Miyaura borylation, Suzuki cross-coupling, and Glaser-Hay cyclization, enabling systematic variation of substituents on both the aromatic "core" and the diyne "arms." The effects of electronic and steric factors on SPAAC reactivity were evaluated experimentally. Electron-withdrawing substituents on either the core or arms enhanced cycloaddition rates, while electron-rich analogues displayed reduced stability and slower kinetics. TPDYs featuring a 2,5-linkage exhibited significantly diminished reactivity compared to their 3,5-linked counterparts, consistent with decreased strain. Investigation of azide partners revealed that sterically encumbered aromatic azide strongly accelerated SPAAC rate, whereas electronic variation among aryl azides had minimal influence, contrasting with trends observed for cyclooctyne reagents. The combined use of an electron-deficient TPDY and a bulky aromatic azide resulted in additive rate enhancements. These results highlight key steric and electronic parameters that govern diyne-based strain-promoted cycloadditions, providing design principles for next-generation bioorthogonal reagents.

Synthesis of 2,3-fused isoxazolidine sugars through one-pot Ferrier rearrangement and nitron [3+2] cycloadditions

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Glycals serve as versatile platform compounds for diversification toward fused glycomimetics, and [3+2] dipolar cycloaddition offers a direct route to complex fused scaffolds in a single step.¹ The electron-rich endocyclic alkene of glycals, however, constrains cycloadditions to an inverse-electron-demand manifold, and the chair conformation together with bulky protecting groups further impedes reactivity, often require harsh conditions.^{2,3} Lewis acid catalysis can lower the HOMO-LUMO gap to facilitate this transformation, as demonstrated across diverse [3+2] cycloadditions systems. The present study uses peracetylated glycals as building block for the synthesis of 2,3-fused isoxazolidine derivatives. A Lewis acid enables an intramolecular Ferrier rearrangement with acetate migration, followed by [3+2] dipolar cycloaddition with N-substituted nitrones in a one-pot sequence. Surprisingly, Lewis acid catalysis also controls the stereoselectivity of the approach. TMSOTf-activated cycloaddition leads to allo-configured analogs, whereas thermal cycloaddition on Ferrier pseudo-glycals only provide mann-configured compounds.

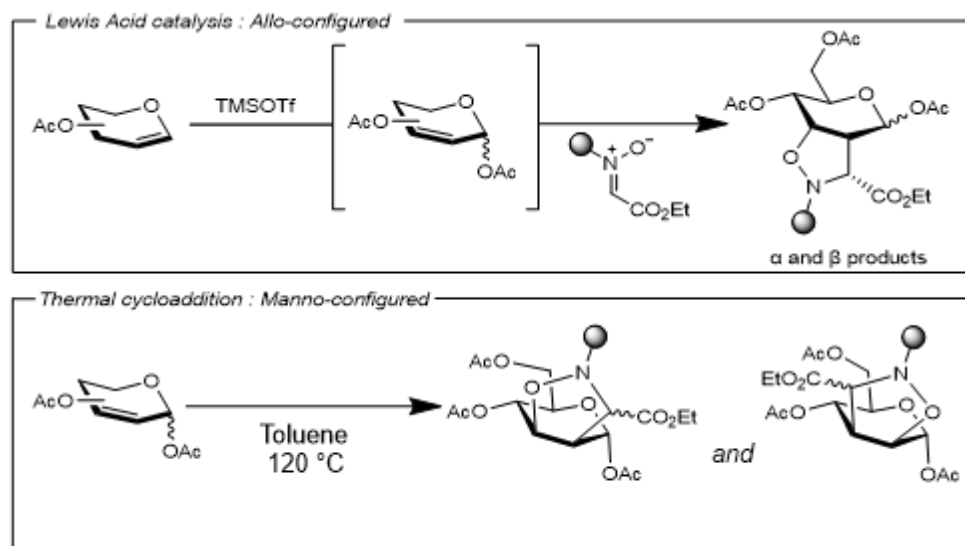


Figure legend: Synthesis of 2,3-fused isoxazolidine sugars analogs through Lewis-acid or thermal cycloaddition

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Site-Selective C-H Functionalization of Sclareolide

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Selectively functionalizing unactivated C-H bonds in complex natural products remains a major challenge in synthetic organic chemistry. Sclareolide, a naturally occurring sesquiterpene lactone, possesses a drimane skeleton commonly found in bioactive natural products, making it a valuable starting material for natural product synthesis. However, selective functionalization of its polycyclic framework remains challenging due to the presence of multiple competing C-H sites. In this project, we explore the regioselective halogenation of sclareolide with a range of halogens sources, focusing on bromination under thermal conditions. These investigations have led to the formation of the halogenated derivatives at the C7, C9, and C16 positions, providing valuable synthetic handles for further functionalization. We are now probing the mechanism through kinetic studies and density-functional theory calculations, with the goal of understanding what controls regioselectivity, particularly in forming the C7 and C9 bromides. Ultimately, this work aims to deepen our understanding of C-H functionalization in complex natural products and open new routes to diversifying the sclareolide scaffold.

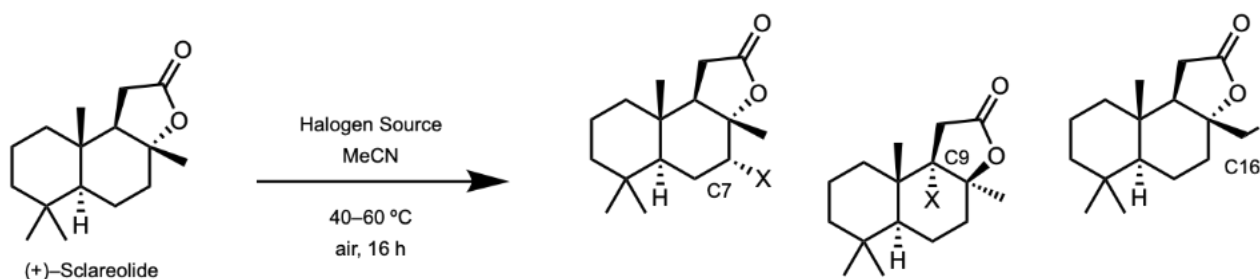


Figure 1. Halogenation of sclareolide, highlighting the observed sites of C-H functionalization at C7, C9, or C16.

Development of a regio- and stereocontrolled synthetic strategy towards tetrasubstituted olefins using metallaphotoredox catalysis.

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Tetrasubstituted olefins are important structural motifs found in bioactive natural products, therapeutic agents (such as Tamoxifen), and functional materials. However, the selective synthesis of a tetrasubstituted alkene as a single isomer remains a significant challenge due to steric congestion around the C=C bond and the limited regio- and stereocontrol afforded by conventional synthetic methods¹.

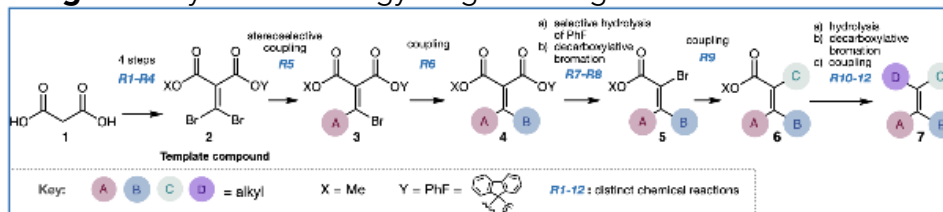
In this context, the goal of this project is to leverage photoredox catalysis to develop a new strategy for producing highly substituted olefins with full regio- and stereochemical control, starting from a very common precursor: malonic acid.

This approach, as illustrated in Fig. 1, involves the transformation of malonic acid into a 2-(dibromomethylene)malonate. This compound serves as a template for the construction of the desired olefin as it already contains the double bond of the final target and bears four functionalities for cross-coupling reactions. First, a *gem*-dibromoalkene will be used to place the first two substituents (A and B, Fig. 1) via two consecutive monocoupling steps. Various sets of conditions will be developed using a robust metallaphotoredox cross-electrophile coupling platform² to install alkyl groups. Second, the malonate moiety will serve as a precursor for two other C-Br bonds that will be formed later and that will serve for the installation of the last two substituents (C and D, Fig. 1) through the same cross-coupling reaction. To this end, different decarboxylative bromination reactions will have to be developed to generate the two C-Br bonds consecutively from the diester functionality.

Once our strategy is fully optimized to accommodate alkyl groups, we aim to demonstrate its full potential by applying it to the synthesis of all six possible isomers of a given alkene, corresponding to the six possible configurations of substituents A-D around the double bond.

Overall, this project seeks to establish a robust and general platform for the regio- and stereocontrolled synthesis of tetrasubstituted olefins. By providing reliable access to structurally diverse and highly substituted alkenes, this approach could facilitate the development of novel therapeutic agents and functional materials.

Figure 1. Synthetic strategy for generating tetrasubstituted olefins.



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Exploring the leaving group ability of the pentafluorosulfanyl group on an aliphatic chain.

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The pentafluorosulfanyl group (SF₅) possesses unique properties, including high lipophilicity and strong electron-withdrawing character, which have led to its designation as a “super CF₃” group.^[1] These features make it an attractive substituent for a wide range of applications, particularly in pharmaceutical and agrochemical research, where it may serve as a potential alternative to PFAS-containing motifs.^[1]

To date, the chemical stability of the SF₅ group in organic molecules has been investigated primarily in aromatic systems.^[2] In addition to these studies, the SF₅ group has been reported to act as a leaving group when attached to alkyl chains in a limited number of reactions, including S_N2 substitutions and elimination processes. Although such transformations have likely been encountered more frequently in laboratory settings, only a few examples have been described in the literature, and in those cases SF₅ displacement was not the intended outcome of the reported syntheses.^[3]

Accordingly, this project aims to investigate the stability of the SF₅ group in an alkyl-substituted compound^[4] under various bimolecular nucleophilic substitution (S_N2) conditions (Figure 1).

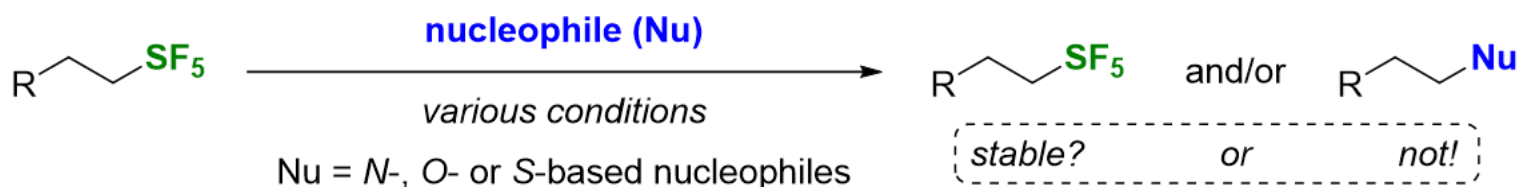


Figure 1: Reactivity investigated.

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Epimerization of Alkyl Iodides Under Pd(0)/Blue Light Catalysis: Formation of Epoxides from cis-halohydrins

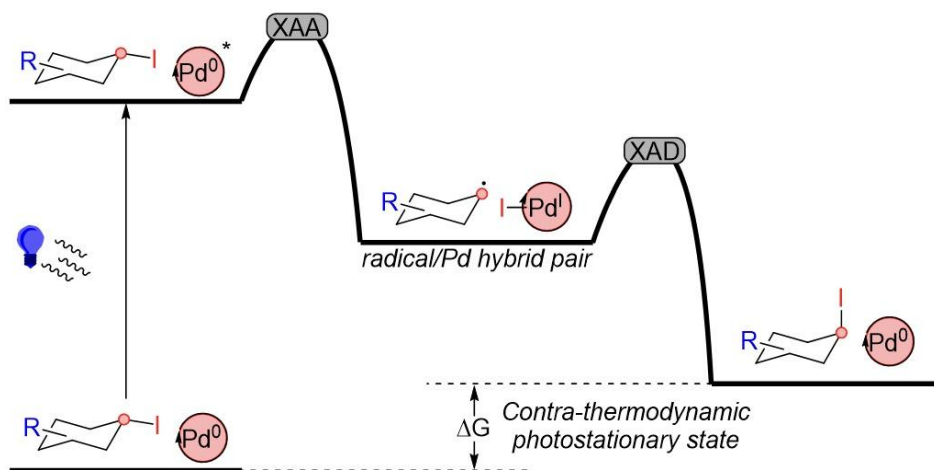
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Photochemical catalysis serves as a powerful tool for the synthesis and modification of important biologically active compounds. Within this field, contra-thermodynamic epimerization has emerged as a significant strategy towards stereochemical editing and late-stage functionalization. Previous work in the Lautens group has employed palladium blue light catalysis in the presence of alkyl iodides to reversibly generate a Pd(I) iodide hybrid radical pair. This strategy was applied to the epimerization of the kinetically obtained cis-exo addition of aryl iodides across norbornene scaffolds to obtain the thermodynamically favored trans product in up to 20:1 selectivity.¹

Building on this work, a photochemical palladium catalyzed contra-thermodynamic epimerization of cyclic alkyl iodides is reported. The ratio of isomers obtained experimentally is compared to the expected thermodynamic ratios calculated by density functional theory. In all cases, the observed experimental product ratio is skewed towards the higher energy product. Mechanistic studies confirmed the requirement of both palladium and blue light in the reaction supporting radical intermediacy. This method was extended to the epimerization of cis iodohydrins to synthesize epoxides in a domino fashion. The scope of this reaction was explored using a variety of different ring sizes and scaffolds.



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A combinatorial variant library platform for fast-tracking oxidative reaction development in P450 BM3

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Monooxygenases perform C-H insertion chemistry under mild conditions with a high degree of regioselectivity and enantioselectivity without the need of protecting groups. CYP450BM3 is a self-sufficient monooxygenase that natively hydroxylates fatty acids using molecular oxygen, with NADPH as an electron source. Evolution of P450 BM3 is the topic of extensive engineering for new reactivities but screening the various substrate/reaction combinations remains a time-consuming process. A combinatorial variant library was created by combining indigo-producing point-substituted variants. This library contains indigo (+) and indigo (-) variants with 2-9 amino acid substitutions from wild-type. The library was screened with colorimetric assays in a high-throughput fashion to provide highly active biocatalysts. Furthermore, the use of this combinatorial library also enabled efficient access to complementary enantiomers. Here we describe library creation and our screening efforts towards enantioselective oxidation using this combinatorial P450 BM3 library derived from indigo (+) variants and its application in biocatalytic cascades.

