Empowering Women in Organic Chemistry Conference 2024

Poster Abstract Booklet

Table of Contents

Information for Attendees

The posters will be displayed on Friday, June 21, 2024 from 4:30–6:00pm. Presenters for posters 1–40 will be available at their posters from 4:30–5:15pm. Presenters for posters 41–79 will be available at their posters from 5:15–6:00pm.

On the poster abstracts pages that follow, the poster number can be found in the upper left corner.

Please do not photograph or record the poster presentations, unless you have the explicit permission of the presenter.

List of Posters for Quick Reference

Poster Number	Presenting Author	Poster Title
1	Sa-adatu Abdullai	Design and Synthesis of δ-Lactone derivatives: Exploring the therapeutic potential of a versatile scaffold
2	Medina Afandiyeva	Addressing Challenges in Nickel-Catalyzed Cross-Coupling with Methyl Benzoate through Mechanism-Guided Catalyst Design
3	Melike Akoglu	Targeted Degradation Of Indoleamine 2,3-Dioxygenase 1 (Ido1) And Tryptophan 2,3-Dioxygenase (Tdo) As A Novel Anti-Cancer Strategy
4	Johanna Asante, Caroline Casey	The Development Of Disinfectant Bisqacs Based On A Bolaamphiphilic Architecture
5	Kaitlyn Breault	Total Synthesis Of Corylfiol A And Related Isolfavone Natural Products
6	Jamie L. Breunig	Total Synthesis Of Heterocycle Containing Natural Products
7	Kelly Burchell-Reyes	Asymmetric Reduction Of Prochiral A-Cf3 And A-Sf5 Ketones
8	Sarah R. Buzsak	Fe/Thiol Cooperative Hat Olefin Hydrogenation: Mechanistic Insights To Inform Enantioselective Catalysis
9	Yun-Pu Chang	Discovery and Development of Chiral Silanol Ligands for Enantioselective Catalysis
10	Madeline Clerici	Reduction of highly conjugated alkenes using photochemical activation of formate
11	Rebecca C. Colandrea	Stereospecific Nickel-Catalyzed Borylation of Tertiary Benzylic Carboxylates
12	Jordie Compton	High-Throughput Experimentation at J&J Innovative Medicine:A Chemistry Capability to Accelerate the Discovery Portfolio
13	Amanda J. Consylman	AI-Assisted Design and Laboratory Synthesis of Novel Disinfectant Amphiphiles
14	Marissa G. Coschigano	Borane-Catalyzed Postpolymerization Hydrosilylation Of Poly(Cyclosilane)S
15	Soumyadipa Das	Studies on alkane dehydrogenation by a 'NCN' type pincer iridium complex
16	Bethany DeMuynck	Iron-Mediated Carbon Atom Insertion To Access 3-Substituted Quinolines Via Trichloromethyl Reagents
17	Simran Dhingra	Synthesis Of Novel Near-IR Azabodipy-Tki-Peptide Bioconjugates And Investigation Of Their Potential In Bioimaging And Photodynamic Therapy
18	Jaika Doerfler	Atroposelective Brønsted Acid-Catalyzed Photocyclization to Access Chiral N-Aryl Quinolones with Low Rotational Barriers
19	Kalina Doytchinova-Weil, Christina Stauffer	Process Chemistry Development At Fmc
20	Justine A. Drappeau	Site-Selective C–H Thiolation as an Enabling Tool for Late-Stage C–H Diversification
21	Emily Du	Modular Iridium Polypyridyl Complexes for Selective C–H Abstraction via Proton-Coupled Electron Transfer
22	Alana D. Duke	Photoexcited Nitroarenes As Tunable Reagents For Methylene Deletion Via Decarboxylative Oxidation
23	Daliah Farajat	Shaking Up the Friedländer Reaction: Rapid, Scalable Mechanochemical Synthesis of Polyaryl-substituted Quinolines

Poster Number	Presenting Author	Poster Title
24	Bria Garcia	Cascade Cyclizations Of Alkene-Tethered Alkylpyridinium Salts
25	Collette T. Gordon	Synthesis And Fabrication Of Conductive Polymers For Environmental Sensing Applications
26	Juana Goulart Stollmaier	Design, Synthesis And Structural Evaluation Of Thiol-Based Inhibitors Of Hdac10
27	Eileen M. Hoang, Naoko Ichiishi, Austin T. Kelly, Xiao Li, Alexis Charaudeau, Alan H. Cherney	High-Throughput Innovation Technologies (HIT) For Late Synthetics
28	Irina Honin	Characterization Of The Binding Kinetics, Anticancer Activity, And Photocaging Properties Of 2-Hydroxy-Benzamides As Selective Inhibitors Of Hdac1 And 2
29	Bianca Imbriaco	Contra-Thermodynamic, Asymmetric Olefin Isomerization
30	Anju Treesa Jose	Palladium Catalyzed Arylation Of Secondary A-Alkoxytricyclohexylstannanes
31	Jyoti Nandi	Design, Synthesis, And Biological Evaluation Of 5-Sulfonyl Thiadiazoles As Control Agents For Asian Soybean Rust
32	Elya Kandahari	Mechanistic Investigations Of Oxoammonium-Catalyzed Hydride Transfer
33	Kaitlyn T. Keasler	Handling Fluorinated Gases As Solid Reagents Using Metal–Organic Frameworks
34	Annemarie A Lee	Characterization Of Chain Reactions in Photochemistry
35	Julia J. Lee	Design, Synthesis, And Evaluation Of Subtype Selective Pparalpha Agonists As Leads For Diabetic Retinopathy
36	Roxanne Lessard	Novel Fluorinated Chiral Auxiliary for the Synthesis of Stereogenic Tertiary Alcohols
37	Yetong Lin	Towards Control Of LMCT Catalysis By Rational Incorporation Of Chelating Ligands On Heteroleptic Titanium Complexes
38	Zheng Sonia Lin	Investigations On The Competition Between Nucleophilic Aromatic Substitution And Metal-Catalyzed Cross-Coupling Reactions In Heterocyclic Aromatic Systems
39	Ashley Lojko,	Functionalization Of Aliphatic C-H Bonds Via LMCT-Mediated Radical HAT From Bench-Stable Titanium Complexes
40	Windsor Lundy	Enantioselective Negishi Arylation Of Amino Acids
41	Vishala Maharaj	Photodecarboxylative Amination Of Carboxylic Acids With Diazirines
42	Jocelyn Marden	The PET Imaging Study Of (2S,4R)-4-18F-Fluoro-L-Glutamine In Two Rat Inflammatory Models
43	Sabina J. Maurer	Cryptic Sulfotransferases For Aziridine Formation
44	Pankti Mehta	Organophotocatalyzed Decarboxylative Fluorination Of Poly(Acrylic Acid)
45	Katrin Nekipelov	Commercial Heparins And Synthetic Derivatives As Potential Immunomodulators In An In Vitro Metastatic Context
46	Eryn Nelson	Regioconvergent Nucleophilic Substitutions With Morita-Baylis-Hillman Fluorides
47	Cody H. Ng	Development Of A Visible-Light-Mediated Aza Paternó-Büchi Reaction Using Sulfonylimines
48	Khue N. M. Nguyen	Harnessing Radicals: For Homolytic Aromatic Substitution And Cyclopropanation

Poster Number	Presenting Author	Poster Title
49	Geneviève F. O'Keefe	Towards Enantioselective Hemiboronic Acid Catalyzed Direct Monophosphorylation Of Polyols
50	Skylar K. Osler	Mechanochemical Reactivity Of A Fluorenyl Naphthopyran Mechanophore
51	Yetunde Oyesakin	Design, Synthesis, And Evaluation Of Covalent Cada Analogues As Potent Tlr4 Downmodulator For The Treatment Of Opioid Use Disorder
52	Pooja B. Pandya	Synthesis Of Diisonitrile Chalkophore Natural Products And Analogues To Elucidate Their Functions In M. Tuberculosis
53	Diana Rachii	Bushy-Tailed Qacs And Qpcs: The Development Of Multicationic Quaternary Ammonium And Phosphonium Compounds With A High Degree Of Alkyl Chain Substitution
54	Abbey N. Ragan	Synthesis, Structure, And Reactivity Of Compounds Bearing The SF5 Group And Its Congeners
55	Emma K. Ralph	Cyclopropanation Of Unactivated Alkenes With Nonstabilized Carbenes
56	Kasmier Reece	Visible Light Mediated Photocatalytic Reduction Of Aryl Sulfonates
57	Asha Reghuvaran Santha	Copper-Controlled Stereodivergent Stille Cross-Coupling Reactions
58	Danielle Rosenberger	Expansion Of LpxC Inhibitors Into The UDP Binding Site
59	Josiah Sanchez	Chemical Synthesis Of Linker To Small Molecule Bioconjugate To Enhance Surface Retention To Cells
60	Stella Rose Schneeberg	Synthesis Of Small-Molecule PAC1R Antagonists To Treat Chronic Pain And Anxiety
61	Grace E. Scofield	A Predictive Model For The Thiol Reactivity Of A-Methylene–Γ-Lactams Using Heteroarenes As Tuning Elements
62	Cassandra A. Sedler	Direct Hock Rearrangement Of Acyclic Alcohols Via Hypervalent I(III) Umpolung Reactivity
63	Meenakshi Sharma	Nitrene-Transfer Chemistry To C–H And C=C Bonds Mediated By Triangular Coinage Metal Platforms Supported By Triply Bridging Pnictogen Elements Sb(III), Bi(III) And An Arene Platform
64	Sandra M. Simmons	Synthesis Of Prochiral Substrates And Investigations Of Chiral Resolution Through Biocatalytic Oxidation
65	Lara Skibbie	Novel PPCS Inhibitors To Prevent Coa Biosynthesis In Drug Resistant Pathogens
66	Olivia Steiner	Activation Of Dithiolopyrrolone Antibiotics By Bacteria
67	Alexis M. Stoorza	The Total Synthesis Of Picrasidine C: A Subtype Selective PPAR Agonist
68	Elizabeth C. Swift	Synthesis Of Highly Functionalized 4-Iodo-7-Azaindazoles Via Condensation/Diels–Alder/Retro-Diels–Alder Cyclization Of Iodoalkynones And 2-Hydrazineylpyrimidines
69	Madelaine P. Thorpe	The Backbone Constitution Drives Passive Permeability Independent of Side Chains in Depsipeptide and Peptide Macrocycles Inspired by ent-Verticilide
70	Aneta Turlik	Unified Approach To Deamination And Deoxygenation Through Isonitrile Hydrodecyanation: Computational And Experimental Studies
71	Linda Ung	Elucidating The Influence Of Remote Stereocenters On Donor/Donor C–H Insertions To Facilitate The Asymmetric Assembly Of Cadinane Natural Products

Poster Number	Presenting Author	Poster Title
72	Oniya Valencia	The Development of a 1,2-Aminoarylation Reaction via Photocatalytic Aryl Radical Generation
73	Katherine L. Verboom	Progress Towards The Total Synthesis Of Gladiolin
74	Autumn Vossler	Synthesis And Derivatization Of Vancomycin Linear Heptapeptide
75	Eleanor Wong	Synthesis And Evaluation Of Cannabigerol-Inspired Antimicrobial Compounds
76	Abigale Wood	Targeting The mRNA Thiamine Pyrophosphate Riboswitch With Small Molecules
77	Jia Yang	Biosynthetic And Structure-Activity Investigations On Translation-Inhibiting Cyclic Peptide Natural Products
78	Cindy Zhang	Thioquinazolinones As Antituberculosis Agents Targeting Phosphopanthethienyl Transferase
79	Patrycia Zybura	Stereocontrolled Synthesis Of Functionalized Tricyclic O-Heterocycles

Poster Abstracts

Poster 1

Design and Synthesis of δ-Lactone derivatives: Exploring the therapeutic potential of a versatile scaffold.

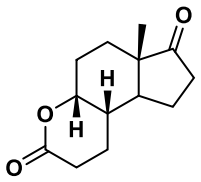
Sa-adatu Abdullai, Michelle Hawk, Dr. Stephen Bergmeier, Dr. Nigel Priestley*

Department of Chemistry and Biochemistry, Ohio University, Athens, OH, USA.

*Department of Chemistry and Biochemistry, University of Montana, Missoula, MT, USA**

Sa902119@ohio.edu.

Small molecules libraries have played a major role in drug discovery studies and lead compound identification. These libraries are often synthesized from simple building blocks, frequently featuring analogous of two-dimensional structures, distinguished by peripheral functional groups and limited structural diversity among molecules. An approach to generate more structurally diverse libraries includes the use of small natural product molecules. The complexity and structural diversity with natural product backbone may increase the chance of identifying lead compounds which can be further developed.[1,2] In this work we focus our attention on the synthesis of different derivatives of δ-lactone. δ-Lactone is a tricyclic compound with a steroidal backbone produced through fermentation of phytosterols. A series of compounds have been synthesized utilizing the δ-lactone backbone through modification of the cyclopentanone and valero lactone units. Important steps in our synthesis include the aminolysis reaction, ring closing metathesis reaction and 1,3-dipolar cycloaddition.



δ-Lactone

(1) Truax, N. J.; Romo, D. Bridging the Gap between Natural Product Synthesis and Drug Discovery. *Nat. Prod. Rep.* **2020**, *37* (11), 1436–1453. https://doi.org/10.1039/D0NP00048E.

(2) DeCorte, B. L. Underexplored Opportunities for Natural Products in Drug Discovery: Miniperspective. *J. Med. Chem.* **2016**, *59* (20), 9295–9304. https://doi.org/10.1021/acs.jmedchem.6b00473.

Poster 2

Addressing Challenges in Nickel-Catalyzed Cross-Coupling with Methyl Benzoate through Mechanism-Guided Catalyst Design

Medina Afandiyeva, Abhishek Kadam, C. Rose Kennedy*

Department of Chemistry, University of Rochester, Rochester, New York, USA

mafandiy@UR.Rochester.edu

Transition metal-catalyzed cross-coupling reactions are widely used in industry and academia. In contrast with traditionally used palladium catalysts, electropositive nickel complexes enable activation of the more polar acyl C(sp^2)–N and C(sp^2)–O bonds found in abundant and less reactive amides and esters. Current methodologies for Ni-catalyzed cross-coupling often require high pre-catalyst loading and elevated reaction temperatures. To design catalysts that address these limitations, a detailed mechanistic understanding of Ni-catalyzed transformations through the identification of catalytically relevant organometallic intermediates is required. In this talk, I will describe a suite of NHC-bound bidentate [Ni] complexes and the role of a pyridine co-ligand in a cross-coupling reaction between methyl benzoate and aniline. Mechanistic experiments provide evidence for unusual activation of the Ni(0) pre-catalyst and formation of a Ni(II) catalyst resting state. Current work on developing a synthetic approach toward an air-stable Ni(II) pre-catalyst will be described highlighting the importance of organometallic chemistry for reaction development.

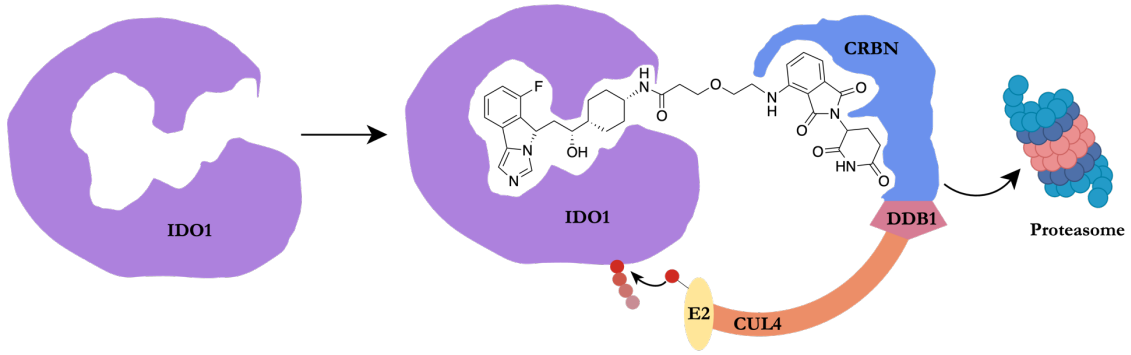
Poster 3

TARGETED DEGRADATION OF INDOLEAMINE 2,3-DIOXYGENASE 1 (IDO1) AND TRYPTOPHAN 2,3-DIOXYGENASE (TDO) AS A NOVEL ANTI-CANCER STRATEGY

Melike Akoglu, Alyssa Pollard, Jinnette Tolentino-Collado, Franchesca Abou Said, Purnima Dela, Bidhata Tripathi, Peter J. Tonge*

Department of Chemistry, Stony Brook University, John S. Toll Drive, Stony Brook, New York 11794-3400, United States
melike.akoglu@stonybrook.edu

The ability to evade the host immune system is a hallmark of cancer and a major contributor to tumor growth and progression. Immunotherapy is a promising strategy for treating cancer that works by stimulating the host immune system. However, many cancers such as breast cancer do not respond to current immunotherapies due to the existence of multiple pathways for tumor immunosuppression and resistance, such as enhanced tryptophan (Trp) catabolism. Indoleamine 2,3-dioxygenase (IDO) and tryptophan 2,3-dioxygenase (TDO) catalyze the rate-limiting step of tryptophan catabolism and have been targets of many medicinal chemistry programs. Two inhibitors, epacadostat and navoximod, have been used successfully as monotherapies and in combination with other therapeutics in phase I/II trials. However, phase III trials were unsuccessful giving rise to concerns about the future of these inhibitors in the clinic. The goal of the present work is to develop and implement two series of proteolysis targeting chimeras (PROTACs) for the degradation of IDO1 and TDO via hijacking of the ubiquitin/proteasome system through E3 ligase recruitment to the target protein to combat some of the issues with these drugs. The event-driven pharmacology catalyzed by degradation of IDO1 is hypothesized to be a more effective therapeutic strategy than the occupancy-driven pharmacology resulting from IDO1 inhibition. Thus far, we have synthesized a small library of IDO1 and IDO1/TDO PROTACs, and we are currently testing the efficacy of these drugs using Western Blots.



Poster 4

THE DEVELOPMENT OF DISINFECTANT BISQACS BASED ON A BOLAAMPHIPHILIC ARCHITECTURE

Johanna Asante, Caroline Casey, Dr. Kevin P.C. Minbiole*

Department of Chemistry, Villanova University, 800 E Lancaster Ave, Villanova, USA.
jasante@villanova.edu, ccasey19@villanova.edu.

Quaternary ammonium compounds (QACs) use their amphiphilic structure to force bacterial cell lysis. Most commercially utilized QACs have a common architectural theme, with an ammonium center and a non-polar tail. However, some QACs such as chlorhexidine use a bolaamphiphilic architecture, featuring two cationic centers at the molecule's periphery, with a non-polar region connecting them. As such, these quaternary ammonium compounds (QACs) have shown the promise to span the bilayer of bacterial cell membranes and cause subsequent disruption, thereby halting the growth of certain pathogenic bacteria. Our efforts are focused on developing novel bolaamphiphiles, featuring flexibility of linker lengths, alkyl tails, relative substituent positioning, and cationic residues.

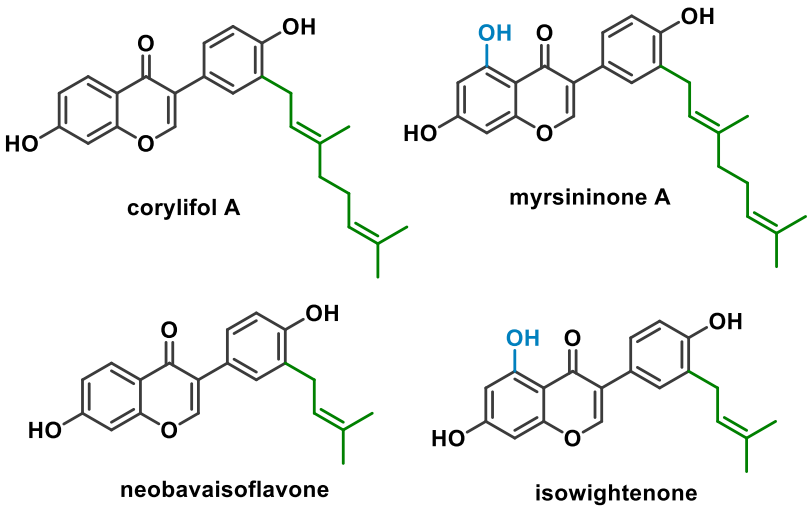
Poster 5

TOTAL SYNTHESIS OF CORYLFIOL A AND RELATED ISOLFAVONE NATURAL PRODUCTS

Kaitlyn Breault, Lauren Irwin, Jakob Magolan*

Department of Chemistry and Chemical Biology, McMaster University, Hamilton, Ontario, Canada
breaultk@mcmaster.ca

Prenylated phenols constitute a prominent class of fungi and plant-derived natural product that demonstrate a multitude of biological effects. In general, relative to their corresponding non-prenylated parent compound, phenols with a -prenyl, -geranyl, or -farnesyl substituents tend to show enhanced bioactivities, potentially due improved cell permeation associated with greater lipophilicity. Four structurally related prenylated phenolic natural products: corylifol A, neobavaisoflavone, myrisininone A, and isowightenone are isolated from distinct fungal or plant species and associated with diverse biological profiles. These natural products are of interest to investigate their biomedical potential, as isoflavones and other prenylated flavonoids exhibit excellent antioxidant and anticancer activity. Here we use these structurally related natural products as synthetic targets to showcase a new synthetic methodology for regioselective *ortho*-allylation of phenols mediated by acidic alumina. Our general approach to these compounds involves alumina-mediated prenylation of phenolic boronic esters followed by a Suzuki cross-coupling.