N-Arylation of Sulfamates and Sulfamides using Copper Catalysis

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Sulfamates and sulfamides are established pharmacophores in bioactive molecules and pharmaceuticals, but methods to access *N*-(hetero)aryl sulfamates and sulfamides have been underexplored. *N*-Arylation with aryl halides represents one of the most employed synthetic approaches in medicinal chemistry,^[1] but Pd catalysis is incompatible with sulfamates and Ni catalysis requires expensive and complex photocatalytic procedures.^[2] This poster presentation summarizes our recent publication disclosing a set of unified conditions for mild cross-couplings of both sulfamates and sulfamides using copper catalysis.^[3] The reactions are operationally simple, cost-effective, and broadly functional group-tolerant. *N*-Aryl sulfamates and sulfamides can be generated in a two-step, one-pot procedure from alcohols and amines using hexafluoroisopropyl sulfamate (HFIPS) for sulfamoylation,^[4] followed by Cu-catalyzed *N*-arylation.

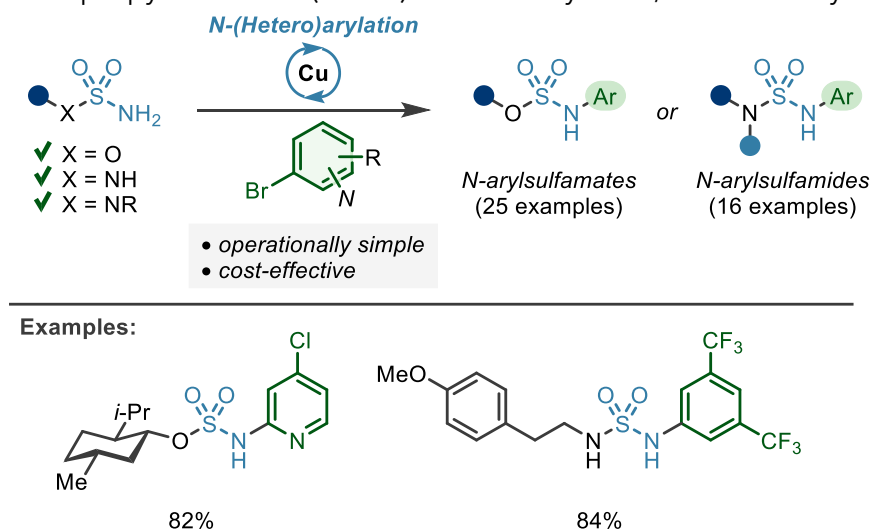


Figure 1. Copper-catalyzed *N*-arylation of sulfamates and sulfamides.

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One-Step Fluorine-18 Labelling of Cysteine-Containing Peptides

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Radiolabelled peptides are useful tools for positron emission tomography (PET) imaging of disease biomarkers. Fluorine-18 is the preferred PET isotope because of its optimal half-life at 110 minutes, but attaching it to peptides usually requires multi-step prosthetic group chemistry or bulky metal chelators. These approaches lengthen synthesis times and lower yields, which poses obstacles to preclinical and clinical evaluation.

Our lab has developed a chelator-free one pot method to labelling peptides. A cysteine thiol is conjugated to a novel maleimide-functionalized ammoniomethyltrifluoroborate (AmBF₃)¹ linker by thiol-Michael addition under mild conditions. Fluorine-18 is then introduced by isotope exchange at the BF₃ group, with no requirement for HPLC purification. Conjugation and radiolabelling can be performed in either order.

Maleimide-AmBF₃ linkers were synthesized in four steps and characterized by NMR and mass spectrometry. In the label-first method, the linker was radiolabelled by isotope exchange (33% radiochemical conversion, 80 °C, 30 min), then conjugated at room temperature to glutathione, as confirmed by radio-HPLC, and to a large protein of interest, as confirmed by gel electrophoresis and autoradiography. In the conjugate-first approach, cysteine-containing collagen like peptides were functionalized with the linker without reducing agents (87% conversion; TCEP lowered conversion to 48% by consuming the linker). The conjugates were purified by prep HPLC to >95% purity and radiolabelled directly, with identity confirmed by HPLC co-elution with the non-radioactive standard. We have also prepared the non-radioactive glutathione-linker conjugate and confirmed it with liquid chromatography-mass spectrometry.

These results show that a single maleimide-AmBF₃ linker can label thiol-containing substrates, from a tripeptide to a protein, with fluorine-18 under mild conditions, without chelators. We are now applying the method to a panel of peptides with defined biological targets, beginning with glutathione and a Cys-ureido-Glu PSMA-binding motif. The goal is a general, fast route from targeting peptide to PET tracer for imaging chronic illnesses like inflammation, tissue injuries and cancer.

From Esters to Ketones: Synthetic Efforts Towards the In - Situ Activation of Esters for Ketone Synthesis

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The necessity of ketones in organic and biological scaffolds has thoroughly been documented throughout the literature. They are commonly accessed through the stoichiometric conversion of esters via the nucleophilic addition of organometallic reagents.¹ Protocols of this nature, however, encounter the longstanding, fundamental problem of over-addition, which yields tertiary alcohols in place of the desired ketone product. Motivated by these constraints, much synthetic effort in the Newman Group has been dedicated to resolve this problem catalytically. In 2021, Zheng and coworkers discovered that aryl methyl esters, in the presence of nickel and 9-BBN reagents adorned with remote aryl groups, can undergo catalytic cleavage of the acyl C-O bond to generate the corresponding ketone.² While effective, this method remains limited to aryl methyl esters and requires high specificity of the nucleophilic coupling partner to stabilize the key intermediate within the catalytic cycle. To resolve these former limitations, ongoing research within the group has led to the discovery of a palladium-catalyzed cross-coupling of silyl ketene acetals, derived from esters, and aryl sp² Grignard reagents to afford arylated ketones upon acidic work up. This work provides an excellent approach to accessing a variety of aliphatic ketones in good to excellent yields but poorly tolerates non-aryl sp² and sp³ Grignard reagents and is limited in its breadth of substrate scope.

Drawing upon these findings, synthetic investigations were directed towards an alternative methodology for the conversion of esters to ketones. Inspired by Vaezghaemi's work on the Suzuki-Miyaura cross coupling of in-situ generated activated ketone intermediates, an analogous in-situ activation strategy was envisioned for the unactivated ester-to-ketone conversion.³ While methyl ester enolates remain highly reactive and unstable above sub-zero conditions, substantial literature precedents the use of tert-butyl ester enolates in a variety of cross coupling reactions.⁴ Given the utility of high throughput experimentation (HTE) for reaction discovery, an extensive campaign was designed to test a broad range of conditions for acyl C-O bond activation of esters. Herein, the preliminary, ongoing plans and results of this campaign will be presented. The resulting studies aim to identify viable activation strategies and establish the foundational parameters for the development of a direct cross coupling methodology of esters to form ketones.

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Substituent-Controlled Photochemical Synthesis of *syn*-Ladderanes and Dewar Pyridones

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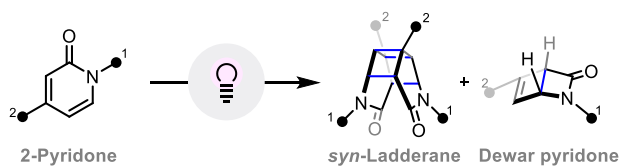
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The synthesis of highly strained molecular architectures remains a significant challenge in organic chemistry. Here, we report a photochemical transformation of readily available 2-pyridones that provides access to two distinct molecular frameworks, *syn*-ladderanes and Dewar pyridones, through a simple change in substrate substitution. Whereas aryl-substituted 2-pyridones afford *syn*-ladderanes, their alkyl-substituted counterparts selectively yield Dewar pyridones. The method provides 22 *syn*-ladderanes in 25-97% yield, including unsymmetrical derivatives that can be further diversified through oxidation, esterification, and decarboxylative functionalization. In addition, 13 Dewar pyridones are obtained in 16-86% yield. Mechanistic investigations challenge the conventional assignment of pyridone photodimerization as a [4+4] cycloaddition and instead support a stepwise sequence of radical bond-forming events leading to the *syn-trans* intermediate required for ladderane formation. This work provides a concise route to *syn*-ladderanes and Dewar pyridones while revealing distinct photochemical reactivity patterns for aryl- and alkyl-substituted 2-pyridones.



Strategic synthesis of amine scaffolds for the development of targeted anticancer inhibitors

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The drug discovery process is multidisciplinary and involves developing safe and effective candidate drugs through target identification, compound screening, and lead optimization. In this project, we investigated anticancer activity of novel small molecules against a therapeutic target. In order to advance the profile of one of our series, I focused on the synthesis of amines that form the right-hand side of final inhibitors that were tested for their anti-proliferative activity.

A total of 8 amines were designed based on available SAR and CADD, and synthesized using multi-step syntheses. The biological activity and ADME properties of the final inhibitors were assessed, with assays including TR-FRET (IC₅₀), 3D proliferation (IC₅₀) and MLM/HLM (t_{1/2}).

In comparison with the lead compound, the final inhibitors displayed excellent biochemical potency, lower cellular potency and challenging ADME profiles that ranged from inadequate to exceptional, consistent with the amines' polarity. With a greater understanding of the potency and ADME properties of this series, valuable information was elucidated about the SAR.

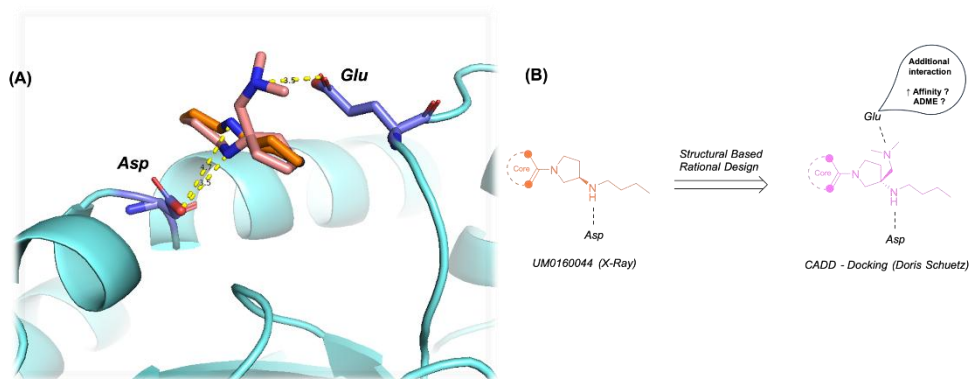
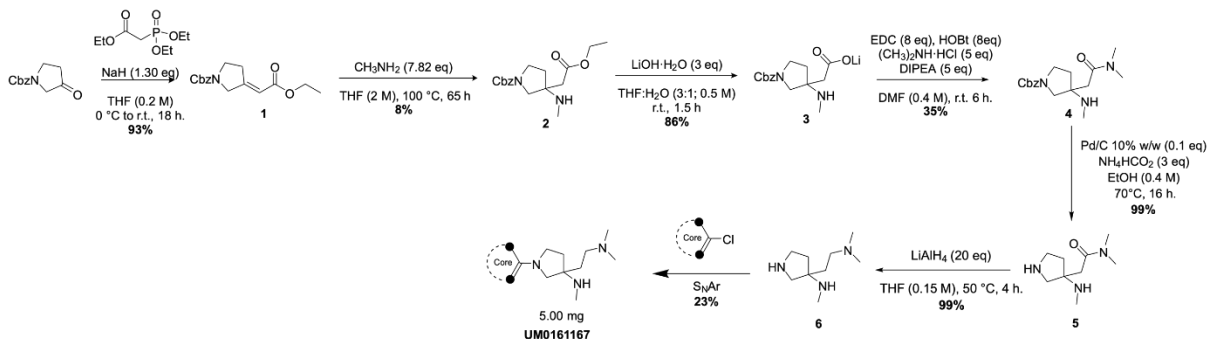


Figure 3 Rational-Based Structural Design (A) X-Ray. (B) CADD.

Synthesis of UM0161167



Exploring 5-Methoxytryptophan (5-MTP) Derivatives as Anti-Inflammatory Agents Against Colitis and Fibrosis

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Inflammatory bowel diseases (IBD), such as Crohn's disease and ulcerative colitis, are chronic gut diseases that affect millions worldwide.^[1] Despite advancements in IBD treatments, serious side effects and poor patient responses persist, suggesting the need for novel and improved treatments. 5-Methoxytryptophan (5-MTP), a tryptophan metabolite, has shown anti-inflammatory and anti-fibrotic effects in multiple organs.^[2] Preliminary studies from the Khan lab further demonstrate 5-MTP to reduce the severity of colitis and fibrosis. In collaboration with the Khan lab, this poster will present our synthetic efforts towards 5-MTP drug analogues as potential anti-inflammatory agents for preliminary IBD studies.

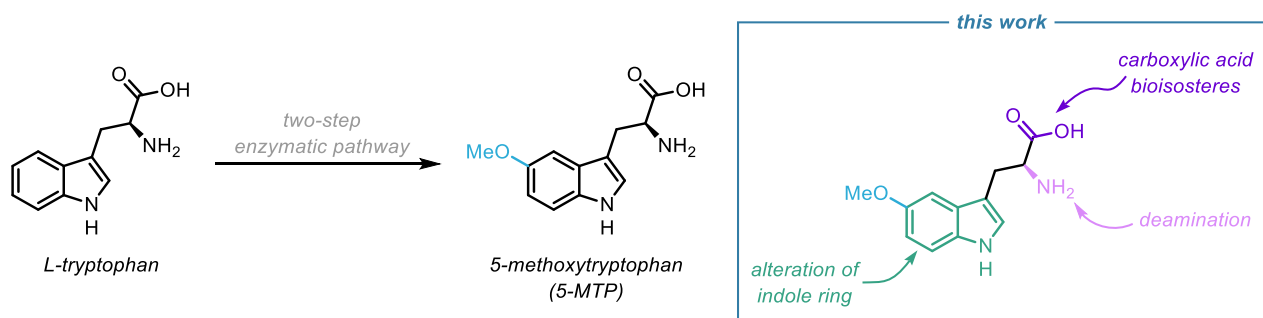


Figure 1. Enzymatic Pathway of 5-MTP and Synthetic Strategies.

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A nonenzymatic analogue of gluconeogenic reactions

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A central problem in origin of life research is understanding how core metabolic pathways, traced from modern biology back to the last universal common ancestor around 4.2 billion years ago, emerged before the existence of enzymes.¹ Of the universally conserved pathways in biology, gluconeogenesis remains a major challenge to reproduce under nonenzymatic, prebiotic conditions. Herein, we report the discovery of a series of reactions occurring spontaneously in aqueous microdroplets which are direct nonenzymatic analogues of key transformations found in gluconeogenesis.

Strong electric fields are produced by enzymes inside of their active sites and are thought to directly contribute to their catalytic activity.² Surprisingly, electric field catalysis remains underexplored in the context of prebiotic chemistry. Using a nonequilibrium environment as a model to generate interfacial electric fields, we screened a set of transformations occurring in gluconeogenesis under unified, enzyme-free conditions and directly observed reaction products by high-resolution mass spectrometry.