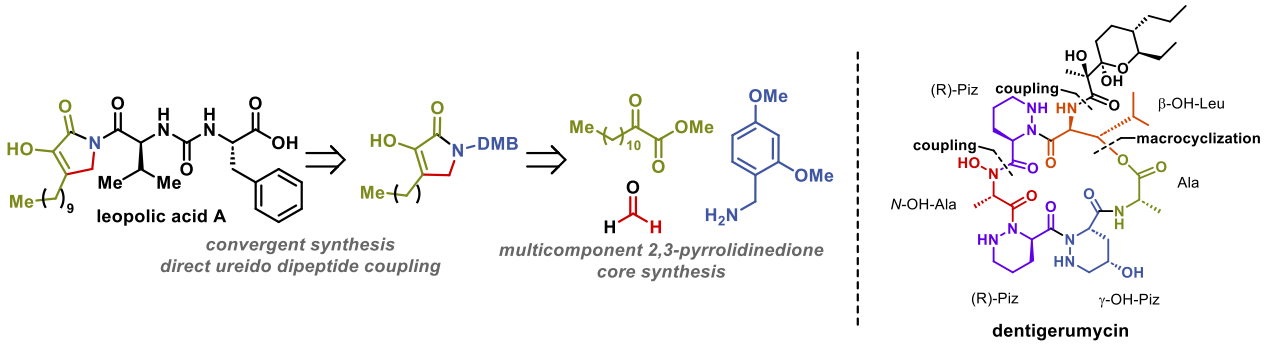
Poster 6

TOTAL SYNTHESIS OF HETEROCYCLE CONTAINING NATURAL PRODUCTS

Jamie L. Breunig, M. Alejandro Valdes-Pena, Andrew W. Ratchford, and Joshua G. Pierce*

Department of Chemistry, Comparative Medicine Institute, and Integrative Sciences Initiative, NC State University, Raleigh, North Carolina 27695, USA
jlbreuni@ncsu.edu

Antimicrobial resistance is an ongoing issue, especially with a lack of new antimicrobial scaffolds. Natural products serve as a promising source of new biologically active molecules, providing access to new antimicrobial scaffolds. Leopolic acid A, a terrestrial natural product, contains a 2,3-pyrrolidinedione headgroup bearing an aliphatic chain appended to a urea containing dipeptide. A convergent 9-step route of leopolic acid A and a series of targeted analogues will be presented.[1] The designed compounds allowed for modification in the 4- and 5-position around the 2,3-pyrrolidinedione core of leopolic acid A and the incorporation of non-natural ureido dipeptide moieties. Leopolic acid A and analogue's antimicrobial (MIC) and antibiofilm (MBEC) potency was evaluated. Leopolic acid A displayed modest activity (32 *μ*g/mL) against MRSA, while most analogues had slightly improved activity (8-16 *μ*g/mL). Several analogues showed MBEC:MIC ratio ~1, showing potential as antibiofilm agents. In addition, the efforts towards the total synthesis of dentigerumycin, a cyclic desipeptide consisting of a polyketide derived side chain and highly modified amino acids displaying modest antifungal activity will be presented.



[1] Jamie L. Breunig, M. Alejandro Valdes-Pena, Andrew W. Ratchford, and Joshua G. Pierce*ACS Bio & Med Chem Au* 0, *0*, pp

Poster 7

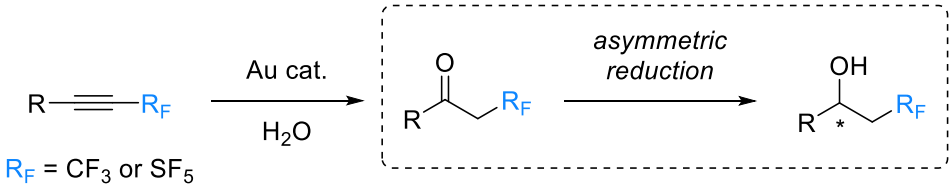
ASYMMETRIC REDUCTION OF PROCHIRAL α-CF_3 AND α-SF_5 KETONES

Kelly Burchell-Reyes, Chloé Depoumps, Jean-François Paquin*

CCVC, PROTEO, Département de chimie, Université Laval, 1045 Avenue de la Médicine, Québec, Canada
kelly.burchell-reyes.1@ulaval.ca

A variety of CF_3- and SF_5-containing compounds have found applications in fields ranging from drug development [1, 2, 3] to material sciences[4]. Given the relevance of chirality in bioactive molecules[5], it is topical to study the synthesis towards novel CF_3- and SF_5-motifs.

Our group has previously described a regioselective gold-catalyzed hydration to efficiently obtain α-CF_3 and α-SF_5 ketones from their corresponding alkynes[6]. We are thus developing enantioselective transformations of these prochiral α-CF_3 and α-SF_5 ketones (Scheme 1). We initially focused on asymmetric reductions to obtain β-CF_3 and β-SF_5 alcohols using tailored reaction conditions. This presentation will provide an overview of our initial results.



Scheme 1. Asymmetric reduction of α-CF_3 and α-SF_5 ketones.

---

[1] Sowaileh, M. F.; Hazlitt, R. A.; Colby, D. A. *ChemMedChem* **2017**, *12*, 1481.

[2] Sani, M.; Zanda, M. *Synthesis* **2022**, *54*, 4184.

[3] Kordzexhadian, R.; Li, B.-Y.; Zogu, A.; Demaerel, J.; De Borggraeve, W. M.; Ismalaj, E. *Chem. Eur. J*. **2022**, *28*, e202201491.

[4] Chan, J. M. W. *J. Mater. Chem. C* **2019**, *7*, 12822.

[5] Calcaterra, A.; D'Acquarica, I. *J. Pharm. Biomed. Anal.* **2018**, *147*, 323.

[6] Cloutier, M.; Roudias, M.; Paquin, J.-F. *Org. Lett*. **2019**, *21*, 3866.

Poster 8

FE/THIOL COOPERATIVE HAT OLEFIN HYDROGENATION: MECHANISTIC INSIGHTS TO INFORM ENANTIOSELECTIVE CATALYSIS

Sarah R. Buzsaki[†], Savannah M. Mason[‡], Julian G. West*[†], Scott J. Miller*[‡], Patrick L. Holland*[‡]

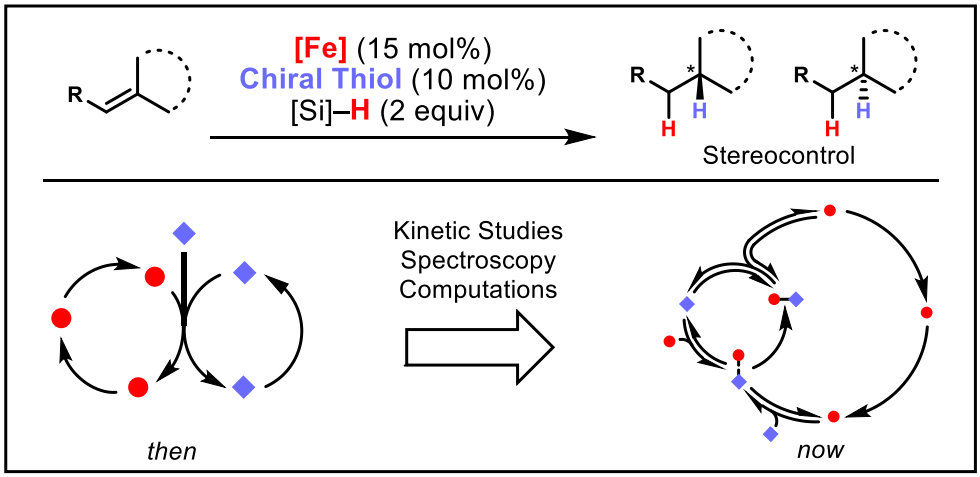
[†] *Department of Chemistry, Rice University, P.O. Box 1892, Houston, TX*

[‡] *Department of Chemistry, Yale University, P.O. Box 208107, New Haven, CT*

Department of Chemistry, Rice University, P.O. Box 1892, Houston, TX

srb12@rice.edu

The hydrogenation of alkenes catalyzed by transition metal complexes is among the most impactful reactions in organic chemistry, with applications in pharmaceutical and agrochemical industries. Classical strategies for controlling the resulting tetrahedral centers via asymmetric hydrogenation rely on expensive precious metal catalysts, carefully designed chiral ligands, and sensitive organometallic mechanisms designed for activated alkenes. Here we show how our asymmetric hydrogenation system[1] builds off our previously developed racemic cooperative Hydrogen Atom Transfer (cHAT) system, dually catalytic in earth-abundant iron and a thiol source. Under mild conditions, we chemoselectively hydrogenate unactivated alkenes in good yields via a radical mechanism. The separated catalytic cycles invite the introduction of chiral reagents to afford enantioselectivity, explored here through bio-inspired chiral thiols. Insights gained from further study of the racemic reaction's mechanism are productively applied to the development of the enantioselective method.



[1] Buzsaki, S. R.; Mason, S. M.; Kattamuri, P. V.; Serviano, J. M. I.; Rodriguez, D. N.; Wilson, C. V.; Hood, D. M.; Ellefsen, J. D.; Lu, Y.-C.; Kan, J.; West, J. G.; Miller, S. J.; Holland, P. L. *Submitted*. **2023.** (Available on Chemrxiv 10.26434/chemrxiv-2023-b9zdf)

Poster 9

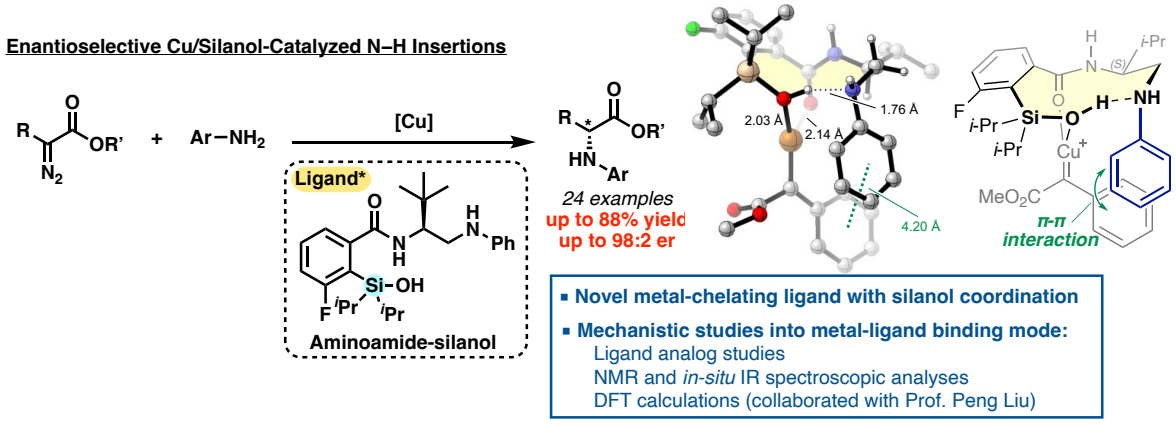
DISCOVERY AND DEVELOPMENT OF CHIRAL SILANOL LIGANDS FOR ENANTIOSELECTIVE CATALYSIS

Yun-Pu Chang,[†] Kevin Blanco-Herrero,[†] Turki, M. Alturaifi,[‡] Peng Liu,[‡] and Annaliese K. Franz*[†]

[†]*Department of Chemistry, University of California−Davis*
[‡]*Department of Chemistry, University of Pittsburgh*

Department of Chemistry, University of California−Davis, Davis, CA, USA
ypchang@ucdavis.edu

Silanol compounds contain a unique Si−OH bond with opportunities to design new ligands for asymmetric catalysis. Although simple alkyl silanols have been previously utilized as ancillary ligands for metal-catalyzed transformations, their application has been relatively underexplored in enantioselective catalysis due to challenges in synthesis and limited investigations of functionalized silanol-containing ligands. Using silanol-containing ligands for asymmetric catalysis offers advantages, including enhancement of reactivity on the metal center and better steric modulation. We have synthesized several novel chiral metal-chelating ligands combining chiral aminoamide and silanol motifs. The catalytic properties of the silanol ligands have been demonstrated through an enantioselective N−H insertion, a method that has received constant attention as an important method for synthesizing chiral amine building blocks. Using a copper salt with a chiral aminoamide-silanol ligand, we have obtained enantioenriched unnatural amino acid derivatives with up to 98:2 enantiomeric ratio and up to 88% yield. This work represents the first case of a transition-metal catalyzed enantioselective reaction induced by chiral silanol-containing ligands. Our investigations into metal-ligand interactions include DFT calculations, ligand analogs, NMR, and X-ray structure analyses, which support the formation of an H-bond stabilized silanol-chelating copper carbenoid complex.



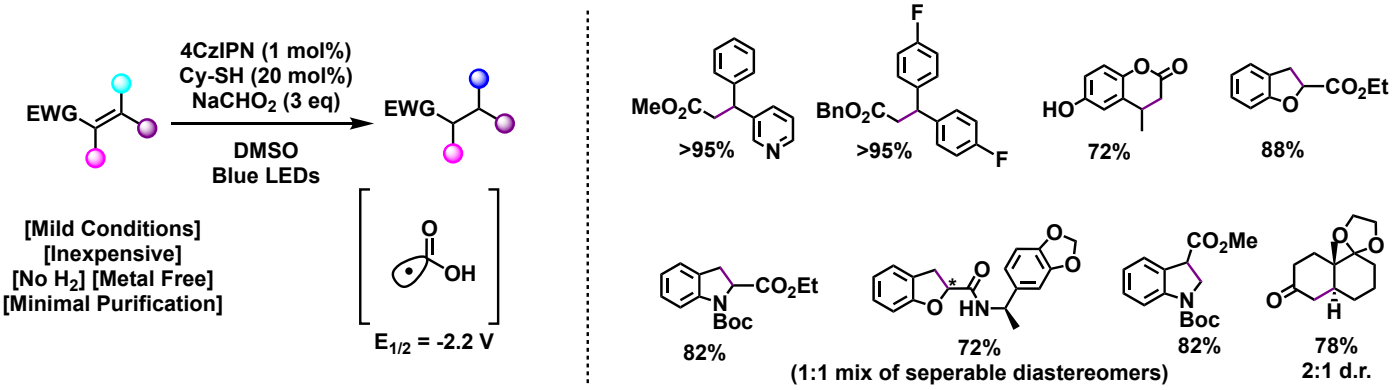
Poster 10

REDUCTION OF HIGHLY CONJUGATED ALKENES USING PHOTOCHEMICAL ACTIVATION OF FORMATE

Madeline Clerici, Carter Brzezinski, Andrew Leblanc, William M. Wuest

Department of Chemistry, Emory University, 1515 Dickey Drive, Atlanta, GA 30322
maddie.clerici@emory.edu

The hydrogenation of alkenes is a laborious and dangerous reaction, often requiring flammable hydrogen gas and precious metals such as Pd/C. Additionally, the hydrogenation of highly conjugated alkenes is even more difficult, typically requiring higher pressures of H_2 and specific reaction apparatus capable of handling such pressure. To address some of these limitations, we developed a photochemical reduction capable of reducing highly conjugated alkenes that is significantly safer and operationally simpler than traditional heterogeneous hydrogenation reactions. Notably, this reduction can also dearomatize activated indoles and benzofurans to the respective indolines and dihydro-benzofurans, as well as other conjugated alkenes. Our reaction conditions are mild, use cheap and readily available reagents, and notably tolerate functional groups that such as benzyl esters and aryl-chlorides that would otherwise be reduced under hydrogenation conditions. To investigate the mechanism of this reduction, we explored alternative radical initiators and performed deuteration experiments that suggest the reaction occurs via single electron transfer followed by radical polar crossover.



Poster 11

Stereospecific Nickel-Catalyzed Borylation of Tertiary Benzylic Carboxylates

Rebecca C. Colandrea, Obieze Enudi, Mary Watson*

University of Delaware
27 Duke Street Apt A Newark, DE 19711 rcoland@udel.edu

Enantioenriched tertiary benzylic boronic esters are valuable synthetic intermediates for organic transformations. However, previous methods to prepare these molecules have required the use of harsh bases and stoichiometric chiral reagents. We are now developing a transition metal-catalyzed cross-coupling to form highly enantioenriched tertiary boronic esters. This reaction is a stereospecific, nickel-catalyzed Suzuki-Miyaura borylation of tertiary benzylic carboxylates. It employs an air-stable Ni(II) salt to transform tertiary alcohol derivatives, which are readily prepared in exceptional enantiomeric excess, to synthesize valuable products with stereochemical fidelity.

Poster 12

HIGH-THROUGHPUT EXPERIMENTATION AT J&J INNOVATIVE MEDICINE:A CHEMISTRY CAPABILITY TO ACCELERATE THE DISCOVERY PORTFOLIO

Jordie Compton, Iulia Strambeanu*, Justin Diccianni, Bo Hao, Wei Liu, Chuck Hendrick, Zhicai Shi*
Johnson & Johnson Innovative Medicine, Global Discovery Chemistry - High Throughput Experimentation
1400 McKean Rd, Spring House, PA 19447; jcompto4@its.jnj.com

HTE has been established as a very effective technology in increasing productivity and cost-effectiveness in Pharma R&D over the past decade by enabling efficient access to complex molecular scaffolds. Especially in early programs, where chemical matter is only available in limited quantities, increased throughput in HTE fashion can drive data-informed decision making and enhance confidence for de-risking purposes. Increasing throughput requires robotic operation and an automated workflow to improve efficiency and consistency. Furthermore, adapting reactions to automated workflow can save human labor and significantly increase throughput.

In the past four years, Johnson & Johnson Innovative Medicine has built a state-of-the-art, highly competitive laboratory and team to champion the identification, evaluation, implementation, and application of HTE capabilities to accelerate the portfolio across all our Discovery Chemistry sites. To this end, several in-house High-Throughput automation workflows and capabilities have been built to successfully impact the Design-Make-Test cycle. These capabilities have been instrumental in facilitating the build of an AI/ML predictive model for challenging reactions and our Direct to Biology and parallel medicinal chemistry workflows.

Poster 13

AI-ASSISTED DESIGN AND LABORATORY SYNTHESIS OF NOVEL DISINFECTANT AMPHIPHILES

Amanda J. Consylman,[1] Alice Wu,[1] Gabe Chang,[1] Dr. Amarda Shehu,[2] Dr. Liang Zhao,[3] Dr. Bill Wuest,[4] and Dr. Kevin Minbiole*[1].

1. *Villanova University Department of Chemistry*
2. *George Mason University Department of Computer Science*
3. *Emory University Department of Computer Science*
4. *Emory University Department of Chemistry*

Department of Chemistry, Villanova University, Villanova, Pennsylvania, USA
aconsylm@villanova.edu

In an effort to thwart the antimicrobial resistance that continues to present human health risks, it is crucial to develop novel disinfectants. Quaternary ammonium compounds (QACs) are among the most popular and effective disinfectants in current use, but their structural variety is lacking. To counter this, an artificial intelligence model was trained using structural information from a SMILES dataset of over 800 QACs along with their antimicrobial activity (measured by MIC) against a set of gram positive and gram negative bacterial pathogens. The deep learning model then predicted new structures for biological assessment, of which nearly a dozen compounds were synthesized and confirmed structurally using ^{1}H NMR. The newly synthesized compounds were tested for their bioactivity, in order to feed back into the AI model and improve future structural predictions for novel and potent disinfectant amphiphiles.

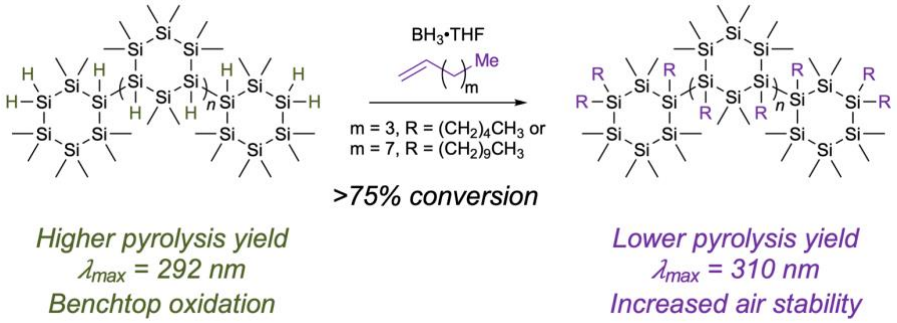
Poster 14

BORANE-CATALYZED POSTPOLYMERIZATION HYDROSILYLATION OF POLY(CYCLOSILANE)S

Marissa G. Coschigano,[1] Sydney L. Gregory,[1] Jonathan Catazaro,[1] Aaron J. Rossini,[2] Rebekka S. Klausen[1]*

[1]Department of Chemistry, Johns Hopkins University, 3400 N. Charles St, Baltimore, MD, 21218, United States.
[2]Department of Chemistry, Iowa State University, Ames, Iowa 50011, United States
mcoschi1@jh.edu

Postpolymerization functionalization is a strategy used to modify polymeric properties and diversify materials. Structurally complex poly(cyclosilane)s provide both end group and internal oxidatively sensitive hydrido (Si-H) side chains possibly prone to postpolymerization functionalization via hydrosilylation to form oxidatively stable Si-alkyl chains. Classical methods of hydrosilylation utilizing heavy metal, such as Pt- or Pd-based catalysts have shown competing Si-Si bond cleavage. Borane-catalyzed hydrosilylation of poly(cyclosilane)s results in high conversion to Si-alkyl chains without Si-Si bond scission.[1] This presentation will cover the chemoselective postpolymerization functionalization of poly(cyclosilane)s and the resulting modulations in physical characteristics, solubility, optical properties, pyrolytic reactivity, and air sensitivity. ^{29}Si cross-polarization magic angle spinning (CPMAS) provides insight on site-selectivity for end group versus internal Si-H groups.



---

[1] Coschigano, M. G.; Gregory, S. L.; Catazaro, J.; Rossini, A. J.; Klausen, R. S. *Macromolecules* **2024**. (Advance Article).

Poster 15

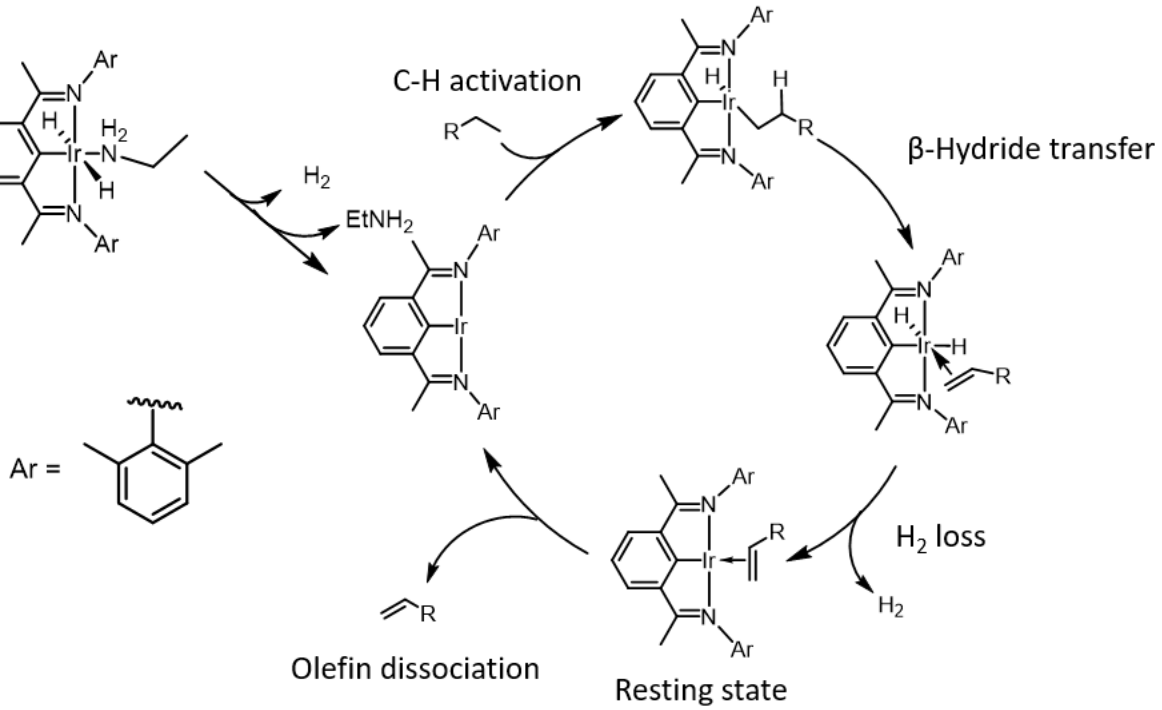
Studies on alkane dehydrogenation by a 'NCN' type pincer iridium complex

Soumyadipa Das, Santanu Malakar, Thomas J. Emge, Alan S. Goldman*

Department of Chemistry and Chemical Biology, Rutgers University, New Brunswick, New Jersey, USA

soumyadipa.das@rutgers.edu

Dehydrogenation of alkanes to yield olefins is of great interest in view of the versatility of olefins as intermediates and reagents. Iridium complexes of PCP-type pincer ligands have been intensively studied as catalysts for alkane dehydrogenation. Their catalytic cycle has been shown to proceed via C-H activation by the 14e fragment (PCP)Ir(I) followed by β-H transfer to give a trans-dihydride olefin complex, olefin loss, and loss of H_2 to return (PCP)Ir(I). However, the economically more viable and air stable option, nitrogenous pincers are less studied in this regard. In this work, we report an NCN-type (phenyl di-(xylyl)imine) pincer Ir complex which we find is the most active catalyst to date for acceptorless dehydrogenation of n-alkanes. DFT studies indicate that the catalytic cycle consists of C-H activation, β-H transfer to give a cis-dihydride olefin complex, followed by H_2 loss to give the 16e Ir(I) olefin complex. This is a new mechanism for Iridium Pincer catalyzed alkane dehydrogenation catalytic cycle.



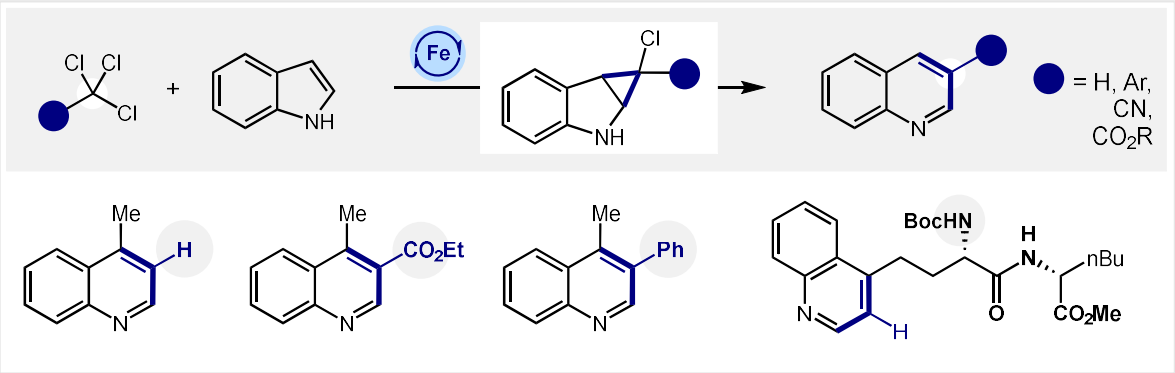
Poster 16

IRON-MEDIATED CARBON ATOM INSERTION TO ACCESS 3-SUBSTITUTED QUINOLINES VIA TRICHLOROMETHYL REAGENTS

Bethany DeMuynck[†], Hojin Kim[†], Victoria Menches[†], Ethan Hyland[‡], Mark Levin[‡], David Nagib[†]*.

[†]Department of Chemistry & Biochemistry, The Ohio State University, Columbus, Ohio, USA.
[‡]Department of Chemistry, University of Chicago, Chicago, Illinois, USA.
Demuynck.1@buckeyemail.osu.edu

Heterocycles are ubiquitous motifs in biologically active molecules. Recently, the ability to directly interconvert from one skeleton to another has gained significant attention. Therefore, a mild, iron mediated carbon insertion reaction has been developed to rapidly access 3-substituted quinolines from indoles. This strategy utilizes a diverse range of trichloromethyl precursors as the carbene source which then react with a broad scope of indoles. This transformation allows for the use of commercial and safe starting materials under mild reductive conditions which allows for wide functional group tolerance. The optimization, scope, and mechanistic understanding of this transformation will be presented.



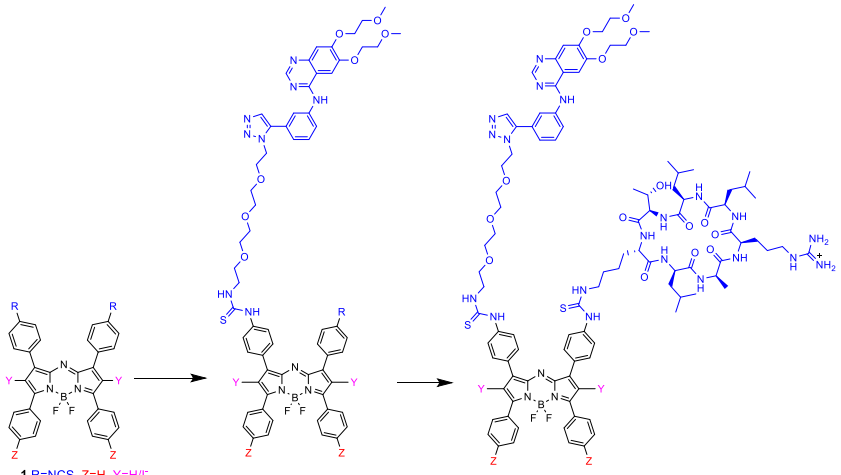
Poster 17

SYNTHESIS OF NOVEL NEAR-IR AZABODIPY-TKI-PEPTIDE BIOCONJUGATES AND INVESTIGATION OF THEIR POTENTIAL IN BIOIMAGING AND PHOTODYNAMIC THERAPY

Simran Dhingra[†], Mistura O. Olajuwon[†], Prajesh Shrestha[‡], Frank R. Fronczek[†], Seetharama D. Jois[‡]*, Maria da Graça H. Vicente [†]*

[†] *Department of Chemistry, Louisiana State University, Baton Rouge, LA 70803, USA*
[‡] *Department of Pathobiological Sciences, School of Veterinary Medicine, Louisiana State University, Baton Rouge, LA 70803, USA*
sdhing1@lsu.edu

AzaBODIPY dyes are related to their parent BODIPY dyes via N-for-C substitution at the C_8-position of the BODIPY core. The highly versatile core structure of these dyes can be fine-tuned to achieve absorption and emission wavelengths within the “phototherapeutic window” where there is least interference from other biomolecules in tissues and maximum penetration is achieved. Previously reported biomolecules such as cyclic peptides and small molecule tyrosine kinase inhibitors (TKIs) show specific binding onto the extracellular and/or the intracellular domain of the Epidermal Growth Factor Receptor (EGFR)[1], overexpressed on colorectal cancer cells. The synthesis of a new series of azaBODIPYs bearing two isothiocyanate groups will be presented. The conjugation of these azaBODIPYs to peptides and to TKI Erlotinib will be discussed. The biological properties of the resulting bioconjugates will be evaluated and compared for potential applications in bioimaging and in photodynamic therapy.



---

[1] Dhingra, S.; Shrestha, P.; Chowdhury, A.; Zhou, Z.; Jois, S.D.; Vicente, M.G.H. *Targets* **2023**, *1*, 48-62.

Poster 18

ATROPOSELECTIVE BRØNSTED ACID-CATALYZED PHOTOCYCLIZATION TO ACCESS CHIRAL *N*-ARYL QUINOLONES WITH LOW ROTATIONAL BARRIERS

Athimoolam Arunachalampillai,[a] Prashantha Chandrappa,[a] Alan Cherney,+[b] Richard Crockett,[c] Jaika Doerfler,*+[c] Gregory Johnson,[c] Venkata Chandrasekhar Kommuri,[a] Ali Kyad,[c] Joshua McManus,[c] James Murray,[c] Tessa Myren,[c] Noah Fine Nathel,[c] Ikenna Ndukwe,[c] Adrian Ortiz,[c] Margaret Reed,[c] Huan Rui,[c] Maria Victoria Silve Elipe,[c] Jason Tedrow,[b] Shane Wells,[c] Suha Yacoob,[b] Kumiko Yamamoto[c].

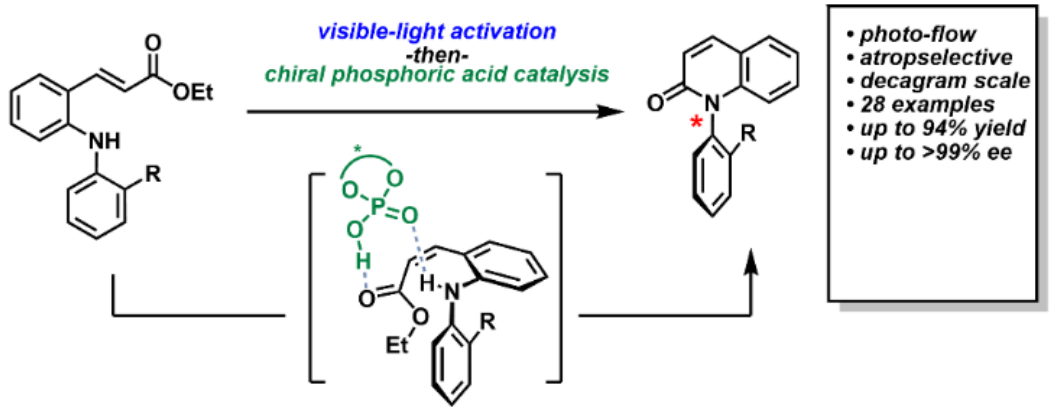
[a] A. Arunachalampillai, P. Chandrappa, V. C. Kommuri, Syngene Amgen Research & Development Center, Biocon Park, Bangalore 560099 India.

[b] A. Cherney, J. Tedrow, S. Yacoob, Amgen, 360 Binney St, Cambridge, MA-02141, United States of America.

[c] R. Crockett, J. Doerfler, G. Johnson, A. Kyad, J. McManus, J. Murray, T. Myren, N. Fine Nathel, I. Ndukwe, A. Ortiz, M. Reed, H. Rui, M. V. Silve Elipe, S. Wells, K. Yamamoto, Amgen, One Amgen Center Drive, Thousand Oaks, CA-91320, United States of America.

Jaika Doerfler – Amgen, One Amgen Center Drive, Thousand Oaks, CA 91320, United States of America; Email: jdoerfle@amgen.com.

Axial chirality arising from hindered rotation about a nitrogen-carbon bond is prevalent in an increasing number of natural products and pharmaceutical agents. Nevertheless, limited synthetic methods to selectively access single atropisomeric species of this type exist. Herein we present a cooperative dual activation approach to access *N*-aryl quinolones via a Brønsted acid-catalyzed photocyclization of readily-available amino cinnamates. The novel transformation occurs under mild conditions, allowing for the preparation of diverse products with low rotational barriers. To illustrate the utility of the atrop-selective photocyclization for large-scale synthesis, this methodology was developed in a continuous flow system to access multi-gram quantities on enantioenriched material. The mechanism as well as solvent dependcies of the racemization of the atropisomers were studied.



Poster 19

PROCESS CHEMISTRY DEVELOPMENT AT FMC

Kalina Doytchinova-Weil and Christina Stauffer

Stine Research Center, FMC Corporation, Newark, DE, USA
kalina.doytchinova-weil@fmc.com; christina.stauffer@fmc.com

Food insecurity is a growing crisis affecting hundreds of millions of people worldwide.[1] At FMC, we develop innovative crop protection products that control weeds, harmful insects, and plant diseases to help growers raise production levels and improve the quality and sustainability of food. This poster will provide an overview of how we work to develop safe and cost-efficient manufacturing processes by highlighting an example from the development of an enantioselective hydroxylation process toward the active ingredient indoxacarb.

Indoxacarb is a commercial insecticide with high activity against pests and excellent safety toward non-target organisms. Initially developed as a racemic product, it was found that the (S)-enantiomer is the active form, while the (R)-enantiomer is inactive.[2] To reduce the environmental burden of applying this non-active form, as well as its associated manufacturing waste, development of an enantioselective process was investigated. The first breakthrough came with the use of cinchonine, which catalyzed the key asymmetric hydroxylation, resulting in a product with 50% enantiomeric excess.[3] Further development led to the discovery of a chiral zirconium-diamine catalyst, which resulted in the first fully enantioenriched product with >98% ee.[4] These developments and their effect on establishing a less waste-intensive manufacturing process will be presented.

---

[1] The-Sustainable-Development-Goals-Report-2022.pdf (un.org)
[2] S.F. McCann *et al. Pest Manag. Sci.* **2001**, *57*, 153-164
[3] R. Shapiro *et al. ACS Symposium Series* **2001**, *800*, 178-185; WO2003040083
[4] WO2003002255

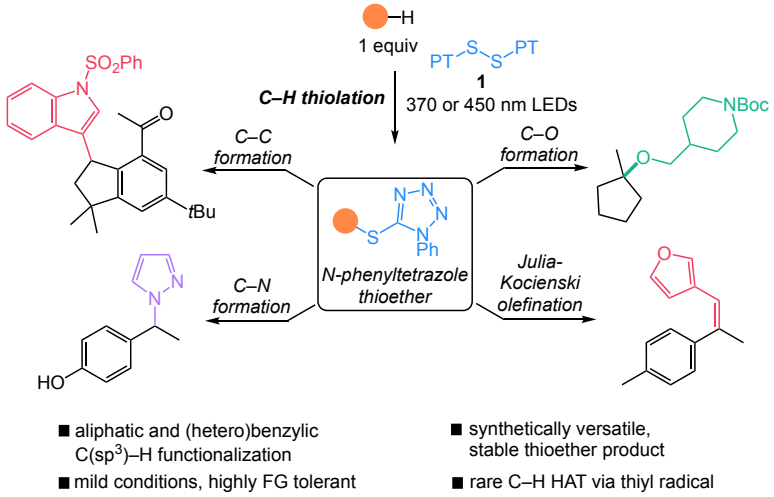
Poster 20

SITE-SELECTIVE C–H THIOLATION AS AN ENABLING TOOL FOR LATE-STAGE C–H DIVERSIFICATION

Justine A. Drappeau, Ashley K. Z. Zachmann, Shubin Liu, Erik J. Alexanian*

Department of Chemistry, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA
jdrappeau@unc.edu

Methods enabling the broad diversification of C(sp^3–H) bonds from a common intermediate are especially valuable in synthesis as they provide a straightforward strategy for the rapid construction of chemical libraries. Given this synthetic value we developed a site selective (N-phenyltetrazole)thiolation of aliphatic and (hetero)benzylic C(sp^3–H) bonds using a commercially available disulfide to access N-phenyltetrazole thioethers.[1] These thioether products are then readily elaborated in diverse fragment couplings for C–C, C–O, or C–N construction. We specifically focused on unactivated tertiary C–H bonds within the aliphatic scope as efficient functionalizations of these sites in a chemoselective and functional group tolerant manner remain extremely challenging. The C–H functionalization proceeds via a radical-chain pathway involving hydrogen atom transfer by the electron-poor N-phenyltetrazolethiyl radical. Hexafluoroisopropanol was found to be essential to reactions involving aliphatic C(sp^3–H) thiolation, with computational analysis supporting dual hydrogen bonding of the N-phenyltetrazolethiyl radical imparting increased radical electrophilicity to facilitate the hydrogen atom transfer. Substrate is limiting reagent in all cases, and the reaction displays an exceptional functional group tolerance well suited to applications in late-stage diversification. The optimization, scope, product elaborations, and mechanistic understanding of these reactions will be presented.



[1] J. Drappeau, A. Zachmann, S. Liu, E. J. Alexanian, *Angewandte Chemie International Edition*, *n/a*, e202404879.

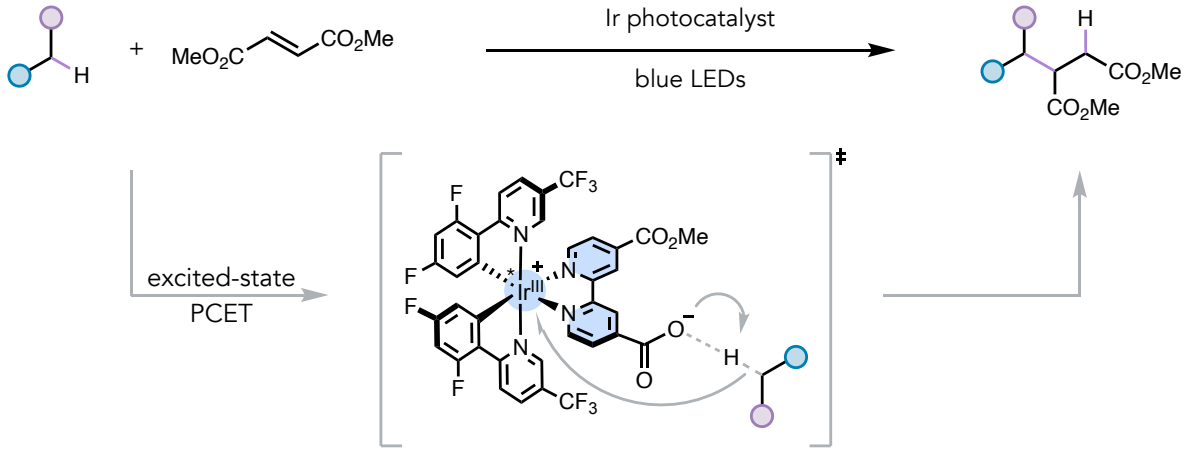
Poster 21

MODULAR IRIDIUM POLYPYRIDYL COMPLEXES FOR SELECTIVE C–H ABSTRACTION VIA PROTON-COUPLED ELECTRON TRANSFER

Diego Granados, Emily Du, Adam Reinhold, Shiloh Andersson, Kai Cui, Gregory Scholes, Sharon Hammes-Schiffer, Robert Knowles*

Department of University, Princeton University, Princeton, New Jersey, USA
emilydu@princeton.edu

The selective functionalization of C–H bonds, ubiquitous in organic compounds, provides a means to rapidly generate complexity within small molecules. In particular, the abstraction of C–H bonds to generate alkyl radicals has allowed for the formation of C–C and C–heteroatom bonds under mild conditions. We are interested in light-driven proton-coupled electron transfer (PCET) as a tunable method to achieve high selectivity for C–H abstractions. We have synthesized a series of isostructural iridium polypyridyl complexes bearing a pendant carboxylate and demonstrated their ability to mediate C–H alkylation through redox-neutral bimolecular C–H PCET, in which the reaction was highly selective for abstraction from electron-rich bonds. Through ultrafast transient absorption spectroscopy, the quenching of the excited state of these complexes was observed to have a kinetic isotope effect, confirming the simultaneous quenching of the photocatalyst and cleavage of the C–H/D bond. We have begun to explore the possibility of tuning the selectivity of abstraction between different electronically biased C–H bonds by modulating photocatalyst structure to generate imbalanced proton and electron driving forces.



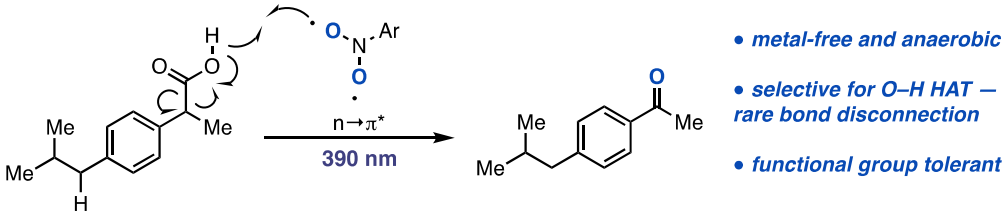
Poster 22

PHOTOEXCITED NITROARENES AS TUNABLE REAGENTS FOR METHYLENE DELETION VIA DECARBOXYLATIVE OXIDATION

Alana D. Duke and Marvin Parasram*

Department of Chemistry, New York University, New York, New York 10003, United States
Email: add8529@nyu.edu

We have previously reported that photoexcited nitroarenes are potent reagents in hydrogen atom transfer (HAT) reactions with hydridic C(sp^3)–H bonds. After HAT, the oxygen-centered radical on the nitroarene recombines with the alkyl radical. The breakdown of the resulting adduct furnishes alcohols. We now report that tuning of the nitroaromatic core provides access to divergent HAT reactivity through photoexcitation. Certain nitroarenes, especially those with *meta*-methoxy substituents, can preferentially abstract hydrogen from the O–H bonds of carboxylic acids, available feedstock chemicals, even in the presence of activated C–H bonds. This HAT event results in a carboxyl radical, which undergoes decarboxylation to furnish alkyl radicals. Recombination with the photoexcited nitroarene and breakdown of the resulting adduct yield valuable carbonyl products in a methylene deletion reaction. Mechanistic experiments, the scope of the reaction, and future directions will be presented.



Poster 23

Shaking Up the Friedländer Reaction: Rapid, Scalable Mechanochemical Synthesis of Polyaryl-substituted Quinolines

Daliah Farajat[†] Jean-Louis Do[‡], Pat Forgione[‡], Tomislav Friščić[†¥], Louis A. Cuccia[‡], and Chao-Jun Li[†*]

[†]*Department of Chemistry, and FQRNT Centre for Green Chemistry and Catalysis, McGill University, 801 Sherbrooke Street West, Montreal, Quebec H3A0B8, Canada*

[‡]*Department of Chemistry & Biochemistry, Concordia University, 7141 Sherbrooke Street West, Montréal, Québec, H4B 1R6, Canada*

[¥]*School of Chemistry, University of Birmingham, University Rd W, Edgbaston, Birmingham, B15 2TT, United Kingdom*

8774 Avenue André-Grasset, Montreal, QC, Canada, H2M2L4 *daliah.farajat@mail.mcgill.ca*

Abstract. Quinolines are a ubiquitous heterocyclic aromatic scaffold, which can be found in many natural and synthetic products. They are highly valued for their pharmacological and electrochemical properties, encouraging the discovery of new routes for quinoline synthesis and diversification. Polyaryl-substituted quinolines have recently surged as useful substrates for a wide variety of applications, yet their synthetic routes remain difficult and inefficient. Herein, we report a rapid and novel mechanochemical Friedländer synthesis of polyaryl-substituted quinolines under basic conditions using ball milling. Optimized reaction conditions result in moderate to excellent yields ranging from 69% to >95% and demonstrates broad functional group tolerance. We further demonstrate a new route for the synthesis of photocatalyst DPQN$^{2,4\text{-di-OMe}}$ and photo-ligand PPQN$^{2,4\text{-di-OMe}}$ as well as OLED donor-acceptor pCzPPQ, electron transport material oligoquinoline TQB and organic semiconductor DPA. A gram-scale reaction was also achieved using Resonant Acoustic Mixing (RAM), providing 87% isolated yield after simple recrystallization.