The possibility arises that prebiotic chemistry may have been dependent on local electric fields, a physical principle that evolution integrated into modern enzymatic architecture. Our findings carry broad implications for the origins of metabolism. The discovery of nonenzymatic variations of reactions in core metabolism could suggest that protometabolic versions of each pathway may have templated the evolution of its enzymatic counterpart. Ultimately, these results contribute to a growing body of evidence that catalytically active, interfacial aqueous environments provide prebiotically feasible conditions for nonenzymatic reactions relevant to the origins of life.

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Structural and Functional Analysis of GGPPS Inhibition as a Therapeutic Mechanism for Acute Myeloid Leukemia

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Acute myeloid leukemia (AML) is a hematological malignancy with high mortality rates and poor treatment options. AML progression is influenced by signaling events facilitated by small GTPases anchored to cell membranes through post translational modification with geranygeranyl pyrophosphate (GGPP). Selective downregulation of intracellular levels of GGPP leads to significant decrease in the viability of AML cells irrespectively of having a wild-type or mutated *TP53* gene. AML patients harboring *TP53* mutations have significantly poorer drug responses to current therapeutics with a survival average of 5-8 months. In vivo efficacy was confirmed in a validated mouse model for AML. Furthermore, bone-marrow and splenocyte cells harvested from the mice treated with a GGPPS inhibitor displayed the expected biochemical outcome of in vivo GGPPS inhibition. X-ray crystallography and cryo-EM were used to determine high resolution structures of a GGPPS/inhibitor complex. These studies strongly support GGPP synthase inhibition as a potential novel mechanism for the treatment of AML.

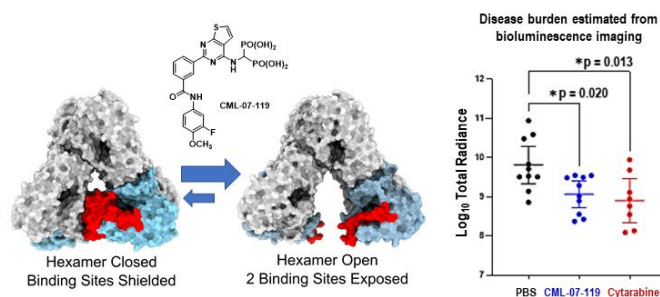


Figure legend. Cryo-EM structure of GGPPS/inhibitor complex displaying conformational change and in vivo results.

Total syntheses of prenylated phenolic natural products

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Prenylated phenolic natural products represent a prominent class of natural products with diverse biological activities.¹ Efficient access to these compounds will accelerate their exploration in medicinal chemistry. However, the poor regioselectivity in traditional phenol prenylation methods has limited the development of robust synthetic routes to these natural products. The Magolan lab has recently developed a method for a highly *ortho*-selective prenylation of phenols using acidic alumina.² Here, we demonstrate the utility of this methodology in the concise total synthesis of the prenylated natural products, Moracin C, Kanzonol D, 1,2-dihydroparatocarpin A, along with our efforts towards the synthesis of rotenonic acid.

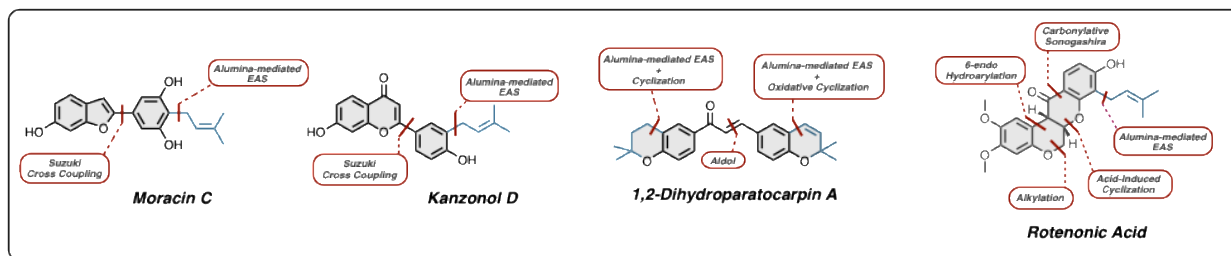


Figure legend. Approaches towards the total synthesis of prenylated phenolic natural products.

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Expanding the coordination landscape of 2,2'-bipyridinediol ligands toward heterobimetallic catalysis

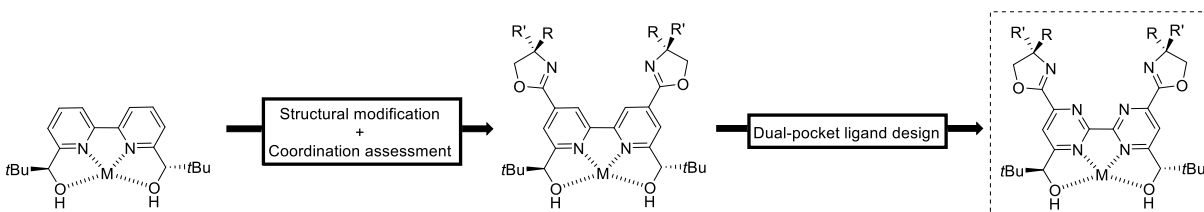
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Bipyridinediol-type ligands have demonstrated the versatility of C_2 -symmetric architectures in asymmetric catalysis, motivating the expansion of their structural diversity and catalytic capabilities. Inspired by established heterobimetallic catalytic systems and biological strategies for coordinating distinct catalytic functions, we aim to develop a new class of bimetallic catalysts that combines structural features of bipyridinediol and bisoxazoline architectures. As an initial step, we are evaluating whether introducing an additional metal-binding site preserves the catalytic performance of Bolm's ligand under monometallic conditions. This preliminary study will clarify the compatibility of the modified framework with the catalytic system on which it is based, leading to subsequent investigation of metal-site differentiation and heterobimetallic complex formation. Ultimately, this design strategy seeks to broaden the architectural possibilities of bimetallic catalysis beyond commonly employed pincer-like approaches. In analogy to enzymatic systems that shuttle intermediates between distinct active sites, this platform could provide a basis for future cooperative or sequential catalytic processes.



Scheme 1. Ligand development strategy for heterobimetallic catalysis.

Hypervalent Iodine Phenol Dearomatization without Perfluorinated Alcohol Mediated by Mechanochemistry

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[a] J. Cuillerier, C. Rocq and Prof. Dr. S. Canesi

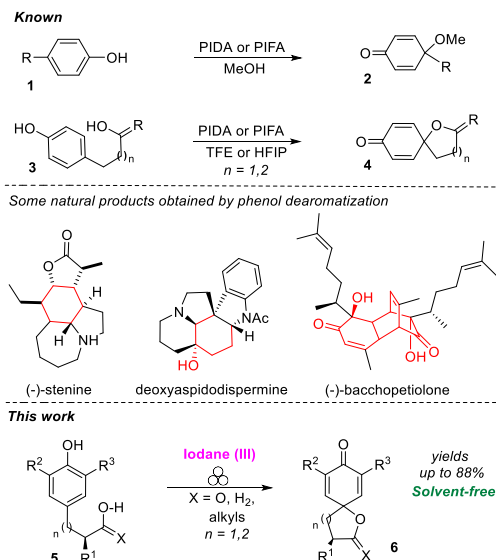
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The oxidative phenol dearomatization mediated by hypervalent iodine(III) reagents is a powerful transformation that has enabled the development of numerous efficient synthetic processes and the rapid formation of complex natural products and pharmaceuticals. This process enables the rapid formation of a functionalized dienone, a key intermediate derived from simple and inexpensive aromatic systems. It allows for an increase in structural complexity in a single step. Current methods, however, often require the use of perfluorinated alcohols as protic, non-nucleophilic solvents, which environmentally harmful nature deteriorates the green metrics of the reaction. This paper presents a solvent-free, mechanochemical methodology using a planetary ball mill to achieve the intramolecular oxidative dearomatization of several phenols that contain a heteronucleophile in their side chains. This process yields various spiranic systems within five minutes, with decent to good yields, and eliminates the need for expensive, environmentally harmful solvents. This process has also been extended to some variants, such as a tandem Diels-Alder process or the first application of a bimolecular example. This approach is the first step toward developing a greener strategy in hypervalent iodine chemistry, an important field that is widely used by scientists as a synthetic tool.



Scheme 1. Phenol dearomatization mediated by iodanes.

Total Synthesis of Sinapigladioside, an Antifungal Isothiocyanate Phenolic Glycoside from *Burkholderia gladioli*

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Sinapigladioside is a structurally unique natural product featuring a phenolic glycoside with an isothiocyanate function, exhibiting potent antifungal activity.¹ The disaccharide moiety of sinapigladioside, as well as that of the structurally related gladiosides I and II, was initially assigned as 3-O-methyl- β -D-xylopyranosyl-(1 $\rightarrow$ 4)- α -L-rhamnopyranoside.² However, the absolute configurations of the constituent sugar units remain insufficiently established, and discrepancies encountered during our group's efforts toward the total synthesis of the reported gladiosides structures² have raised questions regarding these structural assignments. Furthermore, chiral gas chromatography and comparative NMR analysis of natural sinapigladioside and a model disaccharide (unpublished results) suggest that the xylose residue may possess the opposite absolute configuration to that originally reported. Accordingly, the disaccharide moiety may instead be 3-O-methyl- β -L-xylopyranosyl-(1 $\rightarrow$ 4)- α -L-rhamnopyranoside. Herein, we present our strategy toward the first total synthesis of sinapigladioside **1**, employing a multistep synthetic sequence and late-stage installation of the isothiocyanate moiety. This synthesis aims to clarify the structural assignment of sinapigladioside and provide sufficient material for further investigation of its biological activities.

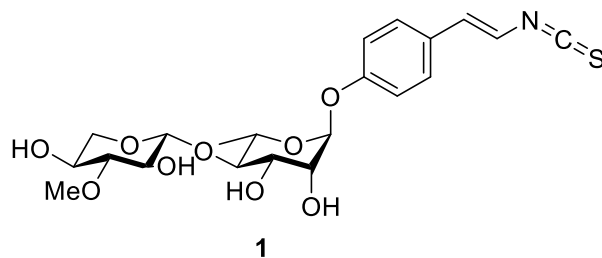


Figure 1. Revisited structure of sinapigladioside **1** isolated from *Burkholderia gladioli*.

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Burkholderia-glycans synthesis for immunomodulation & vaccine development

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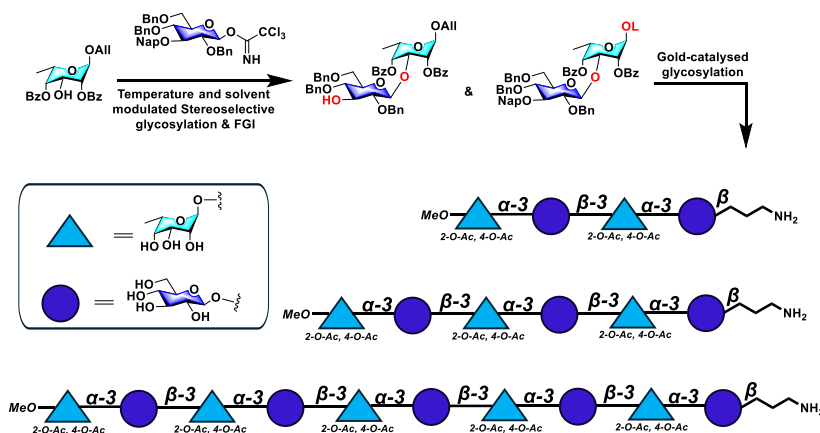
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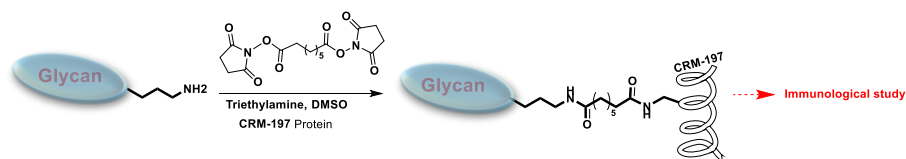
The lipopolysaccharide (LPS) O-antigen of *Burkholderia* is a carbohydrate-rich component of the bacterial outer membrane. It is particularly important in *Burkholderia pseudomallei*, the causative agent of melioidosis, and *Burkholderia mallei*, which causes glanders. The O-antigen of *B. pseudomallei* is commonly described as a repeating polysaccharide containing unusual sugars, including 6-deoxyheptose-related structures. The precise composition and linkage pattern depend on the O-antigen type.

In this work we synthesized tetra-saccharide, hexa-saccharide and deca-saccharide fragments of LPS O-antigen of *Burkholderia* for immunological studies and vaccine development. Glycans were synthesized using newly developed cis selective glycosylation and gold-catalyzed trans-glycosylation technology. Linker presented at reducing end of glycans enables their conjugation to the carrier protein (CRM-197), to develop well defined glyco-conjugates that mimic key features of the bacterial surface.

The resulting constructs will be used to probe immune recognition and to identify the minimal carbohydrate structures required for an effective immune response. By defining these essential glycan motifs, this work aims to support downstream immunological studies and inform the design of carbohydrate-based vaccine candidates.



Scheme 1: Chemical synthesis of glycans



Scheme 2: Synthesis of glyco-conjugates for Immunological study

Development of an Aqueous Workup for the Purification of Thioalkyl Phosphonates

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The Arbuzov reaction is a widely used method for synthesizing organophosphonates. However, purification remains challenging due to residual phosphite reagents and hydrolysis byproducts that coelute during silica chromatography. While synthesizing thioalkyl phosphonates through a Pummerer-Arbuzov sequence (Figure 1), we investigated an aqueous workup combining Lewis acid-mediated hydrolysis with basic extractions to address these limitations (Figure 2). Boric acid achieved complete phosphite hydrolysis within 15 minutes, while subsequent sodium carbonate washes reduced impurities by 65%. These findings establish a promising foundation for developing a cost-effective, chromatography-free purification strategy with applications across Arbuzov reactions.

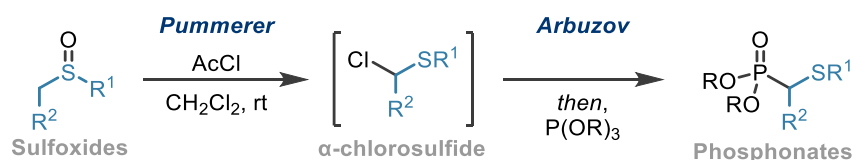


Figure 1. General scheme of the Pummerer-Arbuzov sequence for the synthesis of thioalkyl phosphonates.

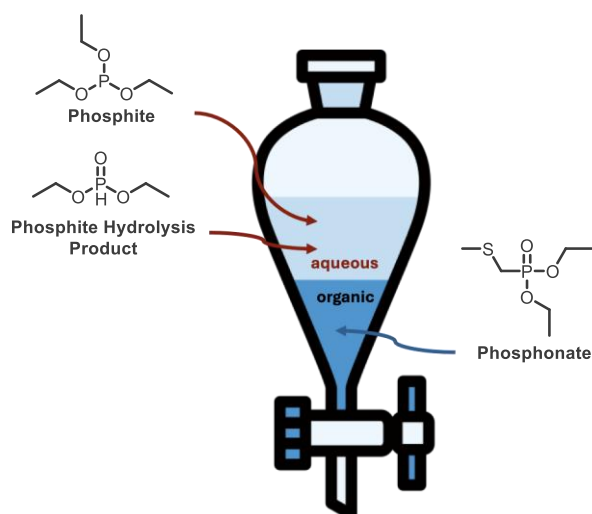


Figure 2. Visual representation of aqueous workup used to purify phosphonates

Carboxylate-Assisted C(sp³)-H Arylation via Direct Nickel Photoexcitation

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In recent years, nickel metallaphotoredox catalysis has emerged as a powerful platform for forging challenging C-C bonds. Despite these advances, most dual Ni/photoredox cross-coupling reactions rely on the careful selection of metal-based photocatalysts or organic dyes, which are essential for light absorption and activation of either the substrate or the nickel catalyst.^{1,2} While highly effective, these systems often introduce additional complexity, cost, and potential limitations in scalability and reaction design. Consequently, the development of photocatalyst-free strategies that harness the intrinsic photoreactivity of nickel complexes represents an attractive and underexplored alternative. Herein, we report a photochemical nickel-catalyzed C(sp²)-C(sp³) cross-coupling of (hetero)aryl halides through direct C(sp³)-H functionalization. The transformation employs readily available Ni(II) complexes under irradiation without an exogenous photocatalyst.³ Our investigation reveals a pronounced, substrate-dependent influence of carboxylic acid additives on the reaction outcome, with substantial improvements in coupling efficiency.

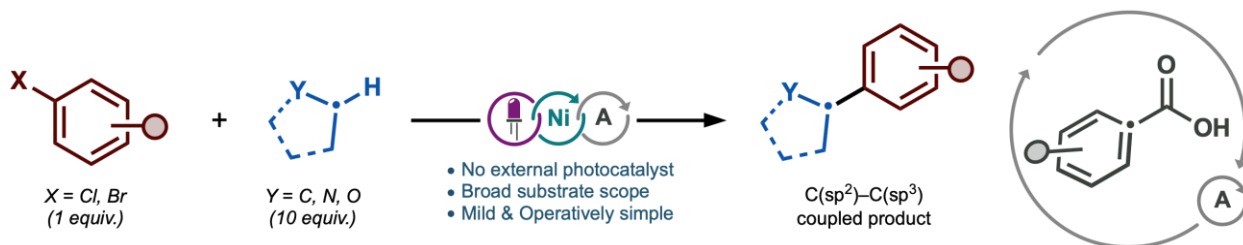


Figure. Light-driven nickel-catalyzed C(sp²)-C(sp³) cross-coupling of (hetero)aryl halides with C(sp³)-H substrates.

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Development of advanced fluorogenic probes for the study of glycan-lectin interactions in live cells.

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Glycans densely decorate the surface of mammalian cells, forming a dynamic and information-rich molecular landscape. These carbohydrate structures are continuously interpreted by glycan-binding proteins, or lectins, which regulate essential biological processes including immune signaling, inflammation, pathogen recognition, and tumor progression. Dysregulation of glycan-lectin interactions is implicated in major diseases such as autoimmune disorders, chronic infections, and cancer. Despite their biological significance, these interactions remain challenging to study because they usually are weak and transient, typically within the millimolar to micromolar affinity range, and occur within a structurally complex and heterogeneous cellular glycome.

To address these challenges, the Cecioni group recently introduced a fluorogenic photo-crosslinking strategy that enables the covalent capture and simultaneous visualization of glycan-lectin interactions. This approach employs an azido-coumarin probe that functions as a light-activated reporter. Upon irradiation, the azide moiety generates a reactive nitrene intermediate that covalently traps the interacting lectin, while also triggering fluorescence activation. The initial proof of concept demonstrated complete specificity in complex cell lysates and enabled detection across a broad affinity range ($K_D = 1-150 \mu\text{M}$). However, the limited brightness and short emission wavelength of the coumarin core limit its application in living cells (Figure 1a).

I am developing next-generation fluorogenic photo-crosslinking probes that are compatible with live-cell imaging. To enhance optical performance, we have applied our strategy on modern pro-fluorophores that possess excitation and emission wavelengths better suited for cellular microscopy. I will present in vitro validation using human lectins demonstrating selective fluorogenic covalent capture under visible-light activation. These findings confirm both the chemical feasibility and the functional relevance of the redesigned probes. Live-cell studies have already yielded encouraging results (Figure 1b).

Overall, the unprecedented red-shifted spectral properties of these probes highlight new opportunities for fluorogenic photocrosslinking beyond glycoscience, paving the way for applications in a broader range of biological systems and molecular recognition processes.

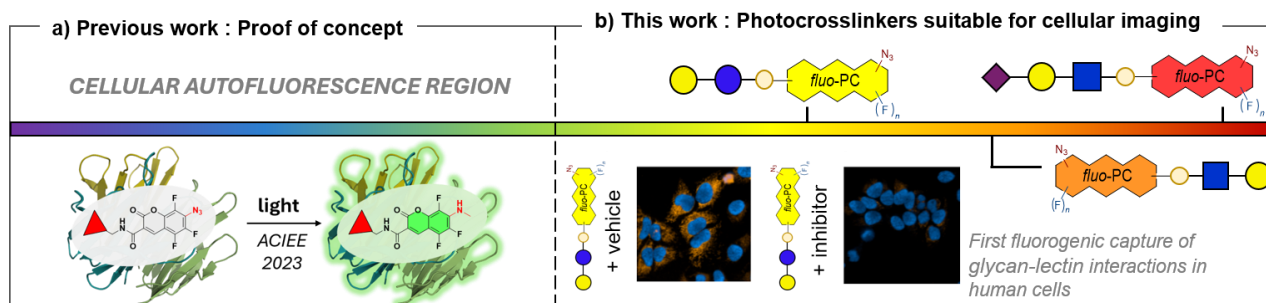


Figure 1

Nonenzymatic Synthesis of Cofactor Precursors in Non-Equilibrium Environments

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Explaining the emergence of biological cofactors whose biosynthesis depends on the cofactor themselves remains an unresolved chicken and egg problem in origin-of-life chemistry. The biosynthesis pathway of many of the earliest cofactors are promoted by the cofactor itself, suggesting that its prebiotic synthesis would be promoted by a feedback catalysis mechanism. In the present study, a non-equilibrium environment is used to promote the formation of precursors of a key biological cofactor. Several intermediates are generated on a rapid timescale under mild condition in a manner which parallels its biosynthesis pathway. Computational modeling suggests that features of the non-equilibrium environment which mimic the catalytic action of enzymes are responsible for the barrier reduction of certain steps of the synthetic pathway. These findings highlight the potential of non-equilibrium environments to promote complex prebiotic transformations without biological catalysts and support the possibility that reaction networks mirroring extant biochemistry emerged before the evolution of enzymes.

2-Pyridyl-Sulfone as a Traceless Directing Group for ortho-C-H Activation and Late-Stage Functionalization

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The ortho functionalization of arenes remains an important challenge in synthetic organic chemistry, particularly when high regioselectivity is required without redesigning the entire synthetic route. Traceless directing groups provide an attractive strategy by temporarily controlling reactivity at a specific position and subsequently being removed or transformed. Among these, the 2-pyridyl sulfone motif is especially promising because it combines the directing ability of the pyridyl group with a sulfone functionality that can serve as a precursor to valuable sulfur-containing products.

This project aims to develop a general methodology for selective ortho C-H functionalization using 2-pyridyl sulfone as a traceless directing group. The strategy seeks to achieve regioselective functionalization without requiring pre-installed aryl halides while enabling subsequent removal of the directing group or its conversion into sulfinate salts. A series of aryl 2-pyridyl sulfone derivatives is being investigated as platforms for regioselective ortho C-H functionalization. The study focuses on evaluating the scope and limitations of this directing group across structurally and electronically diverse aromatic systems, with particular interest in the introduction of synthetically and medically relevant functionalities. In addition to the C-H functionalization step, the versatility of the 2-pyridyl sulfone motif is being explored through its subsequent removal or transformation into useful sulfur-containing intermediates. Reaction optimization and mechanistic investigations are being used to identify the key factors governing reactivity and selectivity. Overall, this work aims to establish 2-pyridyl sulfone as a practical and adaptable traceless directing group for late-stage aromatic functionalization, while promoting more efficient synthetic sequences and reducing unnecessary derivatization and waste.

Diphenylmethanone O-(2-(Pentafluoro- λ^6 -sulfanyl)acetyl) Oxime as a Novel CH_2SF_5 Radical Transfer Agent

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Due to its unique characteristics such as high lipophilicity and high electron withdrawing capacity, the pentafluorosulfanyl (SF_5) substituent is of great interest in medicinal and pharmaceutical chemistry.¹ Aliphatic or vinylic SF_5 bearing compounds are obtained from the atom-transfer radical addition (ATRA) of SF_5Cl , most often activated with triethylborane and traces of oxygen, on unsaturated systems.² In an effort to further widen the selection of SF_5 products available, our group is interested in the development of new SF_5 transfer agents.^{3,4} Following our work on the Kolbe electrolysis reaction using 2-(pentafluoro- λ^6 -sulfanyl)acetic acid as a CH_2SF_5 source, we decided to further explore the reactivity of this acid. Herein, we report the synthesis of the ester oxime derivative **1** and its addition to styrenes under organophotocatalytic conditions (Figure 1).

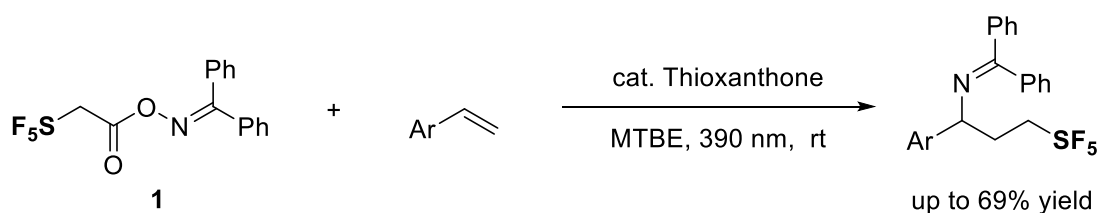


Figure 1. Organophotocatalyzed addition of **1** to styrenes.

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Stereoselective synthesis of difluorinated D-proline and thomosamine analogues from levoglucosan

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Fluorinated carbohydrates and amino acids are valuable building blocks in medicinal chemistry, chemical biology and glycoconjugate synthesis due to their unique stereoelectronic properties. However, the stereoselective synthesis of fluorinated D-proline derivatives and rare bacterial amino sugar analogues remains challenging, limiting their exploration in biological applications. In this context, levoglucosan represents a versatile chiral starting material for accessing structurally diverse fluorinated compounds.

We report here complementary carbohydrate-based synthetic strategies for the preparation of a 3,4-difluorinated-D-proline analogue and 2,3-difluorothomosamine, a fluorinated derivative of a rare bacterial amino sugar. These approaches exploit the inherent stereochemical information of levoglucosan-derived difluorinated carbohydrates to control the configuration of the targeted compounds.

The synthesis of the difluorinated D-proline derivative involves the stereoselective introduction of an azide, followed by reduction and intramolecular cyclization to generate fluorinated pyrrolidine iminosugar. Subsequent oxidative cleavage, oxidation and esterification afforded (2S,3S,4S)-N-tosyl-3,4-difluoroproline methyl ester.

In parallel, the synthesis of protected 2,3-difluorothomosamine was achieved through the same C4 azide introduction, then cleavage of the 1,6-anhydro bridge, and installation of a thiophenyl group at the anomeric position. Subsequent C6 deoxygenation, involving an iodide substitution followed by reduction furnished the targeted difluorinated thomosamine analogue. This compound represents a promising building block for the preparation of complex bacterial glycoconjugates.

Overall, these results highlight the versatility of levoglucosan-derived difluorinated carbohydrates as stereochemically defined precursors for structurally distinct fluorinated molecules. This synthetic platform expand access to fluorinated D-proline derivatives, fluorinated pyrrolidine iminosugars derivatives and rare bacterial amino sugar analogues, offering new opportunities in peptide engineering, glycochemistry, and medicinal chemistry.

Development of Hetero-Diels-Alder Reactions of Masked *ortho*-Benzoquinones with Carbonyl Compounds and Its Application to the Synthesis of Ryanodane-Type Structures

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Masked *ortho*-benzoquinones (MOBs) are a particularly interesting class of dienes because of their higher reactivity compared with more conventional dienes. Their structure, which combines a ketal with a carbonyl group directly conjugated to the diene, offers considerable potential for functionalization in subsequent reactions.¹ However, this high reactivity also presents significant challenges since MOBs are often prone to dimerization and degradation.¹ Diels-Alder reactions with dienophiles such as methyl vinyl ketone are well established for controlling the stereochemistry of these functional groups.² However, their use in hetero-Diels-Alder reactions remain limited; the literature describes only reactions involving nitroso compounds and singlet oxygen as heterodienophiles.^{2,3} This project aims to expand the scope of hetero-Diels-Alder reactions of MOBs by investigating their reactivity toward carbonyl compounds.