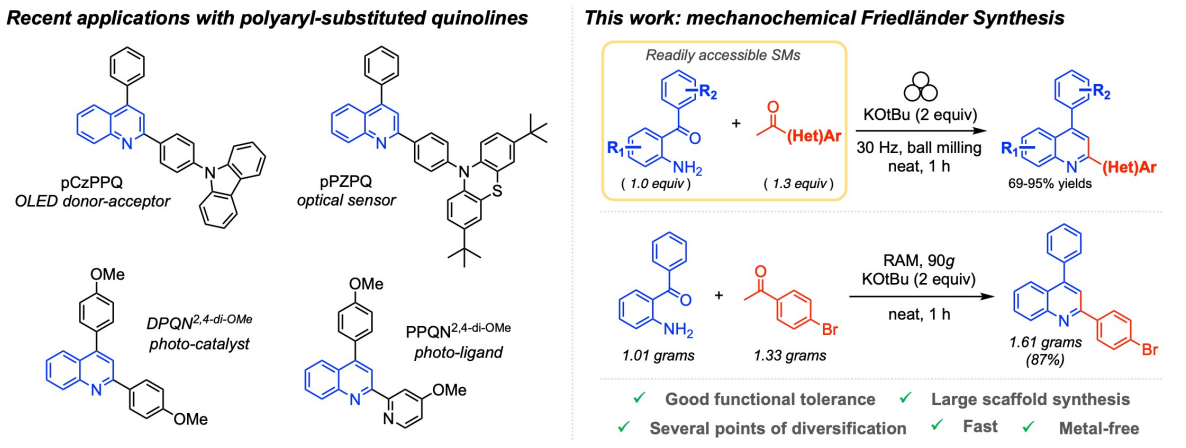


Figure 1. Examples of recent polyaryl-substituted quinolines applied to organic catalysis for small molecule synthesis and organic electronic materials chemistry for design of devices (left) This work: rapid generation of polyaryl-substituted quinolines *via* ball milling mechanochemical Friedländer synthesis under basic conditions using ball milling and resonant acoustic mixing (RAM) (right).

Poster 24

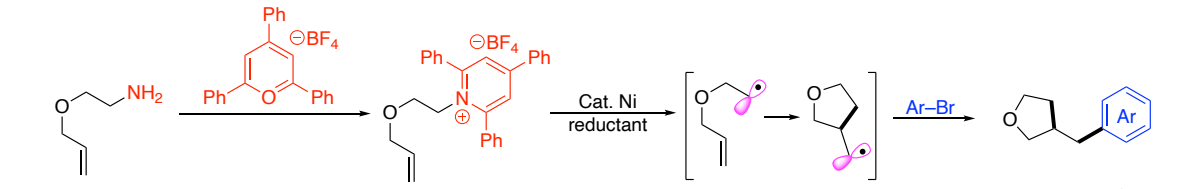
CASCADE CYCLIZATIONS OF ALKENE-TETHERED ALKYLPYRIDINIUM SALTS

Bria Garcia, Pankti Mehta, Jianyu Xu, Mary P. Watson*

University of Delaware
Department of Chemistry & Biochemistry, University of Delaware, Newark, Delaware 19716, USA. briagar@udel.edu.

Bioactive molecules are essential to human health to combat disease, and the need for new medicines is persistent due to new disease development, pathogenic antibiotic resistance, etc. Alkyl amines are an abundant and diverse substrate class, offering tremendous opportunities for diversity-oriented medicinal chemistry campaigns and late-stage functionalization. Their attractiveness had led them to be incorporated as electrophiles in cross-coupling reactions to form new carbon–carbon (C–C) bonds via carbon–nitrogen (C–N) bond cleavage. To make further contributions to this field, this research will focus on a deaminative transformation. Efficient methods to synthesize highly substituted, saturated heterocycles are needed to obtain existing and new derivatives of bioactive molecules. To meet this need, a cascade cyclization of alkylpyridinium salts is being developed.

Alkyl amine starting materials can be easily functionalized with alkene tethers and activated as Katritzky pyridinium salts. When subjected to reductive nickel-catalyzed conditions, deamination will occur to give an alkyl radical, which can then cyclize on the pendant alkene. Subsequent coupling with an aryl halide then allows the formation of two new C–C bonds in one step. Of particular interest is the development of diastereo- and enantio-selective examples of this reaction. This chemistry will provide a revolutionary method of access to saturated (hetero)cyclic molecules.



Poster 25

Synthesis and Fabrication of Conductive Polymers for Environmental Sensing Applications

Collette T. Gordon[1], Sohyun Park,[1] Timothy M. Swager[1]

1. Chemistry, Massachusetts Institute of Technology

Conductive polymers (CPs) are a class of organic polymers that conduct electricity along the pi-conjugated backbone. Interest in these materials has largely been driven by their semiconductive properties, redox activity, and thermal stability. The tunable doping of these materials allows for opportunities in the quantitative sensing of environmental analytes. CPs are attractive materials due to their potential for facile processibility, low cost, and yet high performance. Common CPs include polythiophene, polyaniline, and polypyrrole, however, in many applications, device fabrication remains a challenge due to limited solubility, mechanical stability, and adhesion to substrates. Recent research from our group utilized conductive polymers for quantitative sensing of environmental analytes in electrically read lateral flow assays (e-LFAs). We explore oxidative polymerizations to target CPs materials for enhanced selectivity for new generations of CP-fabricated devices. The synthesis of these conductive polymers will be discussed and their fabrication into conductive-based sensors, and sensing responses will be presented.

Poster 26

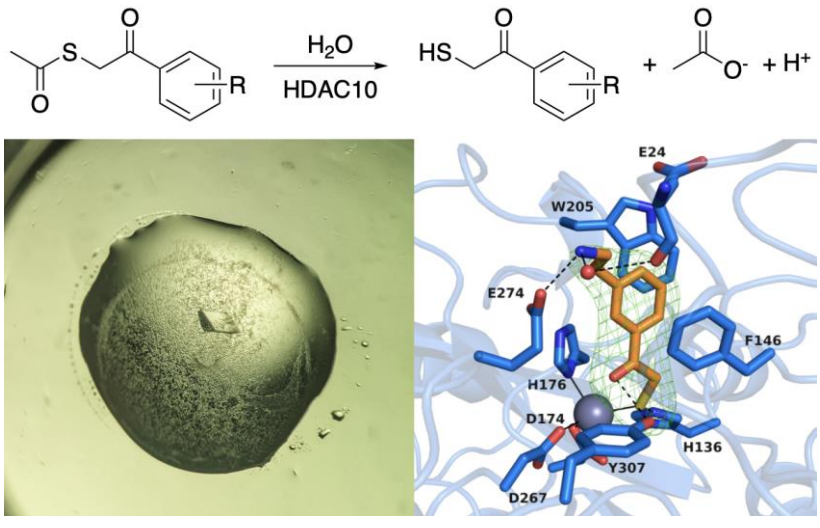
DESIGN, SYNTHESIS AND STRUCTURAL EVALUATION OF THIOL-BASED INHIBITORS OF HDAC10

Juana Goulart Stollmaier, Paris R. Watson, David W. Christianson*

Roy and Diana Vagelos Laboratories, Department of Chemistry, University of Pennsylvania, 231 South 34th Street, Philadelphia, PA 19104-6323 USA

jgstoll@sas.upenn.edu

Histone deacetylase 10 (HDAC10) is unique among the greater HDAC family due to its unusually narrow substrate specificity as a polyamine deacetylase, specifically, an N^8-acetylspermidine hydrolase. Polyamines are essential for cell growth and proliferation; consequently, inhibition of polyamine deacetylation represents a new strategy for cancer chemotherapy. In this work, we have designed six acetylated phenylthioketone inhibitors of HDAC10 containing positively charged *para*- and *meta*-substituted amino groups designed to target interactions with E274, the gatekeeper that recognizes the positively charged ammonium group of substrate N^8-acetylspermidine in the active site of HDAC10. We synthesized each of these inhibitors through a short synthetic route of six steps. By adapting a low-cost colorimetric activity assay, we measured low-micromolar IC_{50} values for these compounds against a humanized construct of zebrafish HDAC10 (A24E-D94A zHDAC10). Selected inhibitors were cocrystallized with A24E-D94A zHDAC10 and zebrafish HDAC6 CD2 to provide insight on isozyme affinity and selectivity.



Poster 27

High-Throughput Innovation Technologies (HIT) for Late Synthetics

Eileen M. Hoang, Naoko Ichiishi, Austin T. Kelly, Xiao Li, Alexis Charaudeau, Alan H. Cherney*

High-Throughput Innovation Technologies, Drug Substance Late Development, Sanofi
350 Water St., Cambridge, MA 02141
eileen.hoang@sanofi.com

High-throughput experimentation (HTE) is a technique to generate knowledge through larger datasets by running multiple reactions in parallel. The High-Throughput Innovation Technologies (HIT) team within Sanofi Process Chemistry was established as part of our mission to leverage technological innovation to combat the increasing molecular complexity of synthetic APIs and fulfill our process efficiency and eco-design goals. Our cross-functional and cross-site team utilizes scientific and platform-based expertise throughout multiple stages of API development, from early proof-of-concept route-scouting to process optimization and scale-up studies. The HIT team has developed a toolbox that includes workflows for metal-catalyzed transformations, amidations, high-pressure reactions, and photocatalyzed reactions. The early incorporation of HTE- and automation-based platforms demonstrates our strong commitment to deliver “right-first-time” manufacturing processes for our small molecule portfolio, resulting in accelerated development, decreased costs, and lowered environmental impact.

Poster 28

CHARACTERIZATION OF THE BINDING KINETICS, ANTICANCER ACTIVITY, AND PHOTOCAGING PROPERTIES OF 2-HYDROXY-BENZAMIDES AS SELECTIVE INHIBITORS OF HDAC1 AND 2

Irina Honin*, Tao Sun, Finn K. Hansen

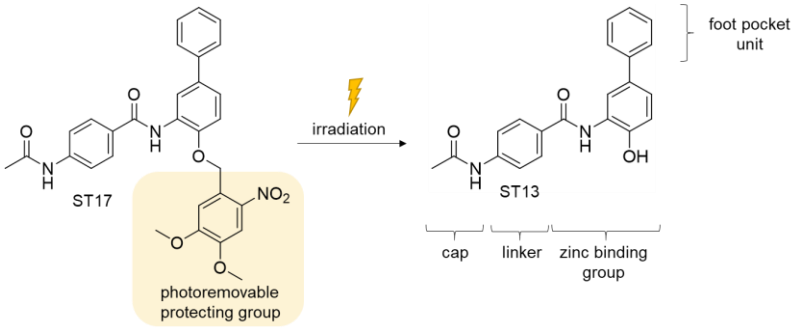
Pharmaceutical Institute, University of Bonn, 53121 Bonn, Germany
ihonin@uni-bonn.de

Selective inhibitors targeting class I histone deacetylases (HDACs) have gained significant attention in research as potential novel drugs to treat cancer. Especially the class I isoforms HDAC1 and HDAC2 are often overexpressed in different cancer entities.[1] Inhibiting these enzymes can significantly impact epigenetic regulation and slow tumor progression.[1,2] However, while 2-aminobenzamides are well characterized inhibitors of HDAC1 and HDAC2, the corresponding phenol analogs have not been sufficiently investigated so far.[3,4]

The aim of this work was to characterize a 2-hydroxybenzamide derivative (ST13) regarding its HDAC inhibitory potential, binding kinetics, and activity in different cancer cell lines. ST13 was compared with the FDA-approved pan-HDAC inhibitor vorinostat and Cpd-60, a highly selective 2-aminobenzamide targeting HDAC1 and HDAC2. In addition, we caged the phenol moiety of the zinc-binding group in ST13 with a 4,5-dimethoxy-2-nitrobenzyl group to generate the light activatable prodrug ST17.

We could confirm that ST13 is a selective, slow- and tight-binding HDAC1 and HDAC2 inhibitor. Furthermore, we demonstrated that the light activatable prodrug ST17 readily releases ST13 upon irradiation with ultraviolet (UV) light, thereby allowing the precise control of its HDAC inhibiting as well as antiproliferative properties.

Overall, this study provides new insights into the binding kinetics, anticancer properties, and utility of 2-hydroxybenzamides as HDAC1 and HDAC2 inhibitors.



[1] D. Banik, S. Moufarrij, A. Villagra, *Int. J. Mol. Sci.* **2019**, *20*, 2241.
[2] J. Roche, P. Bertrand, *Eur. J. Med. Chem.* **2016**, *121*, 451–483.
[3] L. Schäker-Hübner, R. Haschemi, T. Büch, F. B. Kraft, B. Brumme, A. Schöler, R. Jenke, J. Meiler, A. Aigner, G. Bendas, F. K. Hansen, *ChemMedChem* **2022**, *17*, e202100755.
[4] J. L. Methot, P. K. Chakravarty, M. Chenard, J. Close, J. C. Cruz, W. K. Dahlberg, J. Fleming, C. L. Hamblett, J. E. Hamill, P. Harrington, A. Harsch, R. Heidebrecht, B. Hughes, J. Jung, C. M. Kenific, A. M. Kral, P. T. Meinke, R. E. Middleton, N. Ozerova, D. L. Sloman, M. G. Stanton, A. A. Szewczak, S. Tyagarajan, D. J. Witter, J. Paul Secrist, T. A. Miller, *Bioorg. Med. Chem. Lett.* **2008**, *18*, 973–978.

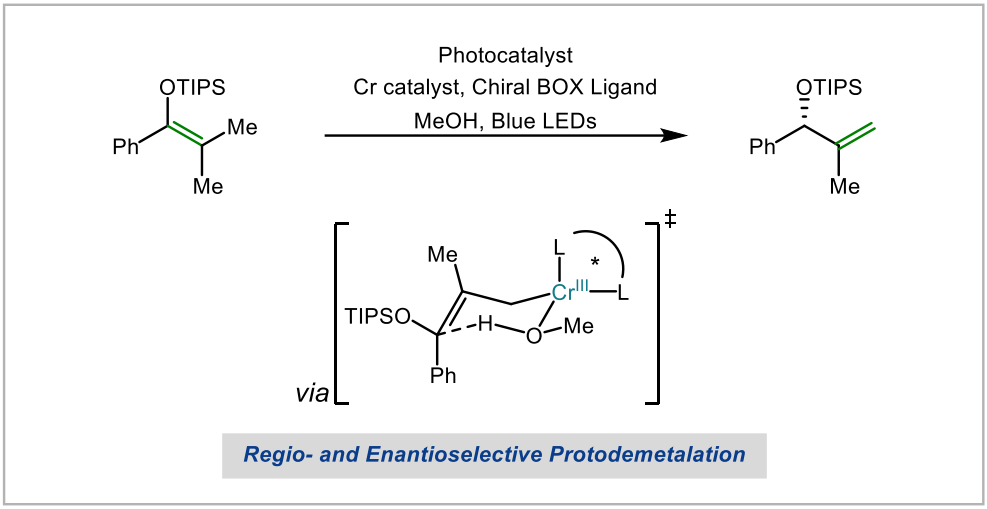
Poster 29

CONTRA-THERMODYNAMIC, ASYMMETRIC OLEFIN ISOMERIZATION

Eve Y. Xu, Bianca Imbriaco, Sumin Lee, Kuo Zhao, Robert R. Knowles*

Department of Chemistry, Princeton University, Princeton, New Jersey, USA
Presenting author: *bianc@princeton.edu*

Recognized for its exceptional atom economy, asymmetric olefin isomerization is a powerful strategy for constructing stereogenic centers in substituted olefins. Positional isomerization of olefins often occurs exothermically, leading to the formation of thermodynamically more stable internal olefins. However, this thermodynamic bias can be overcome using photocatalysis by leveraging the differences in redox properties among olefins. In this regard, we developed an enantioselective, light-driven method for the contra-thermodynamic positional isomerization of olefins. The sequential oxidation and deprotonation of a tetra-substituted enol ether substrate generates an allyl radical, which undergoes radical capture by a Cr(II) cocatalyst bearing a chiral bisoxazoline (BOX) ligand. Protodemetalation of the nascent Cr(III) allyl complex by methanol is highly regioselective and enantioselective, yielding an enantioenriched terminal olefin product in good yields and up to 95:5 er. Mechanistic studies suggest an enantiodetermining protodemetalation as well as reveal a complicated Cr speciation during the reaction. Computational studies were carried out to explain the observed enantioselectivity.



Regio- and Enantioselective Protodemetalation

Poster 30

PALLADIUM-CATALYZED ARYLATION OF SECONDARY α-ALKOXYTRICYCLOHEXYLSTANNANES

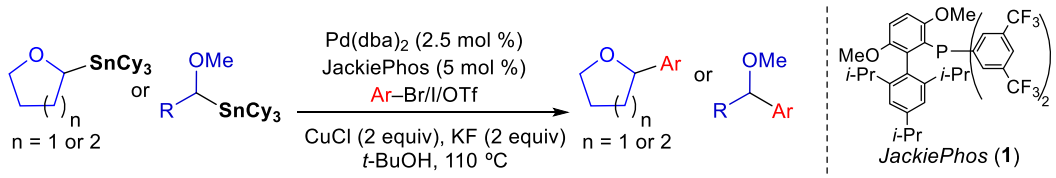
Anju Treesa Jose,[†,‡] Haoran Zhao,[†,‡] and Mark R. Biscoe*[‡]

[†] Ph.D. Program in Chemistry, The Graduate Center of The City University of New York, 365 Fifth Ave, New York, NY 10016

[‡] Department of Chemistry & Biochemistry, The City College of New York, 160 Convent Ave, New York, NY 10031

ajose@gradcenter.cuny.edu

The vast number of biologically active molecules possessing oxygen-containing heterocycles necessitates the development of new synthetic methods that readily enable the incorporation of oxygen-containing heterocycles into organic structures. Although seminal work by Falck established a Pd-catalyzed cross-coupling reaction of secondary α-alkoxytributylstannanes, this process requires the presence of a coordinating/directing O-protecting group to achieve selective transmetalation of a secondary α-alkoxy group.[1] Building upon our laboratory's prior works and observations,[2,3] we have developed a general process for the formation of α-aryl ethers via Pd-catalyzed arylation of secondary α-alkoxytricyclohexylstannanes.[4] We found that for non-glycosidic cyclic and acyclic α-alkoxy molecules, both the incorporation of cyclohexyl spectator ligands into the alkylstannanes (i.e., $RSnCy_3$) and the use of electron-deficient biarylphosphine ligand JackiePhos (**1**) are critical to achieve selective alkyl transfer. As $RSnCy_3$ compounds tend to be more crystalline and less toxic than their corresponding $RSnBu_3$ compounds, the use of $RSnCy_3$ derivatives in synthesis has an additional practical advantage. We are currently investigating stereospecific extensions of this method to the preparation of carbohydrate amphiphiles via C-glycosidic bond-construction, and the applications of such molecules in materials chemistry. The optimization, scope, and a comparative study of these reactions will be presented.



[1] Goli, M.; He, A.; Falck, J. R. Pd-catalyzed cross-coupling of α-(acyloxy)-tri-n-butylstannanes with alkenyl, aryl, and heteroaryl electrophiles. *Org. Lett.* **2011**,*13*, 344−346.
[2] Li, L.; Wang, C.-Y.; Huang, R.; Biscoe, M. R. Stereoretentive Pd-catalyzed Stille cross-coupling reactions of secondary alkyl azastannatranes and aryl electrophiles. *Nat. Chem.* **2013**, *5*, 607−612.
[3] Ma, X.; Zhao, H.; Binayeva, M.; Ralph, G.; Diane, M.; Zhao, S.; Wang, C.-Y.; Biscoe, M. R. A general approach to stereospecific cross-coupling reactions of nitrogen-containing stereocenters. *Chem.* **2020**, *6*, 781−791.
[4] Zhao, H.; Jose, A. T.; Asany, A.; Khan, S. M.; Biscoe, M. R. Pd-catalyzed arylation of secondary α-alkoxytricyclohexylstannanes. *Org. Lett.* **2022**, *24*, 8714-8718.

Poster 31

DESIGN, SYNTHESIS, AND BIOLOGICAL EVALUATION OF 5-SULFONYL THIADIAZOLES AS CONTROL AGENTS FOR ASIAN SOYBEAN RUST

Jyoti Nandi*, Rachel Slack, Daniel Akwaboah, James Bereznak, Zhengao Feng, Sheng-Ying Hsieh, Alice Trivellas, Debra Yuhas

FMC Agricultural Solutions, Stine Research Center, Newark DE, 19711

** jyoti.nandi@fmc.com*

Resistance of agricultural pests toward commercial pesticides threatens the global food supply. The discovery of novel mode-of-action agrochemical small molecules plays a vital role in protecting crops from plant diseases, insects, weeds, and other organisms. Asian Soybean Rust (ASR) is a devastating plant disease with global impact. ASR damages photosynthetic tissue, leading to premature defoliation, early maturation, and yield losses up to 80%. In this presentation, we will describe a retrospective fungicide screening of selected compound libraries, which led to the identification of novel 5-sulfonyl thiadiazoles with impressive control of ASR. Exploration of 5-sulfonyl thiadiazoles through bioisosteric replacement led to the discovery of related molecules. This presentation will describe the synthetic methods, fungicidal activity, and structure-activity relationships of the prepared compounds.

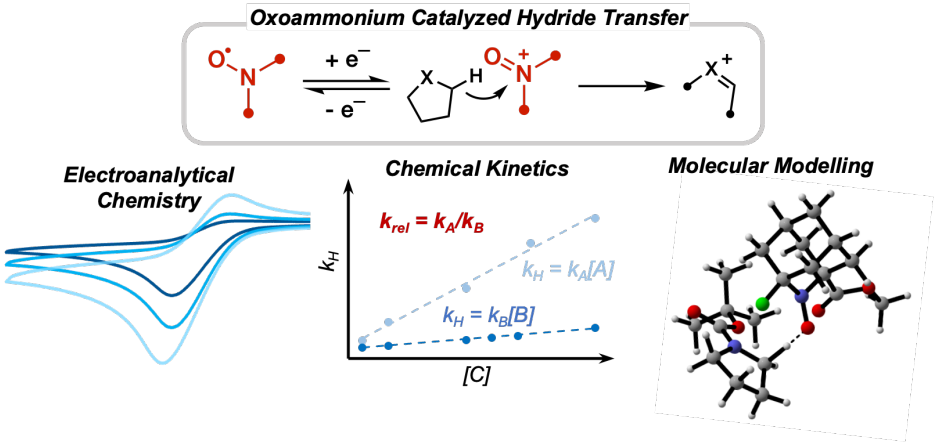
Poster 32

MECHANISTIC INVESTIGATIONS OF OXOAMMONIUM-CATALYZED HYDRIDE TRANSFER

Elya Kandahari, Jonas Rein, and Song Lin*

Department of Chemistry & Chemical Biology, Cornell University, Ithaca, New York, USA
ek648@cornell.edu

Oxoammonium cations are powerful oxidation catalysts that have emerged as popular alternatives to traditional transition metal catalyzed methods. A key mechanistic feature of oxoammonium catalysis is the direct abstraction of hydridic C–H bonds to provide cationic intermediates. Harnessing this unique property, our lab developed the first catalytic and asymmetric variants for the α-oxidation of a diverse scope of amides and ethers. Herein, we describe a detailed mechanistic study illuminating the underlying factors governing hydride abstraction. Cyclic voltammetry was found as an ideal technique to interrogate the reactivity of transient oxoammonium ions. Rate measurements were obtained over a range of substrates representing a gradient of electronic and steric effects, providing clear structure-property relationships. Current efforts are aimed towards the development of predictive statistical models that will provide the foundations necessary to drive the rational design of next generation C–H activation.