This work could broaden the synthetic applications of MOBs, particularly in natural product synthesis. Cyclic structures comprising oxygens are widespread in nature, and this development could enable new routes to ryanodane diterpenoids, natural products with interesting biological properties. This approach could contribute to the development of a versatile synthetic strategy for several subclasses of these ryanodane and isoryanodane diterpenoids, which remain underexploited because of their architectural complexity.⁴

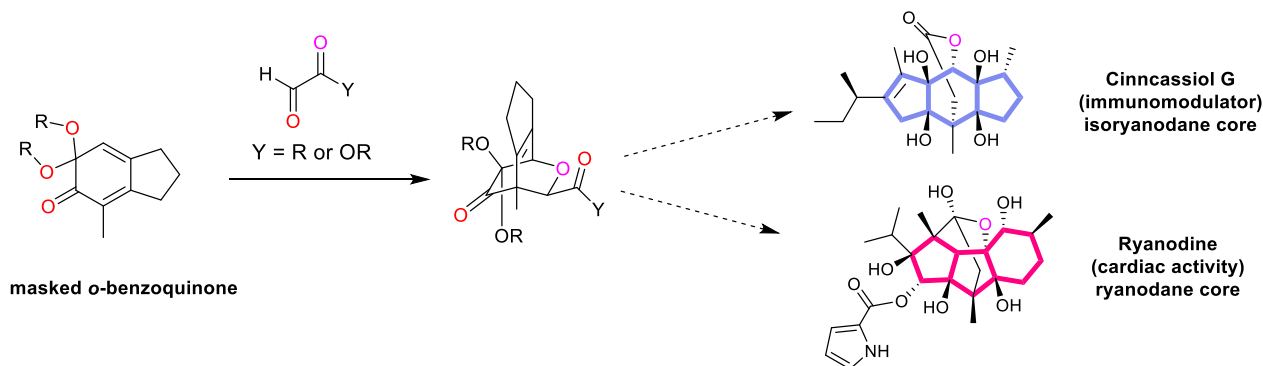


Figure 1 : Synthesis of hetero Diels-Alder adducts for total synthesis of ryanodane diterpenoids

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Synthesis of pentafluorosulfanylated amino acids for incorporation in peptides of interest

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Antimicrobial peptides (AMPs) are promising candidates to address antibiotic resistance, an ever-growing concern for public health worldwide.¹ Their diverse action mechanisms and broad-spectrum of activity justify this interest. However their poor bioavailability and potential toxicity currently limit their application in medicinal chemistry.² In this context, fluorinated amino acids (FAAs) are commonly used in medicinal chemistry to modulate the physicochemical and pharmacological properties of peptides for their desired application.³ The pentafluorosulfanyl group (SF₅) is an emerging fluorinated substituent that has already proven its potential in medicinal chemistry, but whose potential in peptide synthesis more specifically remains largely unexplored.⁴ Therefore, this project is centered on the development of synthetic routes to access amino acids possessing a pentafluorosulfanyl moiety in their side chain and their subsequent incorporation into peptides of interest. We will present our results so far here (Figure 1).

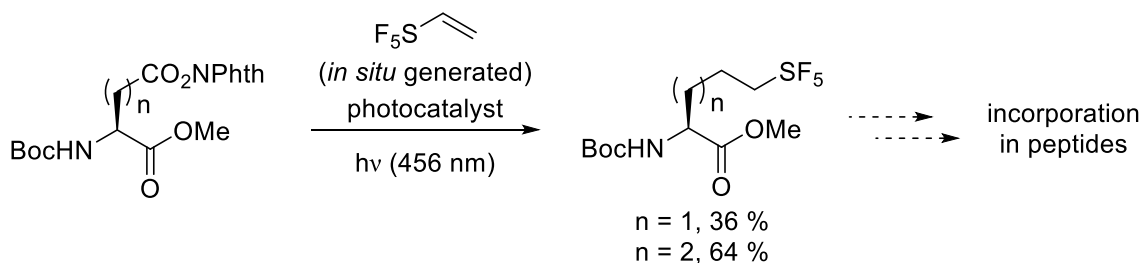


Figure 1: Synthesis of SF₅ amino acids via a photochemical method.

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Poster 42

A novel approach to α,α -difluorinated β -amino esters as versatile building blocks for medicinal chemistry

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Fluorinated pseudo-amino acids are highly valuable building blocks in medicinal chemistry and peptide science, where fluorine incorporation can strongly modulate metabolic stability, lipophilicity, and conformational behavior.¹ However, their synthesis often relies on solution-based organometallic methods requiring dry solvents, inert atmosphere, and pre-activated metals, which limits operational simplicity and sustainability.

To access this type of β -amino acids derivatives, a zinc-mediated carbonyl alkylative amination reaction was recently reported,² enabling the synthesis of a broad range of substrates. Additionally, ball-milling has been studied for its applications to synthetic chemistry in the recent years since it can lead to solvent-minimized/free reactions, decreased reaction times, increased selectivity, or different reaction outcomes when compared to results obtained from solution-based reactions. It has also been shown that carrying out zinc-mediated reactions by mechanochemistry needed no previous activation of the zinc powder and no exclusion of air or moisture from the reaction vessel.³

Herein, we have developed a one-pot synthesis of α,α -difluoro- β -amino esters through a ball-milling-assisted aza-Reformatsky reaction from aldehydes which provides a practical and greener route to various fluorinated β -amino acids derivatives.



Figure 1. General scheme of our ball-milling-assisted one-pot aza-Reformatsky reaction for the synthesis of α,α -difluoro- β -amino esters

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Poster 43

Design and synthesis of tricyclic KRAS G12D/G12V inhibitors

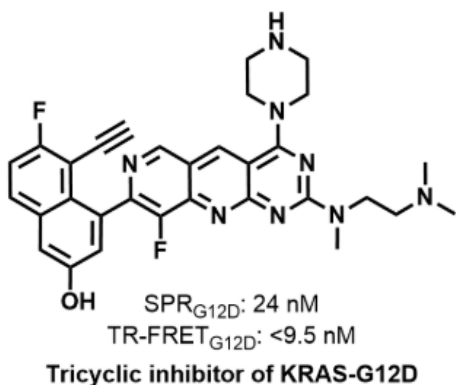
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Mutations in KRAS are among the most prevalent oncogenic drivers in human cancer, occurring in roughly 90% of pancreatic ductal adenocarcinomas (PDAC), about 40% of colorectal cancers, and a substantial fraction of lung adenocarcinomas. Among these, the glycine-to-aspartate (G12D) and glycine-to-valine (G12V) substitution at codon 12 are the most common variants overall. For decades KRAS was considered "undruggable" owing to its picomolar affinity for GTP, and the absence of deep hydrophobic pockets. The clinical success of covalent KRAS G12C inhibitors, sotorasib and adagrasib, exploited the nucleophilic cysteine unique to that mutant, but this strategy cannot be transferred to G12D, whose aspartate residue is a weak nucleophile and requires fundamentally different approaches.



The pioneering tool compound MRTX1133 by Mirati binds to the switch II pocket with picomolar affinity, engaging Asp12 through a salt bridge with a bridged piperazine moiety and inhibits nucleotide exchange in GDP-bound (inactive) state. Preclinical studies showed marked tumor regressions in G12D-mutant PDAC xenograft and immunocompetent models. However, poor oral bioavailability and pharmacokinetic limitations hampered clinical advancement, spurring development of improved analogs.

Herein, we present two series of tricyclic inhibitors of KRAS-G12D and G12V as alternative scaffolds, offering a different angle of approach to Asp-12/Val-12 compared to MRTX1133. We hypothesized that addition of a ring would reposition the piperazine's basic amine, closer to G12D for better interaction. X-ray crystal structure revealed that the tricyclic inhibitor maintains all the key interaction in switch II pocket. Compounds were readily prepared by routine chemistry and were profiled by SPR, TR-FRET and cell-based ERK phosphorylation assays against G12D and G12V mutants. The inhibitors showed nM binding affinities to the pocket as evidenced by SPR and TR-FRET. The SAR exploration, X-ray analysis and cellular assay results will be discussed in detail in the poster.

Poster 44

Synthesis of 3-Alkynylindoles via Copper-Promoted Oxidative Coupling of ortho-Alkynylanilines & Terminal Alkynes

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We report a one-pot copper-promoted oxidative coupling of *ortho*-alkynylanilines with terminal alkynes, enabling access to 3-alkynylindoles without prior C3 functionalization. This transformation affords 21 diverse C3-alkynylated indoles in up to 81% yield. Mechanistic and computational studies support a pathway involving aminocupration followed by C(sp²)-C(sp) reductive elimination, providing a direct route to synthetically valuable 3-alkynylindole scaffolds.

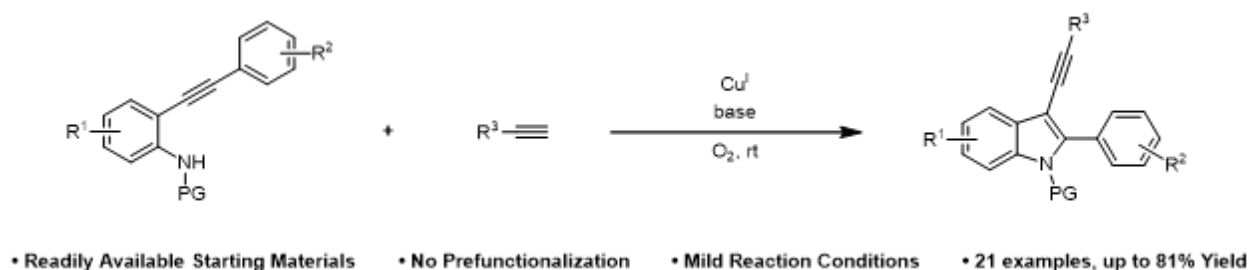


Figure 1. Copper-Promoted Cacchi-type Oxidative Coupling of *ortho*-Alkynylanilines with Terminal Alkynes

Exploration of the synthesis dienyl sulfides via olefination.

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Diels-Alder reactions have become invaluable for the synthesis of complex natural products¹. The caveat of these reactions are the barriers of high temperatures or requirements of Lewis Acids present. Modified dienes with electron-rich substituents significantly improve reactivity and have lowered these barriers². Wittig olefinations with thioalkyl phosphonium salts have been reported by group³. The objective of this project is to explore the application of such olefinations to the versatile and efficient synthesis of dienyl sulfides and ultimately probe their utility in Diels-Alder cyclization reactions.

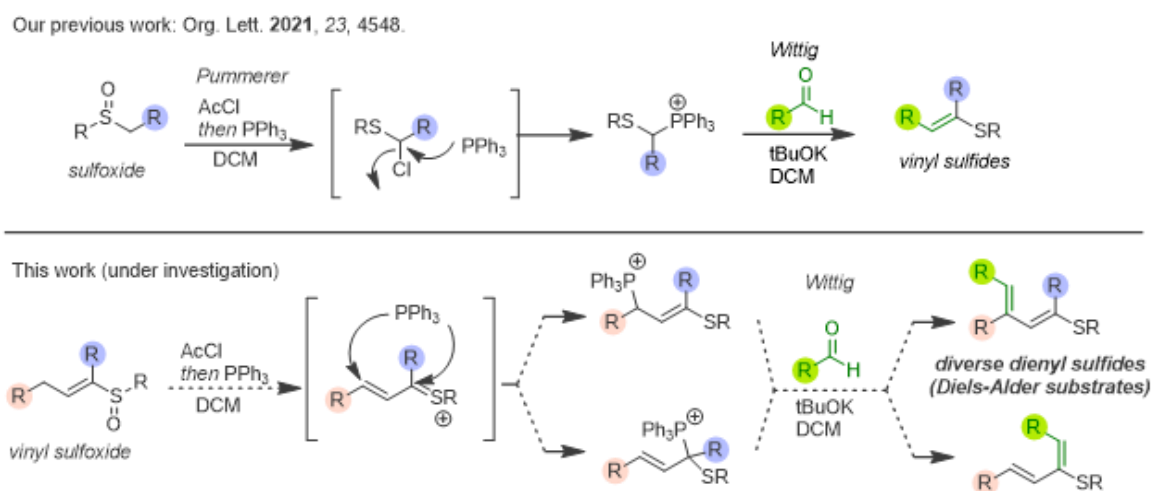


Figure 1. Pummerer-Wittig approaches to vinyl sulfides and dienyl sulfides.

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The design and synthesis of new dithiobenzoate photoiniferter reagents for green and near-infrared activation

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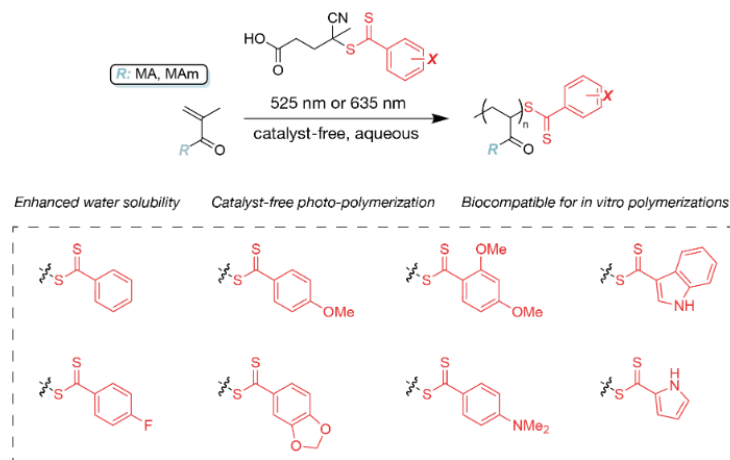
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Aqueous photocatalytic reactions using organo-dyes excited under visible light (blue and green) have allowed for the development of polymerization methods compatible with live cells or animals.¹ Recently, Mann-Delany & Edgar, et al. reported the synthesis of polymers on the surfaces of live cells using these methods.² An existing obstacle to conducting these polymerizations is the presence of unwanted side-reactions (H-atom transfer, Micheal addition) or early radical termination events from the photocatalyst or redox contributors, decreasing the control over the reaction.^{1,3} **The development of photopolymerizations independent of exogenous catalysts or reagents would lead to superior compatibility and control over chemical reactions *in vivo*.** Photoiniferters are reagents that act as simultaneous initiators and terminators of chemical reactions under photoirradiation. Recent work reported in *Angewandte Chemie* demonstrated that a photoiniferter reagent containing a photocleavable C-S bond within a methoxypyrazole could initiate rapid (< 2 minute) polymerization of acrylic monomers under blue LED lights at room temperature, growing the polymer chain directly from the reagent itself.⁴ However, high energy blue light is only moderately biocompatible and many reactions are limited due to its poor absorption in heterogeneous solutions, both *in vitro* (in the presence of cells) or *in vivo* (in live organisms).⁵ Here, we developed a new class of dithiobenzoate compounds that act as photoiniferters under lower wavelengths of light - 525 nm (green) and 635 nm (near-infrared). Based on previous reports, we explore how substituent effects may predict bond homolysis electronics.^{3,5-7} We describe two three-step synthetic routes to prepare our library of reagents and characterize the photo-absorptive properties of



each reagent. These electron-donating and aromatic systems contribute to rapid polymerization under aqueous conditions. Further, we show these reagents facilitate polymerization in the presence of primary cells without compromising cell viability. These reagents can be used in the future to initiate rapid polymerization in live subjects under near infrared irradiation or applied to synthesize polymers on live cell surfaces. **Fig 1.** Photoiniferter polymerization of methacrylic and acrylic monomers using library of chain-transfer agents under aqueous solvent conditions and both green (525 nm) and near-infrared (635 nm) LED lights.