Poster 33

HANDLING FLUORINATED GASES AS SOLID REAGENTS USING METAL−ORGANIC FRAMEWORKS

Kaitlyn T. Keasler,[1] Mary E. Zick,[1] Emily E. Stacy,[1] Jaehwan Kim,[1] Jung-Hoon Lee,[2] Lida Aeindartehran,[3] Tomče Runčevski,[3] Phillip J. Milner[1,*]

1. *Department of Chemistry and Chemical Biology, Cornell University, Ithaca, NY 14850, USA.*
2. *Computational Science Research Center, Korea Institute of Science and Technology (KIST), Seoul 02792, Republic of Korea.*
3. *Department of Chemistry, Southern Methodist University, Dallas, TX 75275, USA.*

305 Highland Rd., Apt 1-1B, Ithaca, NY 14850; km879@cornell.edu

Fluorine is ubiquitous in pharmaceuticals. Fluorinated commodity chemicals such as vinylidene fluoride (VDF), trifluoropropene (TFP), and trifluoromethyl iodide (TFMI) represent intuitive building blocks for the late-stage installation of fluoroalkyl and fluorovinyl groups. However, these reagents are generally overlooked because they are gases at room temperature and pressure, requiring specialized equipment for safe handling. We report that fluorinated gases can be handled as bench-stable solid reagents using a magnesium-based metal–organic framework (MOF) for the first time. Bulk samples of gas–MOF reagents can be stored long-term (cold) or embedded within wax capsules to produce bench-stable, single-use reagents. The gas release can be triggered by simply submerging the gas–MOF reagent in the reaction solvent. Employing these gas–MOF reagents, we established two Pd-catalyzed fluorovinylation reactions using VDF to streamline access to α-fluorostyrenes from (hetero)arylboronic acids and β,β-difluorostyrenes from (hetero)aryl halides. Likewise, TFP can be used to prepare β-trifluoromethylstyrenes from (hetero)aryl halides and TFMI can be engaged in Fe-catalyzed oxidative trifluoromethylation of (hetero)arenes. Beyond C–C bond forming reactions, nucleophiles, such as free (NH)-heterocycles, can react with vinyl fluorides like VDF via a defluorinative pathway yielding *N*-fluorovinylated products. After reactions, the MOF can be easily removed by filtration and recovered. Given the successful delivery of a range of fluorinated gases using MOFs, this strategy represents a universal approach to simplifying reaction discovery using gaseous reagents.

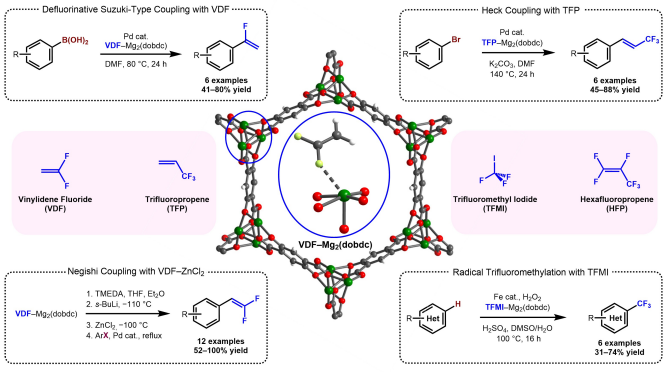


Figure 1: Handling fluorinated gases as solid reagents using metal–organic frameworks to facilitate fluorovinylation and fluoroalkylation reactions.

Poster 34

CHARACTERIZATION OF CHAIN REACTIONS IN PHOTOCHEMISTRY

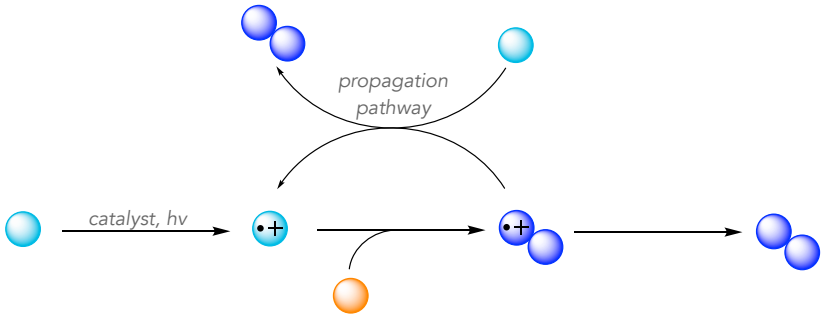
Annemarie A Lee, John R. Swierk*

alee945@binghamton.edu

Binghamton University
Department of Chemistry
4400 Vestal Pkwy E
Binghamton , NY 13902

Photoredox catalysis has become increasingly significant in academic and industrial processes, replacing harsh reaction conditions and high temperatures with visible light. In addition, novel photochemical methods have made certain reactions more accessible, including [2+2] cycloadditions. While several studies have reported on these systems, only a few reports focus on the mechanism proceeding via photochemical chain processes. Recently, Yoon and coworkers investigated ruthenium-catalyzed organic transformations to characterize these chain pathways. Spectroscopic and photochemical analytical techniques are increasingly integral to enhancing our understanding of modern and classical organic transformations. These and other studies have revealed information imperative for extrapolating the kinetics of these systems.

Our current investigation aims to further elucidate the photochemical chain mechanism and identify specific factors encouraging or hindering its success in the Ru-catalyzed Diels-Alder cycloaddition. Though there are a handful of reactions that show chain characteristics, we are still unsure of how prevalent photochemical chain reactions are or how to intentionally design reactions that proceed through this specific mechanism. Our focus centers on Ru(II) catalyzed [4+2] cycloaddition reaction. In-depth mechanistic studies were performed utilizing transient absorption spectroscopy (TAS) in combination with quantum yield measurements to measure the chain lifetime and recognize the distinct pathways involved.



Poster 35

DESIGN, SYNTHESIS, AND EVALUATION OF SUBTYPE SELECTIVE PPARALPHA AGONISTS AS LEADS FOR DIABETIC RETINOPATHY

Julia J. Lee[1], Ziwei Hu[1], Dinesh Nath[2], Adam S. Duerfeldt[1*]

Department of Medicinal Chemistry, University of Minnesota, Minneapolis, Minnesota, USA[1]
Department of Chemistry and Biochemistry, University of Oklahoma, Norman, Oklahoma, USA[2]
lee03421@umn.edu

Diabetic retinopathy (DR), is a severe complication of diabetes that affects over one-third of diabetics. Standard of care (anti-VEGF injection) is invasive and fails to address ~40% of the patient population.[2] These factors, paired with the increased prevalence of diabetes, inspired us to develop mechanistically differentiated small molecules as systemically available options for DR. Fenofibric acid, the active metabolite of fenofibrate and a known peroxisome proliferator-activated receptor alpha (PPARα) agonist, significantly reduces DR progression, as demonstrated in two independent clinical trials (FIELD and ACCORD).[2] Fenofibric acid, however, lacks selectivity and exhibits poor potency.[2] Additionally, dose-limiting toxicities and economic determinants are likely to preclude the utilization of fenofibrate as a mainstream DR therapy.[2] Recently, we published a novel biphenyl aniline PPARα agonistic chemotype, which exhibits improved sub-type selectivity and potency for PPARα, increases cell viability in chemical challenge models, reduces VEGF secretion, and attenuates the release of reactive oxygen species in DR relevant cell-based models.[3] However, due to possible metabolic liabilities of the anilines, we are investigating amides as an alternative linker. Preliminary results for the amide series will be presented in this poster. Concurrently, we have commenced an investigation into the differential behavior of various PPARα agonists when assessed in GAL4-UAS-dependent versus PPRE-dependent cell-based luciferase reporter assays. Activity discrepancies in the two assays provide motivation to interrogate the root of differential downstream effects for different PPARα agonists. Initial results from this comparison study will also be presented.

---

[1] Matuszewski, W.; Baranowska-Jurkun, A.; Stefanowicz-Rutkowska, M. M.; Modzelewski, R.; Pieczyński, J.; Bandurska-Stankiewicz, E. *Medicina (Kaunas)* **2020**, *56* (4), 164.
[2] Dou, X.; Duerfeldt, A. S. *International Journal of Molecular Sciences* **2020**, *21* (23).
[3] Lee, J. J.; Hu, Z.; Wang, Y. A.; Nath, D.; Liang, W.; Cui, Y.; Ma, J.-X.; Duerfeldt, A. S. *ACS Med. Chem. Lett.* **2023**, *14* (6), 766–776.

Poster 36

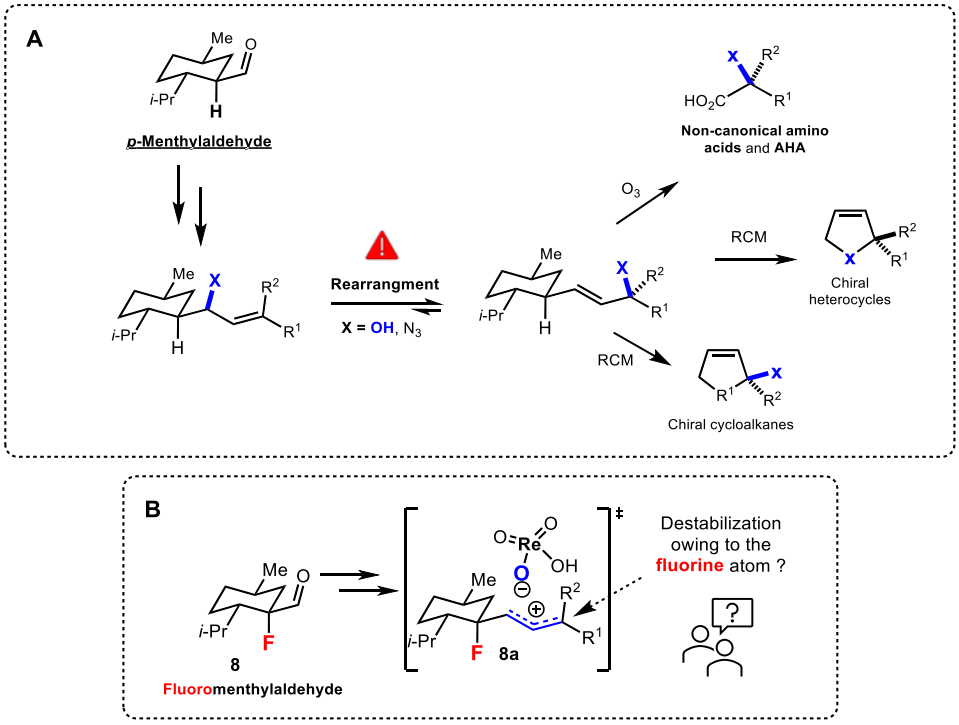
Université de Sherbrooke

Novel Fluorinated Chiral Auxiliary for the Synthesis of Stereogenic Tertiary Alcohols

Roxanne Lessard, Edouard Caron-Duval, and Claude Spino.

Faculty of Sciences, Department of Chemistry, Université de Sherbrooke.
Roxanne.Lessard2@usherbrooke.ca

p-Menthylaldehyde, a chiral auxiliary developed by Prof. Spino's group grants access to strategic **chiral** synthons **5**-**7** via stereoselective rhenium(VII) catalyzed transposition of **allylic alcohols** and other rearrangements [1,2] (Scheme **A**). This auxiliary, although very versatile, exhibits certain problems in its use in the laboratory and in the scope of its applications. To provide **stereoselective control**, the method requires the use of pyrophoric and environmentally hazardous trimethylaluminum ($AlMe_3$) [1]. Also, the unwanted formation of an allylic carbocation during the 1,3-transposition prevents access to stereogenically pure tertiary alcohols (Scheme **A**).[1,2] This project would correct this situation by adding a **fluorine atom** permanently to the chiral auxiliary **8** (Scheme **B**). The research hypothesis is that this *fluoro*menthylaldehyde would provide increased stereocontrol without the need for $AlMe_3$, while allowing the preparation of stereogenic tertiary alcohols (Scheme **B**). The synthesis of the new fluorinated chiral auxiliary was achieved in good yield, and we are currently testing out our research hypothesis.



[1] Spino, C. Chem. Commun. **2011**, *47*, 4872-4883.
[2] Sterically controlled rhenium-catalyzed hydroxyl transposition. Caron-Duval, E.; Spino, C. *Arkivoc* **2023**.

Poster 37

TOWARDS CONTROL OF LMCT CATALYSIS BY RATIONAL INCORPORATION OF CHELATING LIGANDS ON HETEROLEPTIC TITANIUM COMPLEXES

Yetong Lin, Ashley Lojko, Zongle Wei, Emma Scher, Noah Schwartzapfel, and Jeffrey M. Lipshultz*

Department of Chemistry, Stony Brook University

Yetong.lin@stonybrook.edu

Here we would like to discuss an ongoing methodology research project of generating alkoxy radicals from alcohols and tuning their reactivity towards β-scission by employing the Ligand-to-metal charge transfer reactivity of a series of Ti complexes (designed and synthesized in our group). The current results strongly indicate that Ti has the potential to divert the alkoxy radicals to favor β-scission over hydrogen atom transfer, which is more favored in alkoxy radicals with a long aliphatic chain.

---

[1] You may include references at the end of the abstract if you wish.

Poster 38

INVESTIGATIONS ON THE COMPETITION BETWEEN NUCLEOPHILIC AROMATIC SUBSTITUTION AND METAL-CATALYZED CROSS-COUPLING REACTIONS IN HETEROCYCLIC AROMATIC SYSTEMS

Zheng Sonia Lin[a], Kirsten N. Hurdal[b], Rebecca L. Davis[b]*, and Jaclyn L. Brusso[a]*

[a] Department of Chemistry and Biomolecular Sciences, University of Ottawa, Ottawa, Canada; [b] Department of Chemistry, University of Manitoba, Winnipeg, Manitoba, Canada

* *Corresponding author E-mail addresses: jbrusso@uottawa.ca (J.L. Brusso) rebecca.davis@umanitoba.ca* (*R.L. Davis*)

Metal-catalyzed cross-coupling and nucleophilic aromatic substitutions (S_NAr) are common reactions used in the preparation of bioactive molecules. In our studies of heterocyclic aromatic systems of ligand frameworks of MRI contrast agents, we came across competing S_NAr and the cross-coupling pathways. Analysis of high-thoughput screening (HTS) results showed that these two pathways are affected by different variables. In our progress to improve reaction time and yield of the cross-coupling reaction, we found that having additives in the starting reaction mixture suppressed the formation of the S_NAr product and gave the cross-coupling product almost exclusively in quantitative yields. Further investigation of outliers from HTS results revealed a third hidden pathway, in which the S_NAr products were converted to the cross-coupling products, demonstrating the reversibility as well as the opportunity for di-functionalization of the system. Computational studies for the mechanistic investigations for this observed competition are performed through collaboration with Prof. Rebecca Davis (Department of Chemistry at University of Manitoba).

Poster 39

FUNCTIONALIZATION OF ALIPHATIC C-H BONDS VIA LMCT-MEDIATED RADICAL HAT FROM BENCH-STABLE TITANIUM COMPLEXES

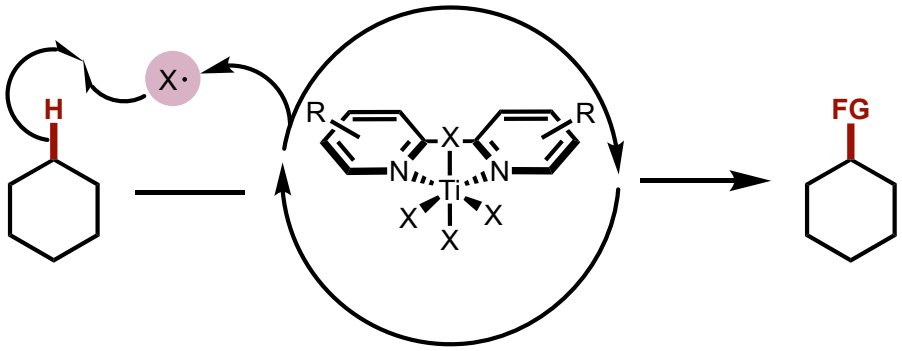
Ashley Lojko, Yetong Lin, Emma Scher, Zongle Wei, and Jeffrey Lipshultz*

Department of Chemistry, Stony Brook University, Stony Brook, New York, USA
ashley.lojko@stonybrook.edu

Heteroatom-centered radicals are powerful HAT agents due to the thermodynamic driving force of the formation of strong X-H bonds when breaking weaker C-H bonds. The electrophilicity of heteroatom radicals poses a challenge in their generation, so they are classically formed via O–heteroatom cleavage. Recently, a mild platform to form heteroatom-centered radicals through Ligand-to-Metal Charge-Transfer (LMCT) has begun to emerge. In this platform, irradiation accesses an LMCT excited state involving oxidation of heteroatom ligand and reduction of the metal center, followed by dissociating of the X-ligand to form the heteroatom radical. Common metals for this include cerium, iron, and copper, all of which have been used to mediate aliphatic C–H functionalization through HAT.

Our research has focused on developing a general LMCT catalysis platform employing titanium complexes. Titanium is quite unique among LMCT-active metals, as the high-valent Ti(IV) state is highly electrophilic but not oxidizing, while the reduced Ti(III) state is still electrophilic, but extraordinarily reducing. Accordingly, Ti-LMCT catalysis could be leveraged for both formal heteroatom-centered oxidations (i.e. chloride to chlorine radical or alkoxide to alkoxyl radical) and reduction of non-oxidizing radicals for efficient catalytic turnover.

A particularly promising scaffold is the novel family of bipyridyl-ligated $TiCl_4$ complexes. The chelating bipyridine ligands ensure bench-stability, while retaining the capacity of the Ti to function as a visible-light LMCT-active center to produce radicals capable of HAT. Through use of a model alkylation reaction, we have evidence of both chlorine radical-mediated HAT and alkoxyl-radical catalyzed HAT reactivity.



Poster 40

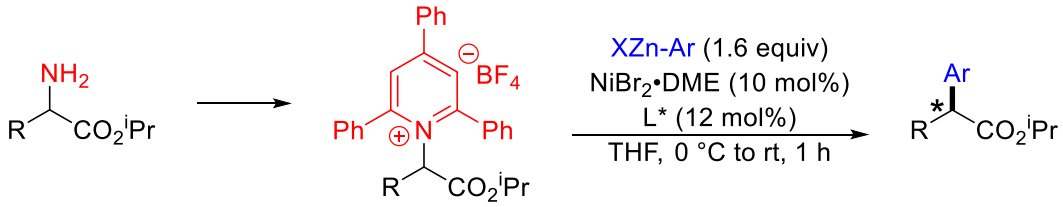
Enantioselective Negishi Arylation of Amino Acids

Windsor Lundy, J. Cameron Twitty, Steven J. Underwood, Megan E. Hoerrner, Mary P. Watson*

Department of Chemistry & Biochemistry, University of Delaware, Newark, Delaware, USA

207 McFarland Drive Newark, DE 19702, wkl@udel.edu

α-Aryl carbonyl moieties are abundant across a wide range of pharmaceuticals, especially non-steroidal anti-inflammatory drugs (NSAIDs). Although many of these drugs are commercially sold as racemic mixtures, their enantiomers can have improved pharmacokinetic properties, making access to enantioenriched α-aryl carbonyl moieties important. In addition, enantioenriched α-aryl carbonyl compounds are useful synthetic intermediates, as the carbonyl fragment can easily be elaborated. To allow for rapid construction of these structures, we have developed an enantioselective Negishi arylation of amino acid-derived alkylpyridinium salts. By utilizing a deaminative cross coupling this method takes advantage of abundant feedstock chemicals to rapidly form chiral drug-like molecules.



Poster 41

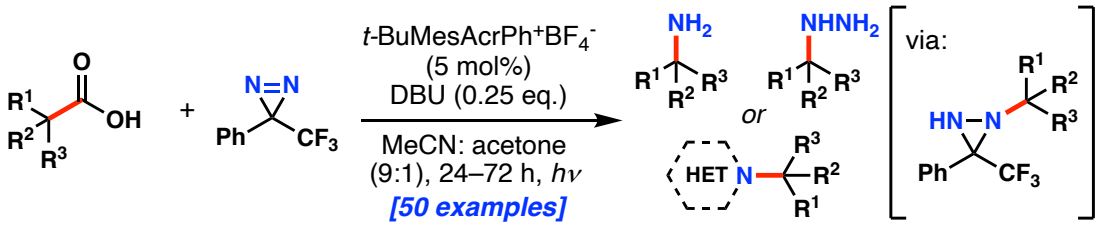
PHOTODECARBOXYLATIVE AMINATION OF CARBOXYLIC ACIDS WITH DIAZIRINES

Vishala Maharaj,[1] Paresh R. Athawale,[2] Preeti P. Chandrachud,[2] and Justin M. Lopchuk[1,2,3,*]

[1]*Department of Chemistry, University of South Florida, Tampa, FL 33620, USA*
[2]*Drug Discovery Department, H. Lee Moffitt Cancer Center and Research Institute, 12902 Magnolia Drive, Tampa, FL 33612, USA.*
[3]*Department of Oncologic Sciences, College of Medicine, University of South Florida, Tampa, FL 33612, USA*

Presenting author email*: vishalam@usf.edu*

Nitrogen containing compounds are prevalent in medicine, agriculture, and materials. Due to this importance, mild methods of late-stage functionalization via C–N bond formations are a synthetic challenge. Diazirines have been previously shown to act as direct aminating reagents in decarboxylative reactions using activated carboxylic acid derivatives such as *N*-acyloxyphthalimides. A new method of photodecarboxylative amination using diazirines, without prior carboxylic acid activation while employing mild transition metal-free photocatalytic conditions will be presented. Several classes of nitrogen containing compounds can be accessed via alkylated amines or hydrazines from a variety of primary, secondary, and tertiary diaziridine intermediates.



Maharaj, V.; Athawale, P. R.; Chandrachud, P. P.; Lopchuk, J. M. Direct catalytic photodecarboxylative amination of carboxylic acids with diazirines: Divergent access to amines, hydrazines, and nitrogen-containing heterocycles. *ChemRxiv*, **2024**, doi: 10.26434/chemrxiv-2024-4vg2s.