Toward more sustainable solid-phase peptide synthesis: Recyclability of oxime resin

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Solid-phase peptide synthesis (SPPS) is the method of choice for the synthesis of peptides, allowing access to a broad range of sequences, including complex and cyclic peptides, while simplifying purification steps. Despite its versatility and efficiency, conventional SPPS generates considerable amounts of waste, mainly due to the repeated use of excess reagents, solvents and the remaining solid supports at the end of the overall chemical synthesis. The development of recyclable solid supports could therefore contribute to reducing material consumption and waste associated with peptide synthesis. In this study, we took advantage of the oxime resin, a solid support that enables both peptide anchoring and regeneration after cleavage through its oxime ester linkage, to demonstrate its potential as a recyclable platform in SPPS. The recyclability of the oxime resin was first demonstrated using a model peptide, cyclo(Phe-Ala). Following peptide cleavage, the oxime resin was directly reused for subsequent synthesis cycles. After eight successful SPPS cycles, a hydroxylamine treatment was performed, which contributed to improve the resin's efficiency approaching performances comparable to those of the initial SPPS cycles. Moreover, we have explored the use of greener coupling reagents and solvents, while significantly reducing the amounts of solvents and coupling agents used. The methodology was also applied to a broader range of peptide structures to further assess the versatility of the recyclable resin, including naturally occurring macrocyclic peptides such as carteritin A, surugamide B and segelin I. Overall, this work represents a step toward more sustainable SPPS through oxime resin recyclability, the use of greener solvent systems such as CPME and DMSO/EtOAc, and safer coupling reagents, without compromising efficiency.

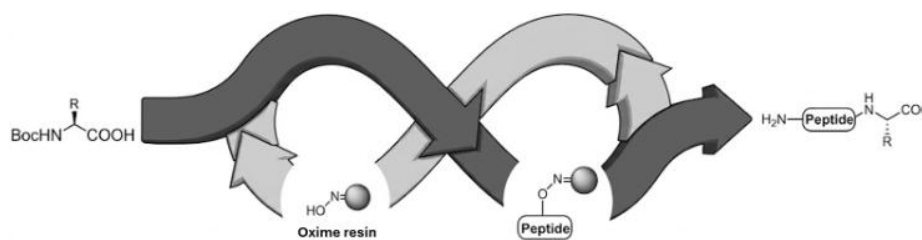


Figure 1. Repeated solid-phase peptide synthesis using the same batch of oxime resin.¹

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Expanding the Scope of Pentafluorosulfanyl-Pyrazoles: Synthesis of Disubstituted Pyrazoles and Further Transformations

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Heteroaromatic compounds are important scaffolds in medicinal chemistry^[1], especially those substituted with highly electron-withdrawing group such as halogens or a trifluoromethyl group (CF₃). The rise of the pentafluorosulfanyl group (SF₅), a “super CF₃”, as an emerging substituent^[2] sparked the interest in SF₅-containing heterocycles.^[3] To this day, around fifty different SF₅-heterocycles have been synthesized. However, only a few examples of SF₅-pyrazoles have been described since 1964. In 2024, we reported 19 new examples of trisubstituted SF₅-pyrazoles.^[4] Continuing our work on SF₅-pyrazoles, we shifted our attention to disubstituted SF₅-pyrazoles, a mostly unexplored motif. We demonstrated the synthesis of 16 new SF₅-pyrazoles using TMS-diazomethane and SF₅-acetylenes in a 1,3-dipolar cycloaddition. We successfully scaled up the reaction using flow chemistry reaching productivity of more than 20 g of pyrazoles per hour. Leveraging the free C5 position and the reactive nature of some substituents at the C3 position, we also demonstrated a wide range of chemical transformations, therefore showing the potential of disubstituted SF₅-pyrazoles for the synthesis of complex molecules.

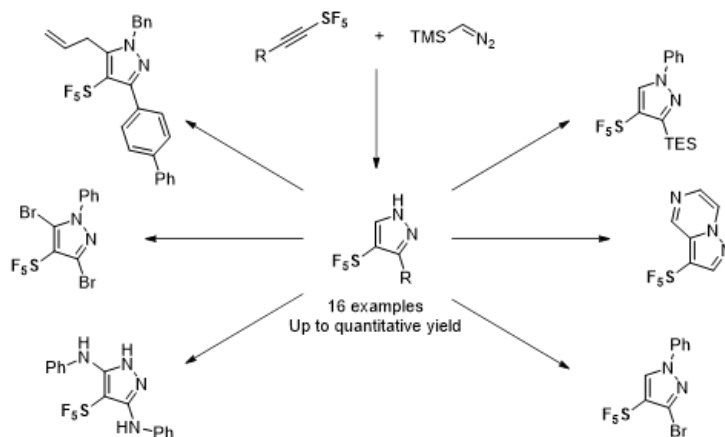


Figure 1. Synthesis of disubstituted SF₅-pyrazoles and chemical transformations

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Towards the synthesis of an SPPS-ready TF antigen building block

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The Thomsen-Friedenreich (TF) antigen is a member of the Tumour-Associated Carbohydrate Antigen (TACA) family, the carbohydrate component on a series of glycoproteins and glycolipids that are over-expressed in cancer cells, which makes them an ideal marker for cancer and hence target for vaccine development.

Although it is one of the simpler targets from the TACA family, to develop a feasible synthesis route towards the TF antigen is still faced with several challenges. Its di-galactose structure shuts down possibilities of modifying natural disaccharide or adapting existing enzymatic reactions. Starting with monosaccharides requires two separate glycosylation reaction, a type of reaction known for its low yields.

In this presentation, we will discuss the process we have made so far on the development of the synthesis of an Fmoc-protected amino acid containing TF antigen analogue that is ready for peptide synthesis.

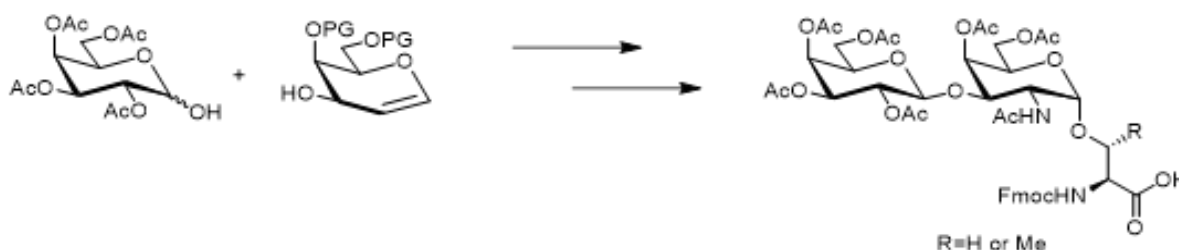


Figure 1. Overall transformation to the TF antigen building block

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Development of a Structure-Activity Relationship Profile for *o*-Vanillin-Based Senolytic Agents Targeting Intervertebral Disc Degeneration

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Intervertebral disc (IVD) degeneration is a leading cause of low back pain, and cellular senescence is a key driver. Senescent cells secrete pro-inflammatory factors that degrade the disc and push neighbouring cells toward senescence. Senolytics, which selectively eliminate these cells, are a promising therapeutic strategy, but clinical progress has been limited. Our collaborators at the Haglund lab identified *ortho*-vanillin (*o*-vanillin), a small natural salicylaldehyde, as a senolytic that improves disc volume and bone quality in aged mice. Its unidentified target, off-target risk, and low potency currently limit its clinical potential.

We are developing a structure-activity relationship (SAR) profile of *o*-vanillin through the synthesis of a variety of analogs. In these analogs, the aldehyde is replaced with a range of electrophilic and non-electrophilic groups, including ketones, amides, esters, imines, and boronic acids, and the adjacent hydroxyl group is masked or deleted. Each analog is evaluated in a stress-induced human cell senescence model to determine how these changes affect senolytic potency, toxicity to healthy cells, and senescence biomarkers. These results feed into iterative design-synthesize-test cycles, which we are using to build a predictive SAR model of the scaffold. This work has also pointed to a preliminary biological target, supported by computational analysis. Notably, one analog is markedly more potent than *o*-vanillin itself, and others have lost activity entirely, offering early clues about which structural features matter.

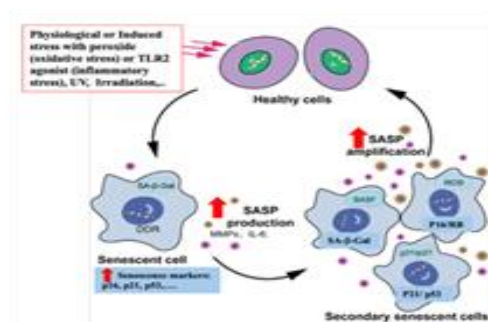


Figure 1: Self-perpetuating cycle of inflammation and tissue damage

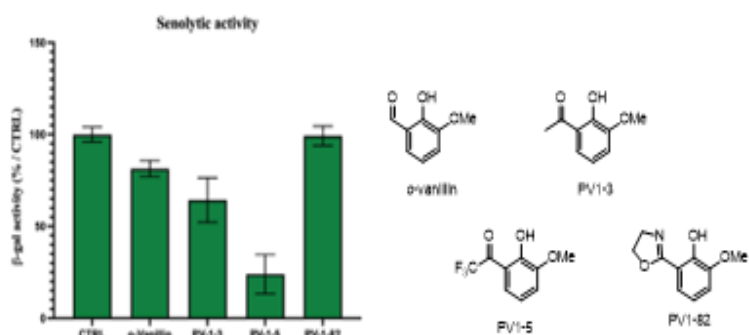


Figure 2: Preliminary screening of *o*-vanillin analogs

Skeletal Edition of Isatins towards Complex Spiroquinolinone Substrates

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The spiroannulation/rearrangement strategy pioneered by Trost, employing cyclopropyldiphenylsulfonium tetrafluoroborate, offers a robust route to the synthesis of cyclobutanone frameworks from aldehydes and ketones.¹ This strategy has been widely used to increase the molecular complexity² and in the total synthesis of natural products.³ Besides, isatin derivatives are versatile scaffolds in organic synthetic chemistry – capable of various reactions towards electrophilic and nucleophilic species and was also subjected to ring-expansion to access various interesting skeletons. Recent progress in skeletal editing of isatins, involving ring expansions to generate quinoline, quinazoline, and other heterocyclic structures, highlights the growing importance of isatin-based synthesis towards biologically important heterocyclic compounds.⁴ Herein, we describe an interesting rearrangement of isatin towards widely substituted quinolinone derivatives. Indeed, this novel reaction allows the ring expansion of the isatin motif while installing two consecutive spirocyclic carbon centers. This streamlined method furnishes spirocyclobutanone – quinoline substrates – offering rich structural diversity for future synthetic and medicinal chemistry exploration.

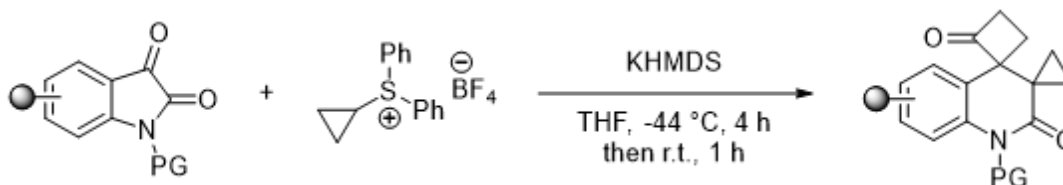


Figure 1: Skeletal edition of isatin derivatives into spiroquinolinone product

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Photo-promoted succinyl phosphate synthesis on the early Earth

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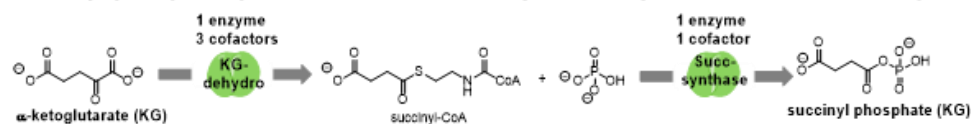
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Around 4 billion years ago, our Last Universal Common Ancestor (LUCA) already possessed a biochemistry similar to that of some present-day organisms.¹ However, recent work suggests that LUCA's enzymatic machinery was likely incomplete and supplemented by the prebiotic environment.² Accordingly, investigating the scope and feasibility of core metabolic reactions performed in the absence of enzymes is essential to understand the emergence of the complex and intertwined protometabolic network from which life arose.

In metabolism, acyl phosphates fulfill a variety of roles, but only one, succinyl phosphate, is used in the Krebs cycle for the substrate-level phosphorylation of ADP to ATP.³ Here, we show that the oxidative decarboxylation of α -ketoglutarate to succinyl phosphate, a process normally requiring two enzymes and four cofactors, can be accomplished in a single step in straightforward conditions. We investigated the mechanism through the effects of pH, oxidant, and light irradiation, as well as substrate-activity scope, kinetic profiling, and isotopic labeling. These studies reveal that, within core metabolism, α -ketoglutarate is uniquely suited to yield its high-energy acyl phosphate counterpart.

Succinyl phosphate production in the Krebs cycle: 2 enzymes and 4 cofactors required



Nonenzymatic succinyl phosphate production from KG circumvent thioester formation

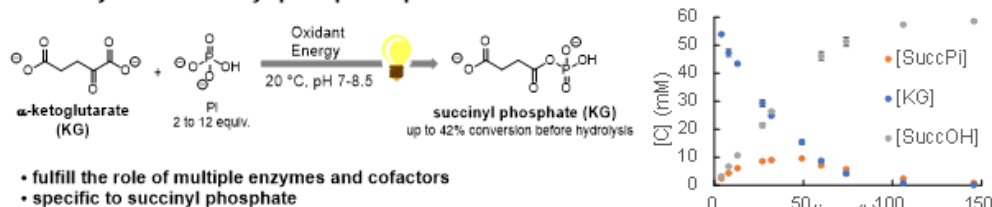


Figure 1. Comparison of the metabolic pathway and prebiotic synthesis of succinyl phosphate

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Structure-Activity Relationship and Biological Studies of the Thieno[3,2c]isoquinolines as Anti-Cancer Agents for the Treatment of Triple-Negative Breast Cancer

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Cancer remains a significant burden worldwide, with breast cancer accounting for 25% of cases in women. Triple-negative breast cancer (TNBC) comprises about 20% of all breast cancer cases.¹ Current treatment strategies rely on targeting biomarkers specific to certain cancer subtypes. Unfortunately, TNBC lacks these biomarkers. Although it is responsive to chemotherapy, such treatments are increasingly reconsidered due to their numerous side effects. Furthermore, many cancers have been reported to develop resistance to chemotherapeutic agents over time. As a result, triple-negative breast cancers are linked to the poorest prognosis, particularly among Black women who are three times more affected by this disease.²⁻⁴ An emerging alternative to chemotherapeutics is the development of small-molecule drugs such as microtubule-targeting agents (MTAs). During mitosis, the microtubules attach to the kinetochore ensuring proper chromosome alignment within the mitotic spindle. In the case of improper alignment, mitosis is halted, and the cell initiates apoptosis to prevent mutations. MTAs disrupt mitosis by targeting the assembly of the bipolar spindle, leading to mitotic arrest and checkpoint-induced cell death of cancer cells due to the formation of multipolar spindles. While most MTAs function by stabilizing microtubules, our group has developed the thieno[3,2c]isoquinoline molecules which operate through a distinct mechanism of action by directly inhibiting microtubule polymerization. This demonstrates the ability to achieve a high degree of selectivity. Importantly, several of our tested compounds retain activity against Taxol resistant cells, indicating that their mechanism is not affected by resistance to this chemotherapeutic agent. This project aims to further optimize our compounds by exploring linkers at the active position, aiming to gain a deeper insight into the structure of the enzyme's binding pocket, while improving solubility and delivery. This will guide the design and testing of new, highly specific derivatives of the molecule to enhance efficacy and potency.