Poster 42

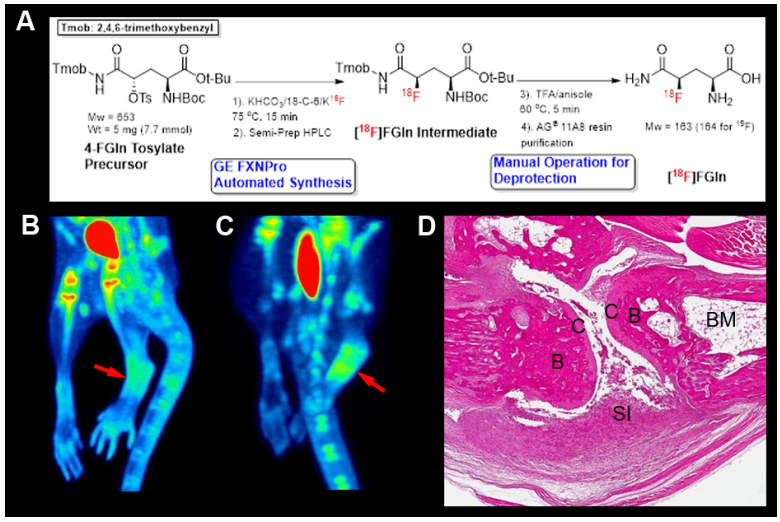
The PET imaging study of (2S,4R)-4-^{18}F-fluoro-L-glutamine in two rat inflammatory models

Min-Jeong Kim[1,2], Hari Akula[1,3], Jocelyn Marden[1], Kaixuan Li[3], Paul Vaska[4,5], and Wenchao Qu*[1,3]

[1]*Department of Psychiatry and Behavioral Health, Stony Brook University School of Medicine, Stony Brook, NY, USA*
[2]*Department of Neurology, Stony Brook University School of Medicine, Stony Brook, NY, USA*
[3]*Department of Chemistry, Stony Brook University, Stony Brook, NY, USA*
[4]*Department of Radiology, Stony Brook University School of Medicine, Stony Brook, NY, USA*
[5]*Department of Biomedical Imaging, Stony Brook University School of Medicine, Stony Brook, NY, USA*

Corresponding author:
Wenchao Qu, wenchao.qu@stonybrookmedicine.edu

(*2S,4R*)-4-^{18}F-fluoro-L-glutamine (^{18}F-FGln) has shown promise as a metabolic imaging marker in various types of cancer. A recent study in humans showed that ^{18}F-FGln is a more specific marker for monitoring the metabolic activities of cancer cells compared to ^{18}F-FDG. Although ^{18}F-FGln PET has not yet been studied in inflammation, there has been ample evidence of the fact that the metabolism of major inflammatory cells relies heavily on glutamine. In this study, we aimed to explore the potential utility of the ^{18}F-FGln as a novel metabolic imaging marker for inflammation in rat models of acute and chronic inflammatory conditions.



[1] Zhou, R., Pantel, A. R., Li, S., Lieberman, B. P., Ploessl, K., Choi, H., Blankemeyer, E., Lee, H., Kung, H. F., Mach, R. H., and Mankoff, D. A. (2017) [(18)F](2S,4R)4-Fluoroglutamine PET Detects Glutamine Pool Size Changes in Triple-Negative Breast Cancer in Response to Glutaminase Inhibition, *Cancer Res 77*, 1476-1484.

Poster 43

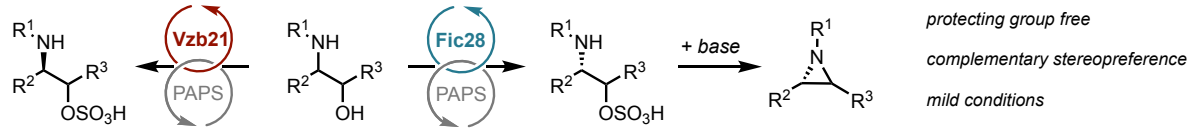
CRYPTIC SULFOTRANSFERASES FOR AZIRIDINE FORMATION

Sabina J. Maurer and Monica E. McCallum*

Department of Chemistry, University of Pennsylvania, Philadelphia, PA, USA 19104
sjmaurer@sas.upenn.edu

Aziridines are small reactive nitrogen-containing heterocycles with applications in medicinal and synthetic chemistry. While many methods for aziridine synthesis exist, most rely on harsh reagents and conditions incompatible with green chemistry principles. By identifying and adapting native enzymes involved in the biosynthesis of aziridine-containing natural products, we have developed a method of chemoenzymatic aziridination, offering a mild alternative to existing methodologies.

Recently, the biosyntheses of bacterially derived aziridine-containing natural products ficellomycin, vazabitide A, and azinomycin A were disclosed, revealing a two-step aziridination process. Sulfation of a 1,2-amino alcohol followed by intramolecular displacement forms the aziridine. Our research has characterized the non-native activity of these “cryptic" sulfotransferases, discovering unprecedented stereoselectivity and promiscuity. By optimizing a basic workup procedure, we can install aziridines on a variety of amino alcohols without the use of protecting groups. With this platform in hand, we are developing larger scale whole cell reactions alongside a native cofactor recycling system for green aziridination.



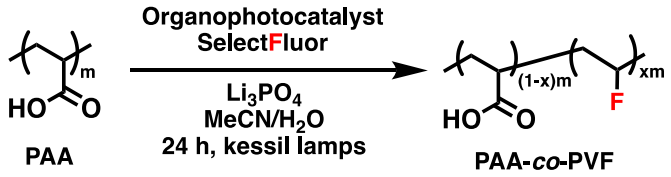
Poster 44

ORGANOPHOTOCATALYZED DECARBOXYLATIVE FLUORINATION OF POLY(ACRYLIC ACID)

Pankti Mehta[1, 2], Max B. Levy[1, 2], Michael R. Talley[1, 2], Mary P. Watson[1, 2, 3]

[1] Department of Chemistry & Biochemistry, University of Delaware, Newark, Delaware, USA
[2] Center for Plastics Innovation, University of Delaware, Newark, Delaware, 19716, United States
[3]Center for Research in Soft matter and Polymers (CRiSP), University of Delaware, Newark, Delaware, 19716, United States
panktim@udel.edu

Poly(acrylic acid) (PAA) is a widely used polymer that predominantly finds application as a superabsorbent polymer for diapers and other single-use hygiene products. Although single-use hygiene products improve our quality of life, they generate nearly 3.5 million tons of waste, which presents an ongoing challenge for both current and future generations. As a result of this issue, there has been growing interest in recycling and upcycling polymer waste. Because superabsorbent polymers are challenging to recycle as they have been designed to withstand degradation, we focused on valorization via chemical modification of PAA. Post-polymerization modification of PAA by photoredox methods has been demonstrated. Photoredox decarboxylative fluorination of PAA using several organic photocatalysts allows for the tunable synthesis of copolymers of poly(acrylic acid) and poly(vinyl fluoride), another highly valued commodity polymer. Conveniently, low and high levels of vinyl fluoride (VF) content can be achieved by varying the concentration of SelectFluor, the identity of the photocatalyst, and the duration of irradiation, allowing the synthesis of copolymers with tunable properties.



Poster 45

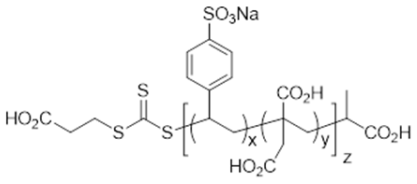
COMMERCIAL HEPARINS AND SYNTHETIC DERIVATIVES AS POTENTIAL IMMUNOMODULATORS IN AN IN VITRO METASTATIC CONTEXT

Katrin Nekipelov * †, Lukas Gockel †, Martin Schlesinger †, Vito Ferro ‡, Gerd Bendas †

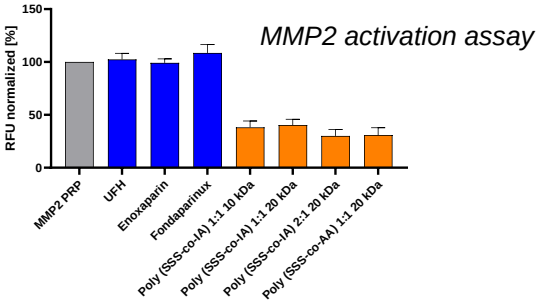
† *Pharmaceutical Institute, University of Bonn, 53121 Bonn, Germany*
Katrin.nekipelov@uni-bonn.de

‡ *School of Chemistry and Molecular Biosciences, University of Queensland, Brisbane, Queensland 4072, Australia*

Thromboses are considered a frequently underestimated risk and reason for mortality in metastatic tumor diseases, which at least partially are based on activation of platelets by cancer cells. Low molecular weight heparin (LMWH) is the guideline-based anticoagulant in thromboprophylaxis and treatment of cancer patients. The ongoing debate whether heparin can act anti-tumorigenic beyond anticoagulation is further complicated by the heterogenous structure of heparin as a natural product. To tackle this issue and allow S/A/R, synthetic non-glycosidic heparin mimetics have been introduced [1], which are copolymers of sodium 4-styrenesulfonate and itaconic acid (Poly(SSS-*co*-IA)) with molecular masses between 10 and 20 kDa. Comparing these mimetics with commercial heparins, this project is focused on platelet-tumor cell interaction and platelet-induced immune deregulation, which has not been addressed yet. The research question is how tumor-activated platelets induce immune-suppressive activities and whether heparin derivatives can reconstitute the immune balance under *in vitro* conditions. The investigations address cytokines and proteins that have been shown to have immunosuppressive effects and are released in higher quantities from activated platelets, whereupon TGF-β and MMP2 were selected. In the MMP2 activity assay, the synthetic polymers (250 µg/mL) showed superiority in the inhibition of this enzyme. While commercial heparins (adopted therapeutic concentrations) showed no effect on the activity of MMP2, synthetic heparin mimetics inhibited the activity significantly. When investigating the impact of TGF-β on the differentiation of $CD4^+$ cells into regulatory T-cells, copolymers with a lower molecular mass showed a lower differentiation rate, suggesting an immunomodulatory effect. Fondaparinux, the smallest commercial heparin, confirmed this result. Binding affinity data, which were recorded in the further course of the investigations, largely underlined this. In summary, LMWH and heparin mimetics can reverse the immunosuppressive activities of platelets and thus provide a novel immuno-oncological perspective for their application in oncology.



Poly(SSS-co-IA)



[1] Gockel, L. M.; Nekipelov, K.; Ferro, V.; Bendas, G.; Schlesinger, M. Tumour cell-activated platelets modulate the immunological activity of $CD4^+$, $CD8^+$, and NK cells, which is efficiently antagonized by heparin *CII* **2022**, *71* (10), 2523–2533

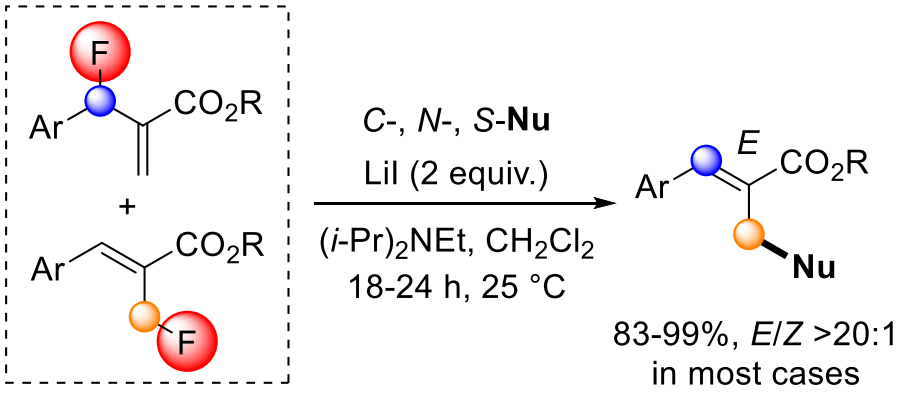
Poster 46

REGIOCONVERGENT NUCLEOPHILIC SUBSTITUTIONS WITH MORITA-BAYLIS-HILLMAN FLUORIDES

Eryn Nelson, Jeffrey S. S. K. Formen, Ciarán C. Lynch, Andi Yuan, Sarah E. Steber, Christian Wolf*

Department of Chemistry, Georgetown University, Washington, DC, USA
cw27@georgetown.edu

The increasing prevalence of fluoro-pharmaceuticals has been met with a growing number of synthetic routes and new methodologies for C-F bond functionalization. To this end, we discovered that lithium iodide enables regioconvergent C-F bond functionalization of isomeric Morita-Baylis-Hillman fluorides with a variety of nucleophiles. The regioselectivity of this reaction differs from previous work and allows both isomers to be utilized, which are typically obtained as a mixture from their corresponding alcohols. Nucleophilic substitutions with carbon, sulfur, and nitrogen nucleophiles yield multifunctional compounds in high yields and with good to high diastereoselectivities at room temperature. The possibility of palladium-catalyzed enantioselective allylation is also demonstrated.



Poster 47

DEVELOPMENT OF A VISIBLE-LIGHT-MEDIATED *AZA* PATERNÓ-BÜCHI REACTION USING SULFONYLIMINES

Cody H. Ng**,** Emily R. Wearing, Dominique E. Blackmun, Julia C. Donovan, Madeleine A. Gonley, Corinna S. Schindler*

Department of Chemistry, University of Michigan, Ann Arbor, Michigan, USA
codyng@umich.edu

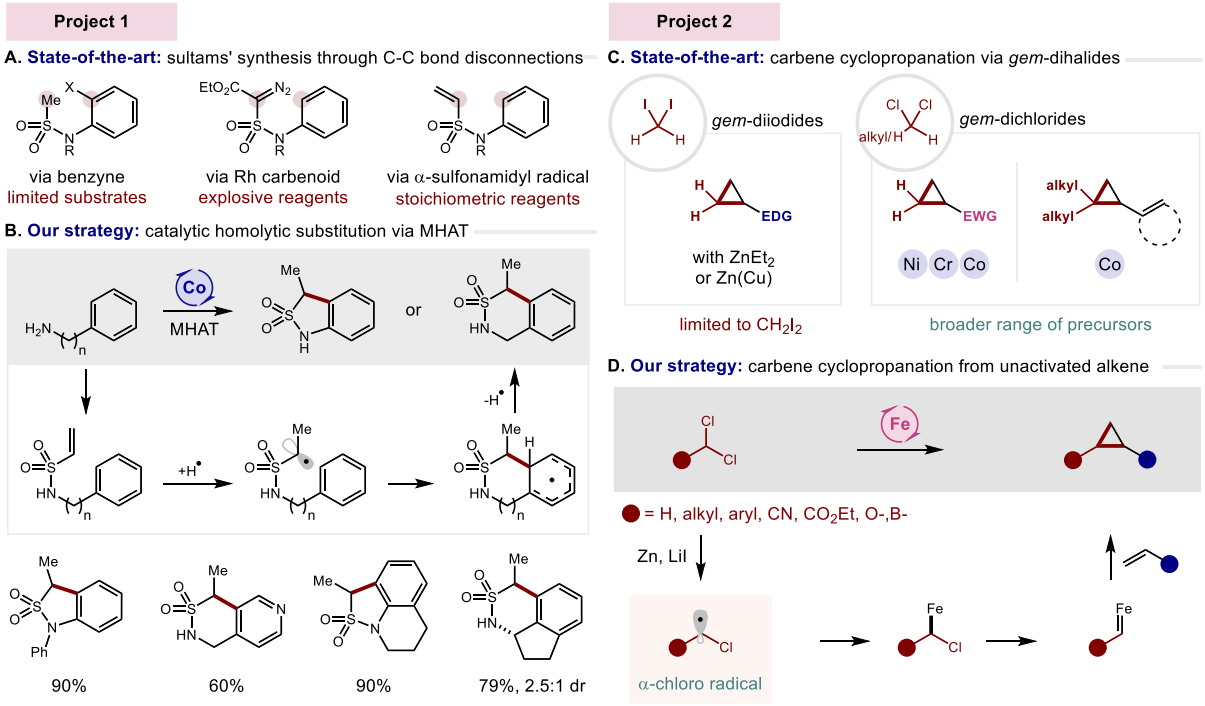
Azetidines are four-membered saturated nitrogen heterocycles that have recently gained interest as new building blocks for compounds with diverse industrial applications. However, extensive exploration of azetidines in this context has remained limited due to the synthetic challenges associated with accessing them. The most atom economical method to access azetidines is arguably via the *aza* Paternó-Büchi reaction, which is a [2+2]-cycloaddition between an imine equivalent and an alkene. Recently, we have discovered that acyclic sulfonylimines are efficient reaction partners in a visible-light-mediated *aza* Paternó-Büchi reaction, enabling direct access to new azetidine products.

Harnessing Radicals: for Homolytic Aromatic Substitution and Cyclopropanation

Khue N. M. Nguyen, Henry C. Sise, James H. Herbort, Duong T. Ngo, Mohamed Elsayed, David A. Nagib*
Department of Chemistry & Biochemistry, The Ohio State University, USA
Email: nguyen.2263@buckeyemail.osu.edu

N-heterocycles are frequently found in FDA-approved small molecule drugs. In particular, sultams have been found to have a wide range of antibiotic reactivity. The synthesis of this motif where the nitrogen is adjacent to the benzene ring has been reported previously, each method possesses challenges, namely complex starting material syntheses, harsh conditions, or high amount of side reactions. Inspired by syntheses via oxidative cyclization, we employed vinyl sulfonamide as the chosen precursor. To overcome the needs to employ stoichiometric reagents and strong oxidants, we combined metal-hydride hydrogen atom transfer (MHAT) and radical addition. As a result, the reaction is catalytic in cobalt with broad functional group tolerance.

Additionally, cyclopropanes have been a rising popular bioisostere in medicinal chemistry. Modern approaches modified the reactive *gem*-diiodides into *gem*-dichlorides, allowing a variety of derivatives for the carbene precursors. These previous strategies focused on electron-poor alkene and vinyl or styrene-like alkenes. I proposed forming α-chloro radical and trapped by Fe catalyst, followed by α-Elimination of the halides to form a metal carbenoid, which reacts with alkenes to form cyclopropanes. This work provides a complementary approach towards electronically unbiased and non-styrene alkenes, along with a wider range of *gem*-dichlorides.



Poster 49

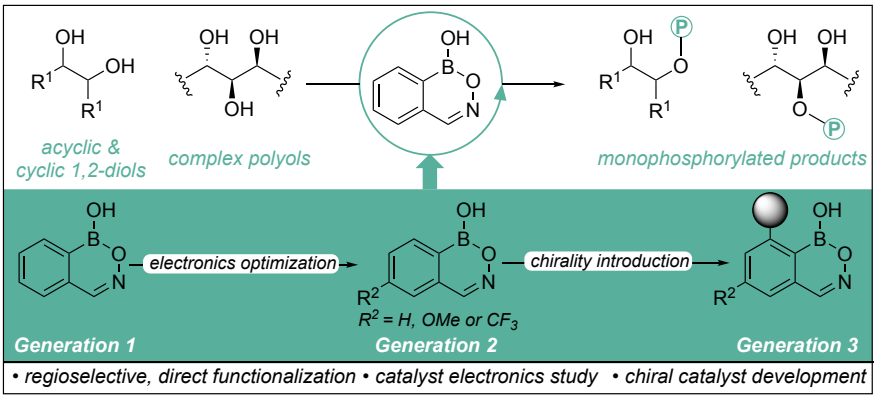
TOWARDS ENANTIOSELECTIVE HEMIBORONIC ACID CATALYZED DIRECT MONOPHOSPHORYLATION OF POLYOLS

Geneviève F. O'Keefe, Dalida L. Akl and Dennis G. Hall*

Department of Chemistry, University of Alberta, Edmonton, AB, T6G 2N4, Canada
gokeefe@ualberta.ca

The phosphorylation of organic molecules is a fundamentally essential chemical transformation.[1] For instance, phosphorylating a single hydroxy group (–OH) on a protein's serine or threonine residue can drastically alter its properties, activating its biological function, therefore playing a critical role in processes like cell signaling and signal transduction. Using kinases, nature is able to phosphorylate complex biomolecules with high selectivity (chemo-, regio-, enantio-). However, the adoption of biocatalytic strategies for the preparation of therapeutic and agrochemical compounds has been limited due to active site specificity requiring substrates similar to the native ligand.[2] Current synthetic approaches fail as enzymatic mimicks as they require impractical conditions, achieve suboptimal yields, and present poor tolerance in substrate variability. Furthermore, these challenges are amplified when multiple –OH groups are present, as state-of-the-art approaches require protecting groups to mediate chemo- and regioselectivity. For this reason, there is high demand for methods that allow for the selective, direct, and catalytic monophosphorylation of diols and complex polyols.

Due to their ability to form reversible covalent bonds with –OH groups, hemiboronic acids present the unique capacity to catalytically activate alcohols in a nucleophilic manner.[3] Preliminary success of this approach for –OH group monophosphorylation was recently exemplified with a benzoxazaborine-catalyzed regioselective phosphorylation of a limited scope of 1,2-diols.[3] To expand the application of this method to a range of polyols, a systematic catalyst optimization was devised. Moreover, the development of an easily accessed chiral catalyst is ongoing.



[1] Ouellette, E. T. *et al. J. Org. Chem.* **2021**, *86*, 7450–7459
[2] Adams, J. P. *et al. Adv. Synth. Catal.* **2019**, *361*, 2421–2432
[3] Rygus, J. P. G.; Hall, D. G. *Nat. Commun.* **2023**, *14*, 2563

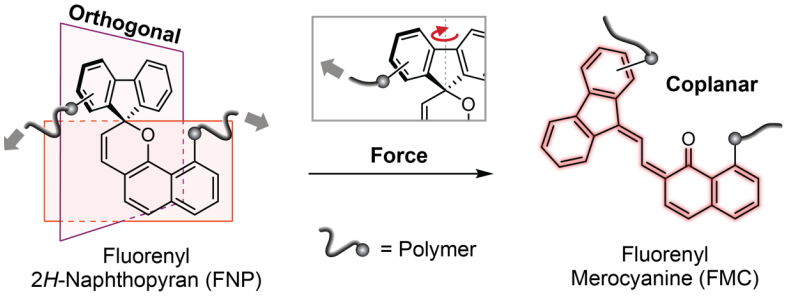
Poster 50

MECHANOCHEMICAL REACTIVITY OF A FLUORENYL NAPHTHOPYRAN MECHANOPHORE

Skylar K. Osler, Maxwell J. Robb*

Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, CA, USA
mrobb@caltech.edu

Mechanophores are stress-sensitive molecules that undergo productive chemical transformations in response to mechanical force, which is transduced *via* covalently-bound polymer chains. The activation of mechanophores has been demonstrated to trigger a wide variety of reactions including retro cycloadditions, electrocyclic ring-opening, homolytic bond scission, and heterolytic bond scission. Remarkably, the reaction pathways that are accessed under force often diverge from those observed under thermal or photochemical stimulus, which has inspired extensive investigations into the structure-activity relationships of mechanophores. In addition to the extension of individual bonds, molecular elongation can apply a torsional force to rotate individual components of a mechanophore and facilitate the desired chemical reaction. We were interested in investigating the role of the effective torsional force on activation rates of mechanophores. We designed a series of rigid fluorenyl naphthopyran (FNP) mechanophores that contain a fluorene subunit (rotator) and naphthyl subunit (stator) and investigated their relative reactivities using computational tools. The activation rates of the FNP mechanophores were found experimentally using ultrasonication experiments performed on polymer solutions. Our results demonstrate that varying polymer attachment position on the fluorene subunit impacts coupling between the external force vector and the effective torsional force, resulting in significant differences in activation rate. This study offers new insight into the factors that govern the reactivity of molecules under force.