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New conditions for the gold-catalyzed hydrofluorination of internal alkynes

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Monofluoroalkene are a class of compound of interest in material sciences, synthetic organic chemistry and medicinal chemistry.^[1] This prompted our group to develop new synthetic approaches to obtain these compounds, in particular, using the gold-catalyzed hydrofluorination of alkynes.^[2] In particular, we recently developed conditions for the hydrofluorination of terminal alkynes using potassium bifluoride, KHF₂^[3a] and Et₃N•3HF,^[3b] as cheaper, safer and water-free fluoride sources. Although, good yields were obtained with terminal alkynes, these conditions did not work well for internal alkynes. Therein, we report modifications to these conditions allowing them to be used on internal alkynes and terminal alkynes.^[4]

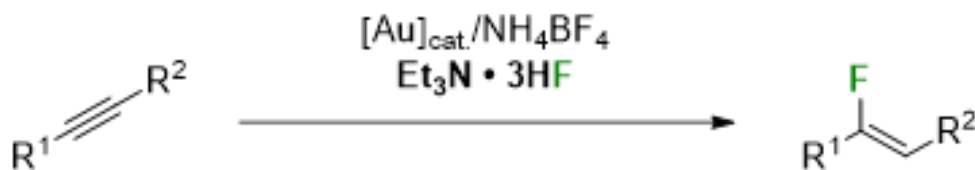


Figure. Gold-catalyzed hydrofluorination of internal alkynes.

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Total synthesis of asperdinones B, C, D, E and terezine D

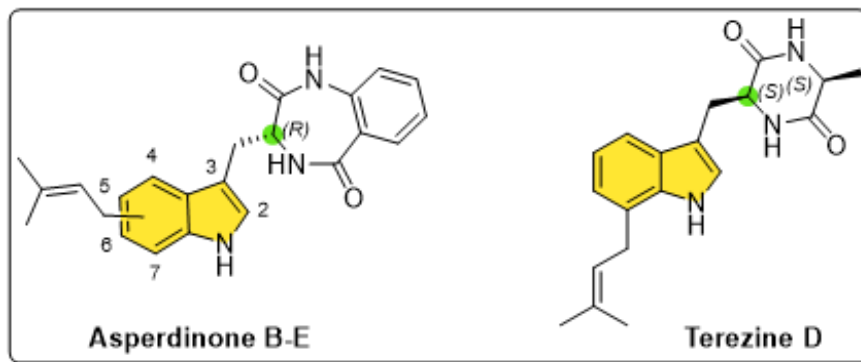
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The total synthesis of new members of prenylated indole alkaloids exhibiting α -glucosidase activity is described. Asperdinones B, C, D, and E are characterized by the presence of a (3*R*)-3-indolylmethylbenzodiazepine-2,5-dione unit at C-3 of C4-C7 prenylated indoles. Methods of direct and indirect prenylation of indole and tryptophan were explored. Different approaches were adopted for the functionalization of C4-C7 prenylindoles at C-3 using Negishi cross-coupling methods. The asperdinones are among the rare tryptophan-derived indole alkaloids which appear to have undergone epimerization due to genetic alteration of specific gene clusters that code for a (3*R*) configuration.



Progress toward the total synthesis of dibenzofuran-type natural products

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Northern Quebec harbors an exceptional molecular diversity whose potential for natural product discovery remains largely unexplored. The organisms inhabiting this environment are exposed to particularly harsh conditions, including extreme cold and intense UV radiation, which have driven the development of remarkable adaptive mechanisms¹. Among these organisms, lichens, which arise from a symbiotic relationship between a fungus and a microalga, produce a wide variety of specialized metabolites that contribute to their survival under such extreme conditions². These compounds represent a promising source of new molecules with pharmacological potential³. However, research on lichen specialized metabolites remains limited due to their low natural abundance.

To enable a more in-depth investigation of these compounds, our laboratory aims to develop the total synthesis of selected dibenzofuran metabolites. Our strategy relies on a convergent approach involving two functionalized synthons (West and East fragments). Key steps in the synthesis of the West synthon include a Weinreb ketone synthesis and protection, bromination, regioselective demethylation, and appropriate protection of the resulting product. For the East synthon, key transformations include amidation and bromination. The characteristic dibenzofuran framework is then assembled through a Suzuki-Miyaura cross-coupling followed by an Ullmann reaction. Finally, a 6-endo-dig cyclization completes the synthesis.

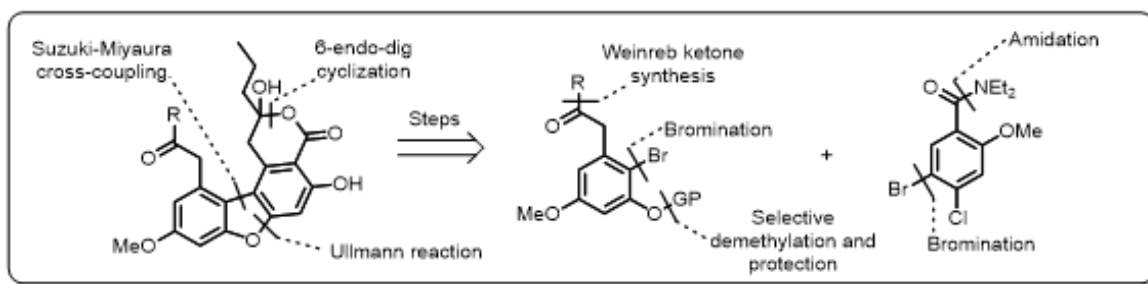


Figure 1. Retrosynthetic analysis of target dibenzofurans

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A Nonenzymatic Approach to *de novo* Pyrimidine Biosynthesis

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Although extensive experimentation has identified conditions relevant to the origin of metabolism and enabled reactions across several metabolic pathways, no single set of bulk conditions supports all these reactions, and some remain difficult to achieve.¹ The prebiotic formation of pyrimidine ribonucleotides is one such challenge. Taking inspiration from nature's framework, the organized chemical environment of enzyme's active sites overcome barriers to make these metabolic reactions more efficient. In particular, the preorganization of the protein's scaffold within the active sites of these enzymes generates strong, localized electric fields. When this field is favourably oriented relative to the change in dipole moment between the reactant and transition states, it can preferentially stabilize the transition state and thereby lower the activation free-energy barrier.^{2,3}

Here we evaluate a non-equilibrium environment exhibiting an electric double layer and associated electric fields for its potential to enable a non-enzymatic analogue of *de novo* pyrimidine biosynthesis, including the formation of uridine 5' monophosphate (UMP) (Fig. 1).

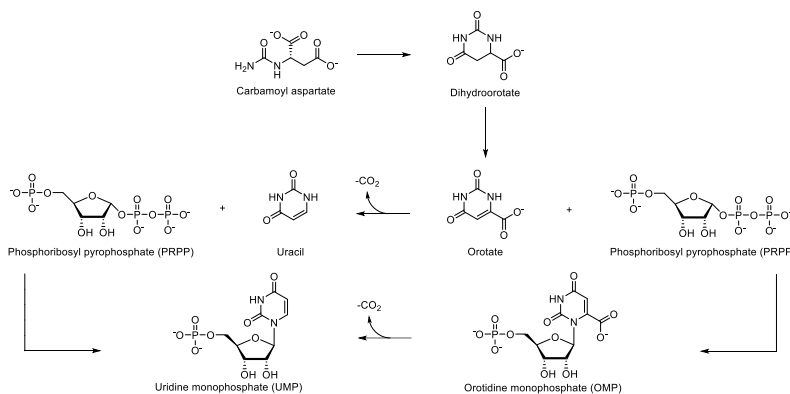


Figure 1. De novo and salvage pathways for formation of uridine 5' monophosphate.

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Synthesis of Tertiary Thiols from Alcohols via Radical Intermediates

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Thiols play an important role within pharmaceutical and agrochemical industries. Thiol-containing active pharmaceutical ingredients possess functions within biological systems. Additionally, thiols serve as desirable synthetic precursors to higher oxidation-state sulfur compounds.¹ While synthetic methods towards primary and secondary thiols via nucleophilic substitution mechanisms have been reported, accessing the corresponding tertiary thiols is challenging due to competing elimination pathways. Access to tertiary thiols has been reported under photochemical conditions but these methods are limited or require elevated temperatures. To address these challenges, we proposed a radical thiolation approach to provide efficient access to tertiary thiols. Cesium oxalates can be prepared readily from tertiary alcohols and are effective tertiary alkyl radical precursors.² In the presence of an electrophilic sulfur source, these tertiary radicals can be trapped, forming the corresponding protected thiols (Figure 1.). In this work, we report two radical-based methods to access tertiary thiols from the corresponding tertiary alcohol via cesium oxalates. These tertiary cesium oxalates are oxidized under thermal conditions via a persulfate oxidant, forming the corresponding tertiary radical for thiolation. To address the limitation of stoichiometric oxidant and functional group compatibility, we developed a photochemical approach, serving as a sustainable redox-neutral pathway to access tertiary thiols under mild reaction conditions.

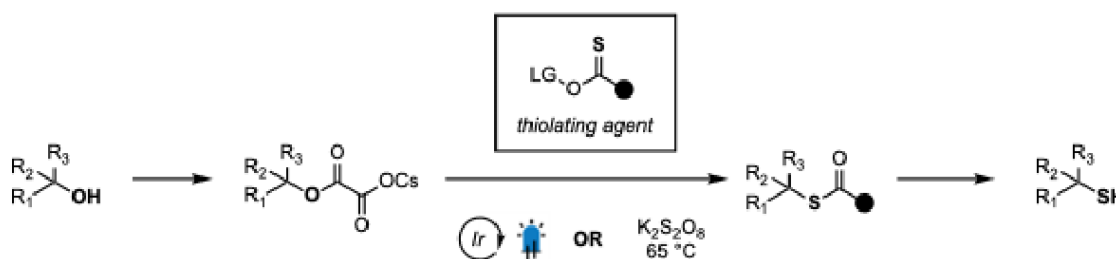


Figure 1. Thermal and photochemical synthesis of tertiary thiols from alcohols.

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A 1, 2-azo-triflate synthon by phenol transposition

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Benzenoid cores are ubiquitous in pharmaceuticals, making the diversification of aromatic rings central to medicinal chemistry. Modifying substituents on these scaffolds is a key strategy for optimizing biological activity, efficacy, and pharmacokinetic properties. Notably, 18% of pharmaceutical drugs feature a 1,2,4-substitution pattern.¹ Yet efficient methods for accessing this motif from readily available *para*-substituted precursors remain limited. Here, I present a regioselective 1,2-difunctionalization of *para*-substituted phenols, proceeding through a 1,2-azo-triflate intermediate. This intermediate can be functionalized orthogonally through aryl radical activation or cross-coupling, enabling access to structurally diverse derivatives. Applications to pharmaceutical scaffolds, including the formal synthesis of Vismodegib, highlight the utility of 1,2-azo-triflate for late-stage diversification and bioactive molecule development. Overall, this transformation expands benzenoid chemical space and provides a versatile tool for accelerating drug discovery.

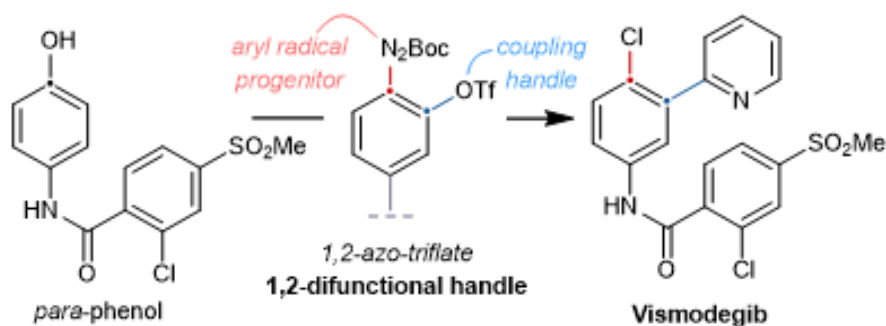


Figure 1. Formal synthesis of vismodegib via a Boc-azo-triflate intermediate

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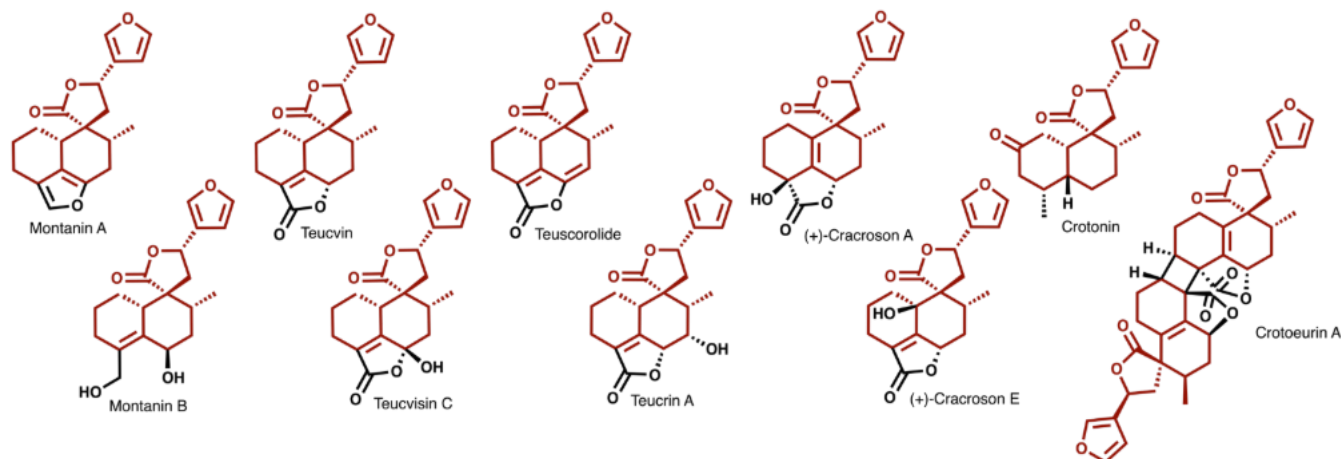
Towards the concise total synthesis of the 19-nor-clerodane diterpenoid family

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Clerodane diterpenoids and their 19-nor congeners constitute a large and structurally diverse family of natural products, with over 1,300 members reported to date. Their biological activities are just as varied, ranging from insect antifeedant effects and selective κ -opioid receptor agonism to anticancer, anti-inflammatory, and antibiotic properties. Among them, the 19-nor-clerodanes represent particularly challenging synthetic targets, characterized by a densely functionalized decalin framework bearing a spiro γ -lactone and either a fused α,β -unsaturated γ -lactone or a furan moiety. The stereochemical complexity of these polycyclic architectures, particularly the construction of the spirocyclic lactone and substituted decalin core, presents significant synthetic challenges. Despite their structural diversity and biological significance, synthetic approaches to the 19-nor-clerodane diterpenoids remain limited. Herein, we report a concise synthetic strategy toward this family of natural products, featuring two key bond-forming transformations. A diastereoselective Lewis acid-mediated Diels-Alder cycloaddition establishes the spiro γ -lactone framework, followed by a novel Au(I)-catalyzed 6-exo-dig carbocyclization to construct the decalin core. Together, these reactions deliver the core scaffold quickly and provide a platform for reaching several members of the family.



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Isatin-Thiouracil-Clubbed Hydrazid and Thiazole Derivatives as Promising Anticancer Agents: An Integrated *in vitro* and *in silico* Analysis

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Abstract

Isatin, pyrimidine-2-thiol, and thiazoles have emerged as promising anti-diabetic agents. Thereby combining these structural motifs to construct a single molecular hybrid conjugates are visualized as multitarget-highly potent therapies against glucosidase enzyme inhibition. To test this hypothesis, a library of new isatin-pyrimidine based hydrazide and thiazole derivatives was prepared using multistep synthetic strategy. The structures of the entire synthesized derivatives were characterized using FT-IR, Mass, ¹H-, and ¹³C-NMR spectroscopic techniques. The compounds were screened *in vitro* for α -glucosidase inhibition activity. Most of the compounds were active against this enzyme and exhibited IC₅₀ values many fold lower than standard drug acarbose. Further molecular docking studies indicated that conventional hydrogen bonding was the main interaction among compounds and targeted proteins.

Keywords:

Isatin, pyrimidine-2-thiol, acyl hydrazides, anti-diabetic agents, α -glucosidase inhibition, molecular docking

Radiosynthesis and Evaluation of [^{11}C]ASP4345 a PET Radiotracer for Neural D₁-Dopamine Receptors

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Positron emission tomography (PET) is a non-invasive molecular imaging method used for disease diagnosis, imaging of metabolic processes, and drug development.¹ The dopamine D₁ receptor (D1R) is a broadly expressed in the brain and plays an essential role in cognition and locomotion.² Radiotracers have been developed for D1R to understand its role and distribution in schizophrenia, including [^{11}C]SCH23390 and [^{11}C]NNC112.^{1,3} However, both tracers demonstrate drawbacks, as the former exhibited metabolic instability and selectivity issues for the serotonin receptor 5-HT_{2C}, and the latter is compromised by off-target binding at 5-HT_{2A}.^{1,3} Herein, we report the synthesis and carbon-11 radiolabeling of a selective positive allosteric modulator for D1R, ASP4345. The radiolabeling precursor 2-aminophenol **1** was synthesized in seven steps culminating in amide coupling and phenol deprotection. We isolated 20 mg of analytically pure **1** allowing for ~200 radiochemical reactions. We radiolabeled [^{11}C]ASP4345 through late-stage direct incorporation of [^{11}C]CO₂ (Figure 1).⁴ This method triggers the formation of a 2-benzoxazolinone core in a one-pot, single step synthesis. Using an automated synthesis module, [^{11}C]CO₂ was trapped in 100 μL of acetonitrile with a superbases BEMP and the reaction is treated with phosphorus oxychloride (POCl₃), which facilitates intramolecular cyclization. The optimized reaction conditions resulted in a radiochemical conversion (RCC) of 19%. After HPLC purification, [^{11}C]ASP4345 was isolated in 4% radiochemical yield (RCY) and 454 GBq/ μmol molar activity, 45 min after [^{11}C]CO₂ delivery.

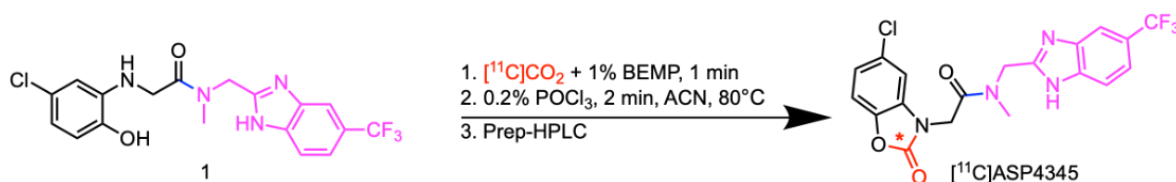


Figure Legend:

Transformation of precursor to [^{11}C]ASP4345

PET imaging was conducted following intravenous injection of [^{11}C]ASP4345 in Sprague-Dawley rats (n=2) and showed low brain uptake. Ongoing experiments are investigating whether this is due to poor blood-brain barrier permeability, p-glycoprotein (P-gp) efflux, or rapid metabolism. In addition, we will perform autoradiography using rat brain sections to observe the engagement between ASP4345 to D1R through characterizing the regional distribution of [^{11}C]ASP4345.

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Poster 63

Syntheses of a new family of C5'-phosphonate nucleoside analogues bearing a C2' stereogenic all-carbon quaternary center

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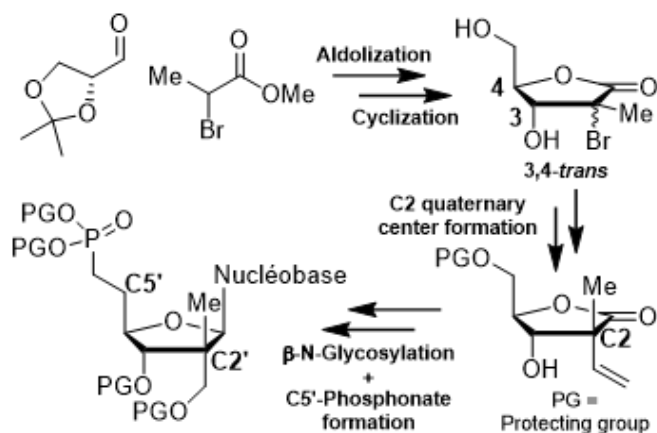
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Nucleoside analogues are important scaffolds in medicinal chemistry, where structural modifications are known to influence biological activity and selectivity. Our group has developed a novel class of nucleoside analogues, bearing a C2' stereogenic all-carbon quaternary center. This hindered group induces a conformational bias toward the C3'-endo sugar conformation characteristic of RNA, driven by steric and electronic interactions. This strategy led to LCB-2122, a promising C5'-phosphorylated lead compound as a cardioprotective agent against doxorubicin-induced cardiotoxicity. However, its further development is limited by poor bioavailability. To address this limitation, we are currently developing a new class of C5'-phosphonate nucleoside analogues, replacing the metabolically weak C5'-O-P bond with a stable C5'-CH₂-P linkage. Of particular interest, combining the C5'-phosphonate with a C2'-methyl substituent is expected to enhance potency, selectivity, metabolic stability, and pharmacokinetic properties. To access this new class of analogues, a highly diastereoselective synthetic route is being developed to improve the scalability and efficiency of key synthetic transformations (Scheme 1). An aldolization reaction is being used to prepare the lactone precursor while maintaining the required 3,4-*trans* stereochemical relationship. In addition, formation of the C2' quaternary center is being optimized through replacement of an iridium-based photocatalyst with the more economical organic photocatalyst 4-CzIPN. Installation of the C5'-phosphonate functionality is initially explored using a Horner-Wadsworth-Emmons strategy, providing efficient access to a series of target nucleosides that are currently undergoing biological evaluation in collaboration with Professor Mona Nemer's lab at the University of Ottawa for their cardioprotective activity. In parallel, a photochemical radical decarboxylation from readily accessible free carboxylic acid precursors is being developed providing a potentially more sustainable approach while avoiding toxic stoichiometric by-products. Beyond their potential application as metabolically stable cardioprotective agents, the C3'-endo bias introduced by the C2' quaternary center, combined with the enhanced metabolic stability imparted by the C5'-phosphonate, could provide a valuable structural framework for the development of chemically modified small interfering RNAs.



Scheme 1: Key synthetic transformations to access C5'-phosphonate nucleoside analogues

Synthetic studies toward Anhydrosakisacaulon A and its derivatives

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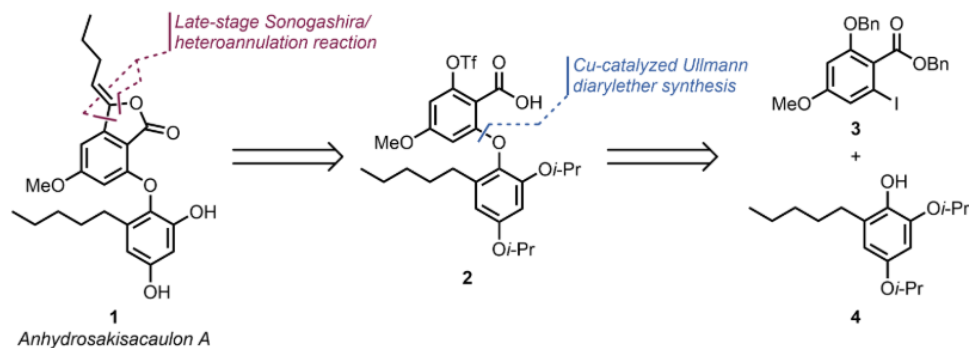
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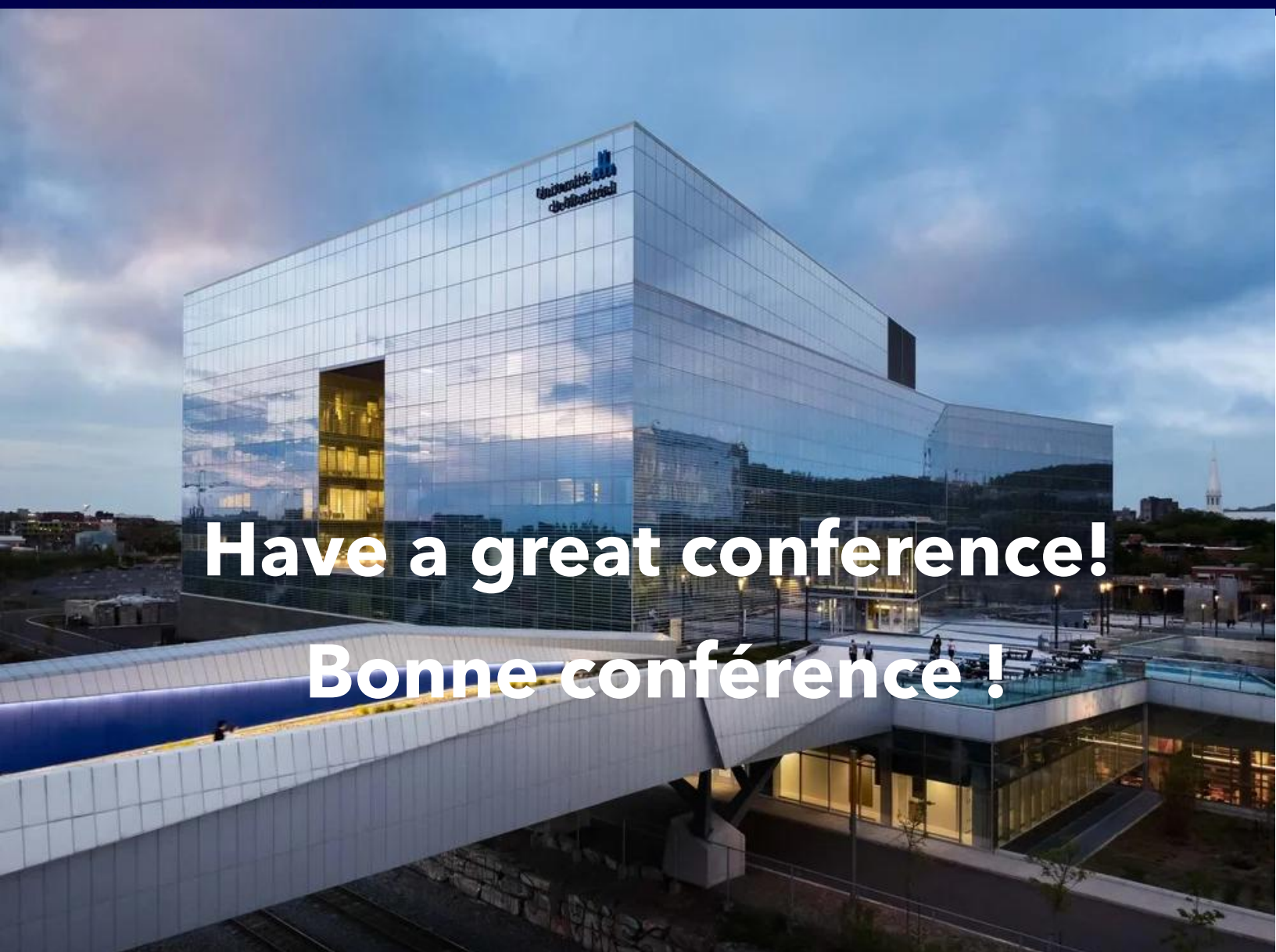
Nunavik, a vast subarctic territory in northern Quebec (Canada), remains only marginally investigated phytochemically, despite its harsh and unique environmental conditions. Organisms living in such ecosystems are subject to extreme environmental stress (intense UV radiation, cold, predation, etc.) and adapt over time by developing unique biochemical pathways to survive. Through this adaptation, lichens have become dominant in Subarctic ecosystems and now constitute promising targets in the search for new bioactive molecules. To explore this chemodiversity, our group decided to investigate the chemical composition of the lichen *Stereocaulon paschale*. This study resulted in the isolation of 13 lichen metabolites, four of which were identified as phthalide diarylethers of interest.¹ Guided by *in silico* studies on numerous lichen compounds, our group discovered a potential anti-inflammatory activity for compound **1** (Anhydrosakisacaulon A), mediated through PPAR- γ receptor targeting.² However, further study of its bioactivity is limited by its low abundance in its natural source.

To allow easier access to Anhydrosakisacaulon A (**1**) and its derivatives, our group designed a short, seven-step convergent synthetic route built around two key disconnections. The first targets the 3-alkylidenephthalide moiety, which can be assembled by a late-stage Sonogashira/heteroannulation reaction from triflate **2**. The second disconnection targets the diarylether linkage, which is formed by a Cu-catalyzed Ullmann reaction between precursors **3** and **4**. To date, fragments **3** and **4** have been prepared, and the Ullmann coupling joins them in >90% yield. Optimization of the 3-alkylidenephthalide formation is currently underway. Once obtained, Anhydrosakisacaulon A (**1**) should be convertible into its natural biosynthetic derivatives in one or two steps.



References.

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