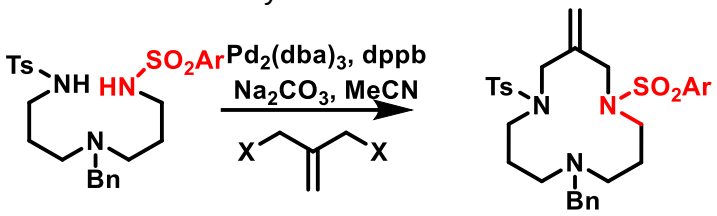
Poster 51

DESIGN, SYNTHESIS, AND EVALUATION OF COVALENT CADA ANALOGUES AS POTENT TLR4 DOWNMODULATOR FOR THE TREATMENT OF OPIOID USE DISORDER

Yetunde Oyesakin[1], Ryan Olsen[1], Thomas Gould[2], and Thomas Bell[1]*

[1]Department of Chemistry, University of Nevada, Reno
[2]Department of Cell and Molecular Biology, University of Nevada, Reno
Department of chemistry, University of Nevada, Reno; yoyesakin@gmail.com

Opioid use disorder (OUD) is a significant health challenge affecting more than thirty million individuals globally with an alarming death rate of one hundred and eighty-seven people per day. While the current drugs for OUD have been proven to be effective in managing this disorder, their prolonged use causes life threatening arrythmia and discontinuation often results in relapse, leading to fatal drug overdose. Therefore, there is a need to develop new drug molecules for this disorder. In this study, we detail the design and synthesis of a series of macrocyclic CADA analogs with 1,5,9-triazadodecane core structure as potent and selective TLR4 inhibitors. Our synthesis strategy involves exploring the Tsuji-Trost N-allylation reaction to generate the macrocyclic intermediate, followed by late-stage functionalization to produce various covalent analogs. Notably, employing the Tsuji-Trost reaction for macrocyclization resulted in a 25% increase in yield compared to the previously utilized Richman-Atkins cyclization method.



So far, approximately 85 different covalent CADA analogues (reversible and Irreversible) have been synthesized and screened in HEK-Blue human TLR4 cells. This effort has identified six potent TLR4 downmodulators, marking significant progress in our pursuit of novel therapies for OUD. Our work highlights the potential of targeting SP-dependent mechanisms in developing safer and more effective treatments for opioid addiction, addressing a critical need in healthcare.

Poster 52

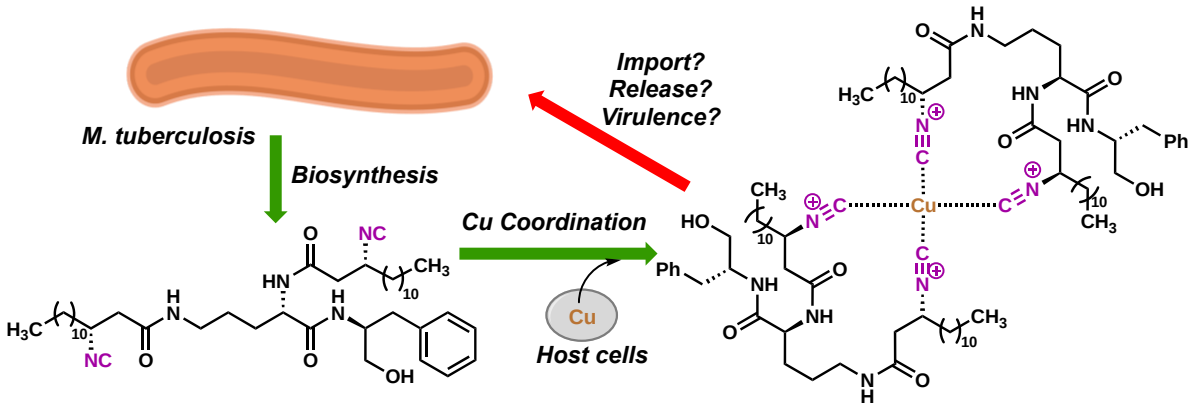
SYNTHESIS OF DIISONITRILE CHALKOPHORE NATURAL PRODUCTS AND ANALOGUES TO ELUCIDATE THEIR FUNCTIONS IN *M. TUBERCULOSIS*

Pooja B. Pandya[1,2], Chad E. Hatch, PhD[2], John A. Buglino, PhD[3], Michael S. Glickman, MD[3], and Derek S. Tan, PhD[1,2]*

[1]*Pharmacology PhD Program, Weill Cornell Medicine, New York, New York, USA*
[2]*Chemical Biology Program, Sloan Kettering Institute, Memorial Sloan Kettering Cancer Center, New York, New York, USA*
[3]*Immunology Program, Sloan Kettering Institute, Memorial Sloan Kettering Cancer Center, New York, New York, USA*

pandyap@mskcc.org

Tuberculosis, the disease caused by *Mycobacterium tuberculosis*, is a leading cause of death worldwide. While first-line treatments are effective for many patients, multidrug-resistant tuberculosis poses a continued threat to global public health. New approaches are needed to provide effective chemotherapy against these drug-resistant pathogens. Extensive evidence indicates that *M. tuberculosis* must acquire copper from the host during infection. Therefore, nutrient acquisition by *M. tuberculosis* presents an attractive target for novel antibiotics. Along these lines, copper-chelating diisonitrile chalkophore natural products have recently been identified in *M. tuberculosis* and implicated in copper acquisition. *In vitro* and *in vivo* studies have demonstrated that diisonitriles play a critical role in copper homeostasis and virulence in *M*. *tuberculosis*, but the molecular mechanisms by which bacteria use diisonitriles to uptake copper are unknown. Our aim is to investigate the structures and functions of these diisonitriles to determine their roles in bacterial physiology and virulence. Toward this end, we have developed a modular synthetic platform that allows efficient construction of diisonitrile natural products and diverse analogues. We are now using these synthetic chalkophore analogues to characterize the metal-binding properties of these molecules, to identify the bacterial proteins involved in chalkophore-mediated copper transport, and to elucidate their roles in virulence.



Poster 53

BUSHY-TAILED QACs AND QPCs: THE DEVELOPMENT OF MULTICATIONIC QUATERNARY AMMONIUM AND PHOSPHONIUM COMPOUNDS WITH A HIGH DEGREE OF ALKYL CHAIN SUBSTITUTION

Diana Rachii,[†] Zachary E. A. Toles,[†] Laura M. Thierer,[†] Alice Wu,[†] Elise Bezold,[‡] Christian A. Sanchez,[‡] Germán G. Vargas-Cuebas,[§] Taylor M. Keller,[‖] Patrick J. Carroll,[‖] William M. Wuest,*[‡] Kevin P.C. Minbiole*[†]

[†] *Department of Chemistry, Villanova University, Villanova, PA 19085, USA*
[‡] *Department of Chemistry, Emory University, Atlanta, GA 30322, USA*
[§] *Department of Microbiology and Immunology, Emory University, Atlanta, GA 30322, USA*
[‖] *Department of Chemistry, University of Pennsylvania, Philadelphia PA 19104, USA*
** Corresponding authors*

diana.rachii@villanova.edu

Quaternary ammonium compounds have served as a first line of protection for human health as surface disinfectants and sanitizers for nearly a century.[1] However, increasing levels of bacterial resistance have spurred the development of novel QAC architectures.[2] In light of the observed reduction in eukaryotic cell toxicity when the alkyl chains on QACs are shorter in nature (≤10C), we prepared 47 QAC architectures that bear multiple short alkyl chains appended to up to 3 cationic groups, thus rendering them "bushy-tailed" multiQACs.[3] Antibacterial activity was strong (often ~1-4 μM) in a varied set of bushy-tailed architectures, though observed therapeutic indices were not significantly improved over QAC structures bearing fewer and longer alkyl chains. While quaternary phosphonium compounds (QPCs, analogs to QACs) have found industrial applications in improving the activity and transport of bioactive agents,[4] the development of QPCs as disinfectants and sanitizing agents is still at an early stage. Taking advantage of our recent discoveries in multicationic QPCs, which show the ability to irradiate bacterial strains that have otherwise deemed pan-resistant,[5] we continue to explore the development of novel "bushy-tailed" QPC

---

[1] Dan, W.; Gao, J.; Qi, X.; Wang, J.; Dai, J. *Eur. J. Med. Chem.* **2022**, *243*, 114765.
[2] Boyce, J. M. *Antimicrob. Resist. Infect. Control.* **2023**, *12 (32),* 1-14.
[3] Toles, Z. E. A.; Thierer, L. M.; Wu, A.; Bezold, E.; **Rachii, D.**; Sanchez, C.A.; Vargas-Cuebas, G. G.; Keller, T. M; Carroll, P. J.; Wuest, W. M.; Minbiole, K.P.C.[Manuscript submitted for publication].
[4] Wang, J.; Li, J.; Xiao, Y.; Fu, B.; Qin, Z. *RSC Med. Chem.* **2020**, *11*, 858–875.
[5] Michaud, M.; Allen, R.; Morrison-Lewis, K.; Sanchez, C.; Minbiole, K.P.C.; Post, S.; Wuest, W. M. *ACS Infectious Diseases*. **2022**, *8*, 2307–2314.

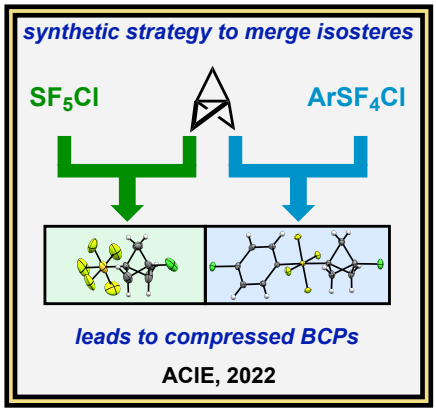
Poster 54

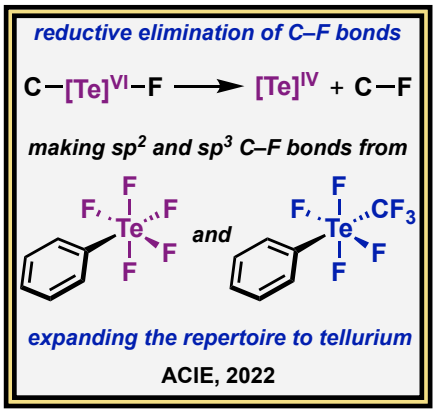
SYNTHESIS, STRUCTURE, AND REACTIVITY OF COMPOUNDS BEARING THE SF_5 GROUP AND ITS CONGENERS

Abbey N. Ragan, Yannick Kraemer, and Cody Ross Pitts*

Department of Chemistry, University of California Davis, Davis, California, USA
anragan@ucdavis.edu

Organofluorine compounds have become increasingly prevalent in medicinal chemistry, with 20-25% of current drugs on the market contain at least one fluorine. Many of these compounds owe their fluorines to the CF_3 group- a group that has garnered much more attention recently as new reagents and methods have been developed. Our group focuses on a bioisostere of CF_3- the SF_5 group. This group is larger, more lipophilic, and also more electronegative than CF_3 giving it its name "super trifluoromethyl group". With a recent increase in accessibility to typical SF_5 transfer reagent, SF_5Cl, our group has been able to utilize it in order to synthesize hybrid bioisosteres through harnessing strain-release functionalization.[1] Our work has also expanded into other perfluorinated compounds, including the discovery that $PhTeF_5$ and $PhTeF_4CF_3$ are both capable of reductively eliminating C–F bonds in the presence of superacidic media.[2]





---

[1] Y. Kraemer, C. Ghiazza, **A. N. Ragan**, S. Ni, S. Lutz, E. K. Neumann, J. C. Fettinger, N. Nöthling, R. Goddard, J. Cornella,* C. R. Pitts* *Angew. Chem. Int. Ed.* **2022**, *61*, e202211892.

[2] **A. N. Ragan**, Y. Kraemer, W.-Y. Kong, S. Prasad, D. J. Tantillo,* C. R. Pitts* *Angew. Chem. Int. Ed.* **2022**, e202208046.

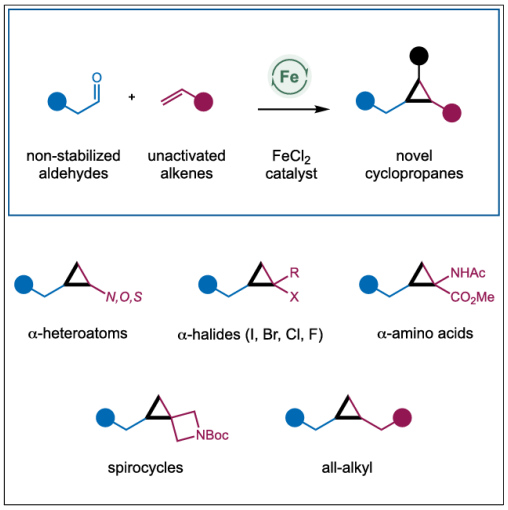
Poster 55

CYCLOPRANATION OF UNACTIVATED ALKENES WITH NONSTABILIZED CARBENES

Emma K. Ralph, Bethany M. Demuynck, Lumin Zhang, David A. Nagib*

Department of Chemistry & Biochemistry, The Ohio State University, Columbus, Ohio, USA
Ralph.82@osu.edu

Cyclopropanes are the 6th most common ring in medicines and the 2nd most common alicycle, making them very useful in medicinal chemistry. Thus, it is very important to develop efficient synthetic methods that can be used with a wide variety of functional groups. The previously developed reaction conditions[1] were optimized to involve an $FeCl_2$-catalyzed cyclopropanation that employs aliphatic aldehydes as carbene precursors. This system also utilizes a wide range of alkenes to form products with alkyl, benzyl, allyl, halide, and heteroatom substituents, as well as spirocyclic, and fused bicycles that were previously inaccessible. Robustness exploration, mechanistic studies, and competition experiments were also done to further explore the system. In conclusion, a robust reaction with high functional group tolerance was developed[2], resulting in a wide range of substituted cyclopropanes that expand the synthetic tools used to access medicinally relevant molecules.



[1] Zhang, L.; DeMuynck, B. M.; Paneque, A. N.; Rutherford, J. E.; Nagib, D. A. *Science*. **2022**, 377, 649-654.
[2] Demuynck, B. M.; Zhang, L.; Ralph, E. K.; Nagib, D. A. *Chem*. **2024**, 10(3), 1015-1027.

Poster 56

VISIBLE LIGHT MEDIATED PHOTOCATALYTIC REDUCTION OF ARYL SULFONATES

Kasmier Reece and Rashanique Quarels

Rowan University
201 Mullica Hill Rd, vicios22@students.rowan.edu, quarels@rowan.edu

Protecting groups play a huge role in synthetic organic chemistry. The addition and elimination of groups to preserve a key functional group throughout a synthesis may require harsh conditions, such as strong acids or bases, and prove to be costly. Tosylates in particular are a common alcohol protecting group that also serves as a good leaving group. However, reagents used for deprotection of aryl tosylates such as samarium iodide, palladium, or trimethylsilyl chloride in refluxing solvent provide moderate yields and are not compatible with many functional groups. More recently, sulfonates have been explored as photoremovable protecting groups. We hypothesize that the use of organic photocatalysts can be used to deprotect aryl tosylates under visible light photocatalytic conditions. These mild conditions to cleave the S-O tosylate bond to generate phenols are an untapped space in organic chemistry with the potential to be used in late-stage deprotections.

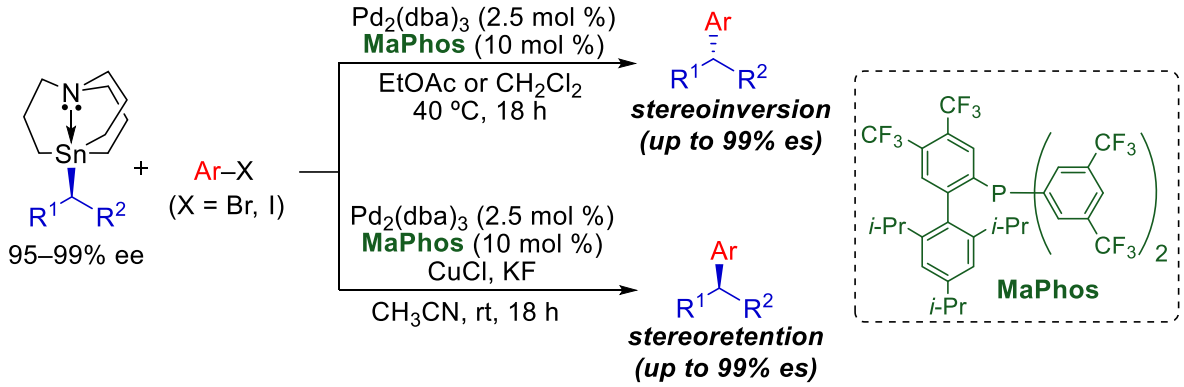
Poster 57

COPPER-CONTROLLED STEREODIVERGENT STILLE CROSS-COUPLING REACTIONS

Glenn Ralph, [†] Asha Reghuvaran Santha, [†,‡] Nana Agyemang, [†,‡] Xinghua Ma, [†,‡] Daniel Zuschlag, [†,‡] Benjamin Murray, [†,‡] Mark R. Biscoe*, [†,‡]

[†]Department of Chemistry & Biochemistry, The City College of New York (CCNY), New York, New York 10031, USA
[‡]Ph.D. Program in Chemistry, The Graduate Center of the City University of New York (CUNY), New York, New York 10016, USA
areghuvaransantha@gradcenter.cuny.edu

Using a new phosphine ligand (MaPhos), we have developed a stereodivergent Stille cross-coupling reaction of unactivated enantioenriched secondary alkylcarbastannatrane nucleophiles and aryl halide electrophiles. The stereochemical outcome of this C(sp^3)–C(sp^2) cross-coupling reaction is determined by the inclusion or omission of CuCl as a co-transmetalating agent. When CuCl is included as an additive, the stereoretentive transmetalation pathway prevails; when CuCl is omitted, the stereoinvertive transmetalation pathway prevails. The flexibility of MaPhos ligand to accommodate both stereoretentive and invertive pathways is a highlight of this study. Substrate scope, solvent effects, and insights into transmetalation will also be discussed.



• *Broad substrate scope* • *Unactivated alkyltin nucleophiles* • *Good/excellent stereocontrol*
• *C(sp^3)–C(sp^2) cross-coupling*

Poster 58

EXPANSION OF LPXC INHIBITORS INTO THE UDP BINDING SITE

Danielle Rosenberger[1], Melike Akoglu[1], Aleena I. Ali[1], Christopher Corbo[2], Alyssa Pollard[1], Robert Rizzo[3], Peter J. Tonge[1]

Center for Advanced Study of Drug Action, Department of Chemistry[1], Biochemistry and Structural Biology[2], and Applied Mathematics and Statistics[3], Stony Brook University, Stony Brook, New York, USA
danielle.rosenberger@stonybrook.edu

UDP-3-O-(R-3-hydroxymyristoyl)-N-acetylglucosamine deacetylase (LpxC), a pivotal enzyme catalyzing the first committed step in Lipid A biosynthesis, has been identified as a validated antibacterial target. Despite its significance, no LpxC inhibitor has successfully completed clinical trials due to safety concerns. We propose a novel approach to address these challenges by focusing on the development of LpxC inhibitors with extended residence time on the enzyme, allowing sustained enzymatic inhibition even at lower drug concentrations. By employing a combination of experimental and computational methods, we aim to synthesize innovative inhibitors that form a long-lasting enzyme-inhibitor complex, which is expected to enhance the post-antibiotic effect (PAE) and improve overall antibacterial efficacy.

Poster 59

Chemical Synthesis of Linker to Small Molecule Bioconjugate to Enhance Surface Retention to Cells

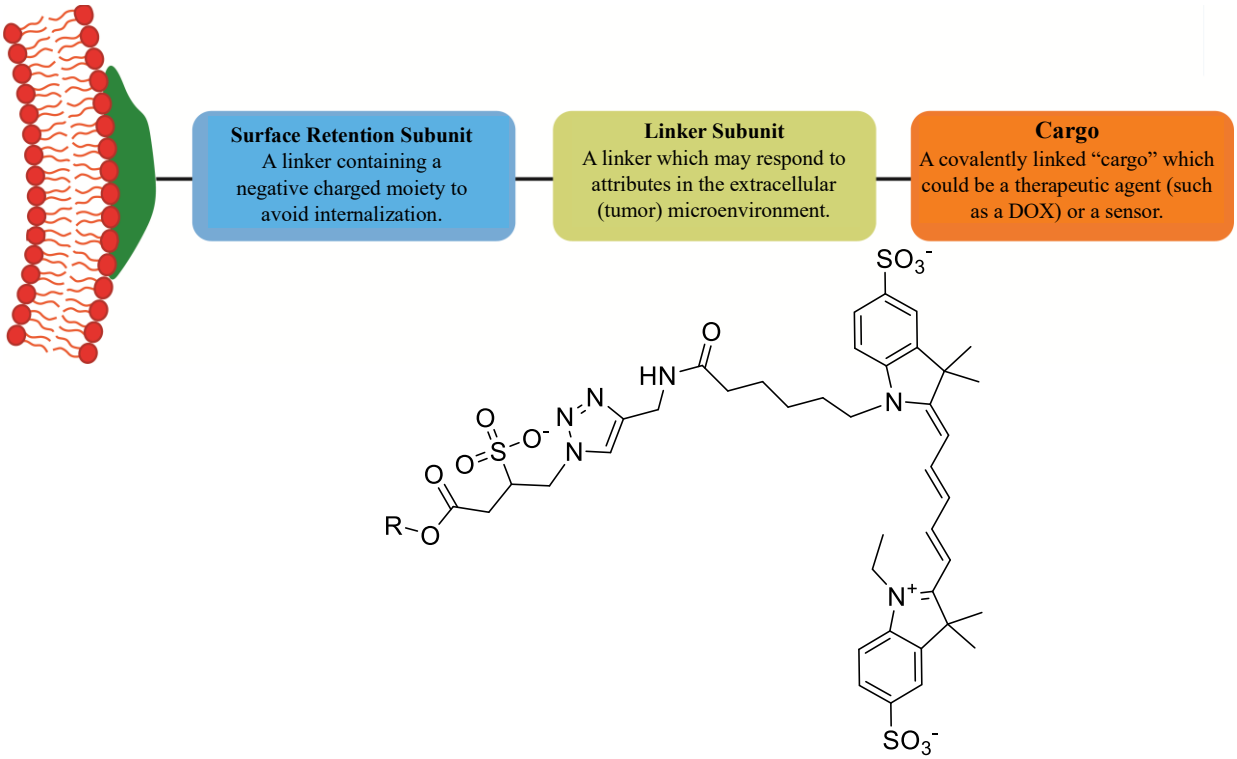
Josiah Sanchez, Aimee Shen, Kyle Winters, Michelle E. Farkas*

Department of Chemistry, University of Massachusetts, Amherst, Amherst, Massachusetts, United States of America, jesjsanchez@umass.edu

Cellular delivery platforms aim to circumvent challenges presented with traditional drug delivery methods. A multitude of delivery systems have been developed. The issue with this traditional system is either they are not specific enough or pose issues with the leakage of cargo and cargo-based toxicity.

A cellular carrier largely addresses the issues of non-specificity as it capitalizes off the biological nature of cells. Functionalizing the surface also aims to resolve the issues of cargo leakage and cargo-to-carrier toxicity. While we functionalize the surface of the cell, internalization can occur over extended periods of time.

We hypothesize that incorporating negative charge on cargo will minimize internalization because of charge repulsion between the cargo and cell surface. We are interested in improving surface retention via a linker which features a negatively charged sulfonate group that, once attached, will be located between the cell surfaces and the cargo. In preliminary studies, we conjugated Cyanine5 (Cy5) in various charged iterations to the cells to assess cargo retention to the surface over time. Cy5 is a fluorescent dye and serves as a traceable surrogate for a cargo molecule, which will be replaced with therapeutics in the future. The synthetic scheme involves a modular installment the aforementioned retention linker involving click chemistry. I synthesized, purified, and characterized the retention linker and Cy5 via ESI-MS, flash chromatography, and analytical HPLC.



Poster 60

SYNTHESIS OF SMALL-MOLECULE PAC1R ANTAGONISTS TO TREAT CHRONIC PAIN AND ANXIETY

Stella Rose Schneeberg, Rebecca Bogart, Islamiyat Lawal, Victor May, Jianing Li, Matthias Brewer*

Department of Chemistry, University of Vermont, Burlington, Vermont, USA
srschnee@uvm.edu

Due to its mediation in a variety of biological activities, the Pituitary Adenylate Cyclase-Activating Polypeptide (PACAP)-selective PAC1 receptor (PAC1R) has emerged as a relevant pharmaceutical target. PAC1R is a class B G protein-coupled receptor (GPCR). GPCRs are the largest and one of the most important receptor families for drug discovery, and class B (vasoactive intestinal peptide (VIP)/secretin/glucagon class) is one of 5 major GPCR classes. PAC1R has been demonstrated to play crucial roles in central and peripheral nervous systems, and activation of the receptor has been shown to initiate different downstream signaling pathways to maintain functional homeostasis. PAC1R's role as a pharmaceutical target is two-fold: agonism may enhance its mitigation in neurodegenerative disorders and maintain energy balance functions in metabolism; while antagonism can potentially treat stress-related disorders, chronic pain/migraine, and other behavioral abnormalities. Our focus lies in developing *antagonists* for the PAC1 receptor. Currently, rational design of PAC1R-selective peptide or small-molecule therapeutics is largely hindered by a lack of structural information regarding PAC1R activation mechanisms. Presented herein are collaborative efforts toward a better understanding of the receptor and its interactions, and the progress toward the development of a small-molecule PAC1R-selective therapeutic to treat chronic pain and anxiety.

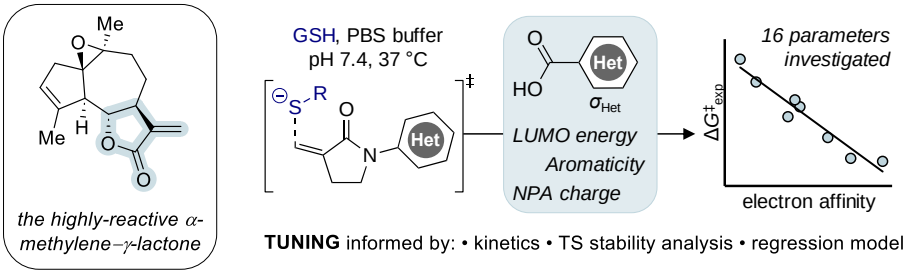
Poster 61

A PREDICTIVE MODEL FOR THE THIOL REACTIVITY OF *α*-METHYLENE–*γ*-LACTAMS USING HETEROARENES AS TUNING ELEMENTS

Grace E. Scofield, Mariah C. Meehan, Corrinne E. Stahl, Peng Liu,* and Kay M. Brummond*

Department of Chemistry, University of Pittsburgh, Pittsburgh, Pennsylvania, USA
ges90@pitt.edu

The *α*-methylene–*γ*-lactone covalent reactive group (CRG) is present in ~3% of known natural products, however, strategies and tools to both modulate and predict the thiol reactivity of this highly-reactive CRG remain elusive. Here, we discuss using DFT studies in conjunction with kinetics experiments to demonstrate that the thiol reactivity of the *α*-methylene–*γ*-lactam CRG can be strategically tuned using *N*-heteroaryl groups. A single-parameter model is developed to predict the thiol reactivity of *N*-heteroaryl lactams as well as other *α,β*-unsaturated amide CRGs through insight-driven selection of CRG ground state descriptors, including LUMO energy, aromaticity, charge from natural population analysis, electron affinity, and a novel Hammett-type parameter for heteroarenes, σ_{Het}.[1] A deeper understanding of the tunability of the *α*–methylene–*γ*-lactam is currently being utilized in the Brummond lab to develop selective covalent modifiers of protein targets.



---

[1] Meehan, M. C.; Scofield, G. E.; Stahl, C. E.; Liu, P.; Brummond, K. M. A Predictive Model for Thiol Reactivity of *N*-Heteroaryl *α*-Methylene–*γ*-Lactams—A Medicinally Relevant Covalent Reactive Group. *Manuscript submitted for publication*.

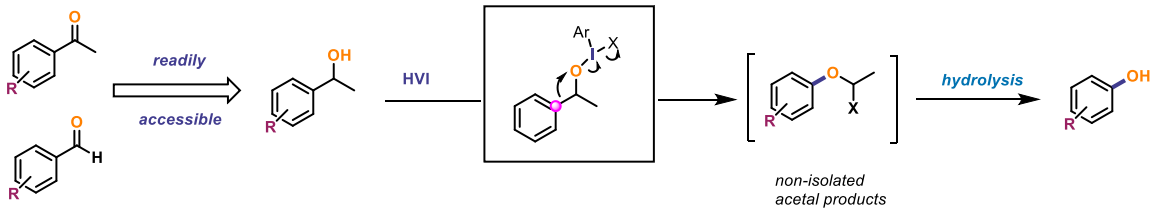
Poster 62

DIRECT HOCK REARRANGEMENT OF ACYCLIC ALCOHOLS VIA HYPERVALENT I(III) UMPOLUNG REACTIVITY

Cassandra A. Sedler and Sarah E Wengryniuk*

Temple University, Department of Chemistry, 1901 N. 13th St., Philadelphia PA 19122.
cassandra.sedler@temple.edu

The Hock Process is among the most important industrial synthetic strategies, making up 95% of the world's production of phenol. Due to the requirement of harsh acidic conditions, mild and versatile strategies that use readily available materials are sought after. The Wengryniuk Lab has developed novel oxidative rearrangement strategies of benzylic alcohols to form cyclic ethers. Facilitated by hypervalent iodine (HVI) reagents, this unique reactivity is of continued interest in our lab. This work describes the HVI-mediated rearrangement of acyclic alcohols with hydrolysis to form phenol derivatives. This methodology could serve as a modern solution to the Hock Process.



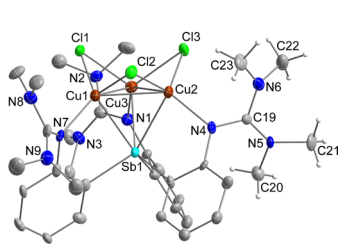
Poster 63

NITRENE-TRANSFER CHEMISTRY TO C–H AND C=C BONDS MEDIATED BY TRIANGULAR COINAGE METAL PLATFORMS SUPPORTED BY TRIPLY BRIDGING PNICTOGEN ELEMENTS Sb(III), Bi(III) AND AN ARENE PLATFORM

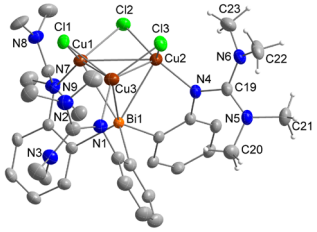
Meenakshi Sharma,* Reece M. Fritz,† Joseph O. Adebanjo,‡ Zhou Lu,‡ Mohammad A. Omary,‡ Thomas R. Cundari,‡ Amitava Choudhury,† and Pericles Stavropoulos†

** Department of Pharmaceutical Sciences, College of Pharmacy, University of Kentucky, Lexington, Kentucky, USA. mshar5672@gmail.com*
† Department of Chemistry, Missouri University of Science and Technology, Rolla, Missouri 65409, United States
‡ Department of Chemistry, University of North Texas, Denton, Texas 76203, United States

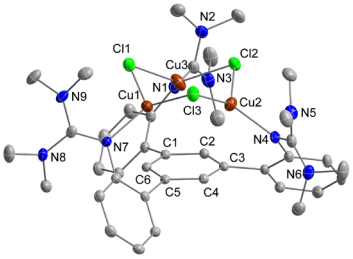
Tripodal ligands (TMG_3trphen-E) that feature heavy pnictogen elements (E = Sb(III), Bi(III)) and tetramethylguanidinyl (TMG) arms have been explored in stabilizing Cu(I) and Ag(I) sites and facilitating nitrene-transfer chemistry.[1] Of particular interest, in ligand development are efforts toward incorporating apical elements that exhibit little if any electron donicity, to enhance the electrophilic nature of a trans-positioned active oxidant (e.g., metal-oxo, nitrene). The tripodal ligand TMG_3trphen-Bz has been synthesized, featuring an arene platform 1,3,5-substituted with phenylene arms possessing tetramethylguanidinyl (TMG) residues.[2] Compounds [(TMG_3trphen-E)$M_3(\mu\text{-}X)_3$] and [(TMG_3trphen-Bz)$M_3(\mu\text{-}X)_3$] (M = Cu(I), Ag(I); X = Cl, Br, I) have been generated upon extraction of $M_3(\mu\text{-}X)_3$ units from MX sources, exhibiting support of the crown-shaped $M_3(\mu\text{-}X)_3$ fragment by M–N_{TMG} bonds and triply bridging E→M_3 interactions. Nitrene-transfer (NTs) to olefins mediated by [(TMG_3trphen-E)$Cu_3(\mu\text{-}Cl)_3$] (E = Sb, Bi) affords aziridines in good yields, primarily for unencumbered styrenes and with the more robust Sb catalyst. Amination of C–H bonds is most effective with sec-benzylic substrates and requires a more electrophilic nitrene (NTces) to achieve practicable yields with halogenated or non-halogenated copper precursors. Hammett plots indicate that the competitive amination of para-substituted ethylbenzenes enabled by [(TMG_3trphen-Sb)$Cu_3(\mu\text{-}Cl)_3$] and [(TMG_3trphen-Bz)$Cu_3(\mu\text{-}Cl)_3$] involves stepwise C–H functionalization.



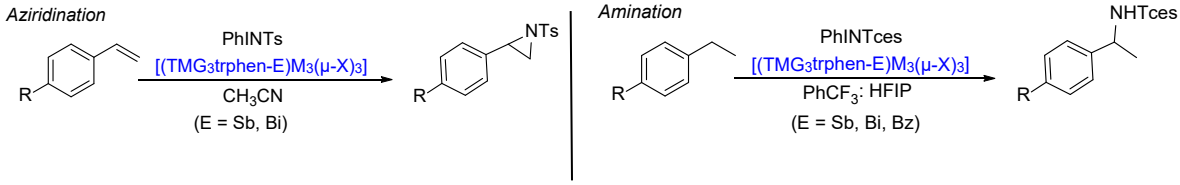
[(TMG_3trphen-Sb)$Cu_3(\mu\text{-}Cl)_3$]



[(TMG_3trphen-Bi)$Cu_3(\mu\text{-}Cl)_3$]



[(TMG_3trphen-Bz)$Cu_3(\mu\text{-}Cl)_3$]



[1] Meenakshi Sharma, Reece M. Fritz, Joseph O. Adebanjo, Zhou Lu, Thomas R. Cundari, Mohammad A. Omary, Amitava Choudhury, and Pericles Stavropoulos. *Organometallics* **2024**, 43, *6*, 634–652.
[2] Meenakshi Sharma, Reece M. Fritz, Joseph O. Adebanjo, Zhou Lu, Thomas R. Cundari, Mohammad A. Omary, Amitava Choudhury, and Pericles Stavropoulos. *Manuscript under preparation.*

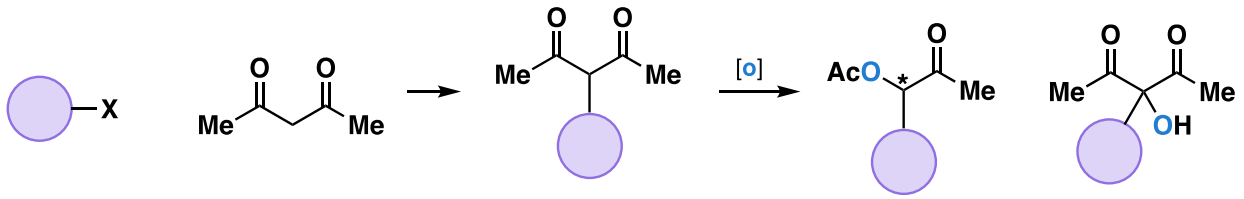
Poster 64

SYNTHESIS OF PROCHIRAL SUBSTRATES AND INVESTIGATIONS OF CHIRAL RESOLUTION THROUGH BIOCATALYTIC OXIDATION

Sandra M. Simmons, Cassie T. Ammerman, Meagan E. Hinze

Department of Chemistry, Sam Houston State University, Huntsville, TX USA
sms179@shsu.edu

The synthesis of bioactive compounds requires precise control over selectivity in where the reaction occurs and bond configuration. Biocatalysts, as enzymes, present eco-friendly alternatives to conventional synthetic methods, showcasing potential for complementary reactivity and dependable substrate selectivity. Within the field of biocatalysis, chiral resolution through biocatalytic oxidation is an underutilized tactic for producing stereoenriched compounds and warrants further investigation. Baeyer-Villiger Monooxygenases (BVMOs) offer an alternative to traditional chemical oxidants with promising implications for chiral resolution applications. To expand our understanding of the capabilities of BVMOs, starting materials with a common ketone backbone derived from acetylacetone were synthesized. Furthermore, authentic product standards were prepared to facilitate the comparison of reaction outcomes between biocatalysts and chemical oxidants. The selectivity differences between chemical and biocatalytic oxidation will be presented along with subsequent implications for chemoenzymatic applications.



Representative prochiral substrate and oxidation outcomes investigated in this work. *Denotes chiral center.

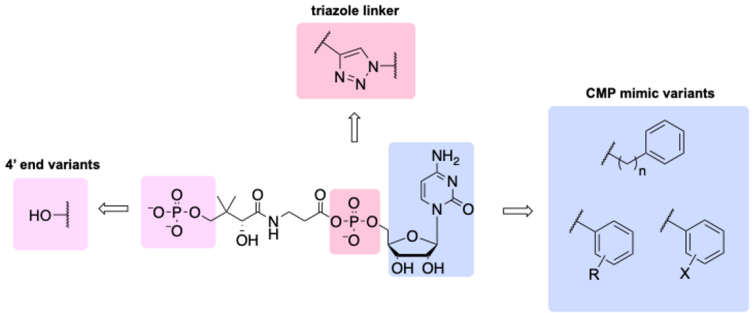
Poster 65

NOVEL PPCS INHIBITORS TO PREVENT COA BIOSYNTHESIS IN DRUG RESISTANT PATHOGENS

Lara Skibbie*, Hailey Butman*, Timothy Scranton*, Rory Smith*, Henry Schrecker*, Kiara Busby*, Timothy Kotze**, Erick Strauss**, and Cynthia Dowd*

** George Washington University*
***Stellenbosch University*
800 22nd St NW, Washington, DC 20052, lskibbie@gwu.edu

With a death toll surpassing 1.6 million per year, tuberculosis (TB) caused by the bacteria *Mycobacterium tuberculosis* (Mtb), is one of the most lethal infections to threaten our society today. Historically, the disease has been treated through a cocktail of anti-TB drugs. However, lapses in completion of the full treatment course, among other issues, have led to the development of drug resistant TB strains. Mtb is not the only drug resistant infective species posing a major threat to global health. The 'ESKAPE pathogens' are a group of six nosocomial pathogens associated with the highest risk of mortality among antibiotic resistant bacteria. Novel anti-infective agents must be developed to combat all of these bacterial species. A commonality amongst these pathogens may provide a solution to address this broad issue. In recent years, the coenzyme A (CoA) pathway has garnered significant interest in the world of drug discovery. CoA is an essential cofactor involved in myriad cellular processes ranging from cellular energy production to cell structure development. A universal CoA biosynthetic pathway exists in all prokaryotic and eukaryotic species, but key differences between the bacterial and human pathways could allow for the development of a selective inhibitor. In particular, distinctive features of the binding pocket of the PPCS enzyme within the CoA pathway provide a unique opportunity for the design of tight binding inhibitors that will preferentially inhibit CoA biosynthesis in prokaryotic species, exhibiting a bactericidal effect. To this end, we have synthesized several structures that will help us probe the PPCS binding pocket, as well as make progress towards the synthesis of bacterial-specific PPCS inhibitors.



Inhibitor Design

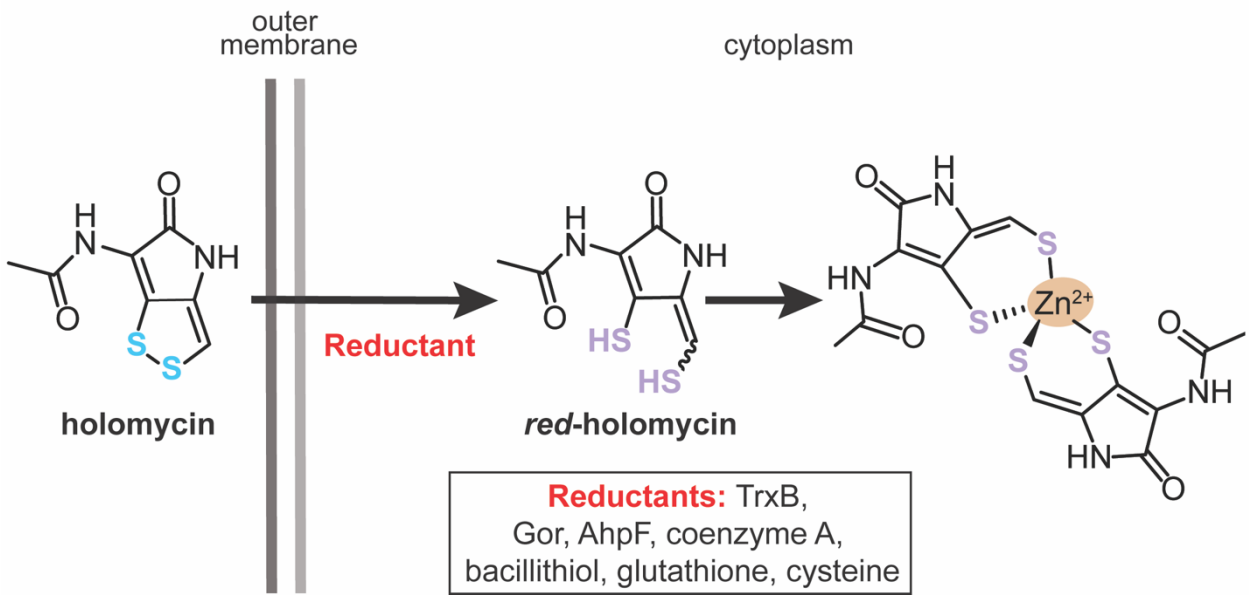
Poster 66

Activation of dithiolopyrrolone antibiotics by bacteria

Olivia Steiner, Rachel A. Johnson, Xiaoyan Chen, Will C. Simke, Bo Li*

University of North Carolina Chapel Hill
250 Bell Tower Drive, Chapel Hill, NC
osteiner@unc.edu

Antimicrobial resistance is a significant global problem. To combat drug-resistant infections, it is essential to identify antimicrobials with novel modes of action. The dithiolopyrrolone (DTP) family of natural products contain a characteristic bicyclic ene-disulfide that can be reduced in the cell and then chelate metal ions.[1] This metal-chelating prodrug mechanism is unique among antimicrobials. We determined that the prototypical DTP holomycin is nonspecifically reduced by several bacterial redox proteins and small-molecule reductants. We also studied the roles of these redox systems in the activation of and resistance to thiomarinol, a marine natural product and unique hybrid antibiotic where the DTP core is covalently linked to an analogue of the clinically used antimicrobial mupirocin. At large, this work contributes to the understanding of prodrug activation by redox systems and will aid in the development of the DTPs as therapeutics.



[1]Chan, A. N., *et al. PNAS* **2017** 114(10)

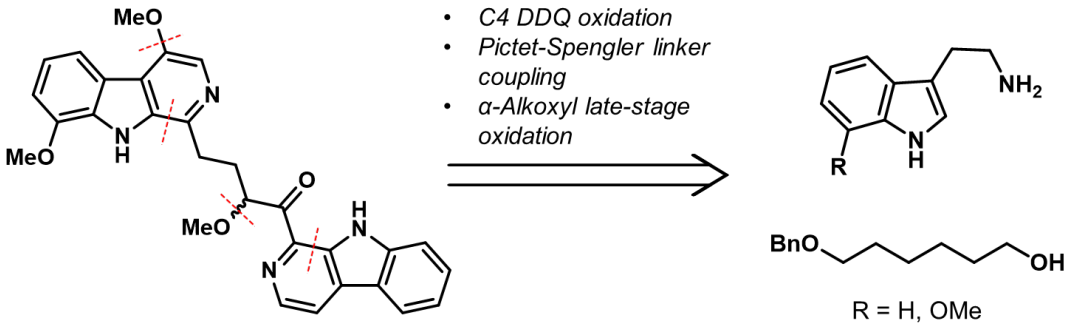
Poster 67

THE TOTAL SYNTHESIS OF PICRASIDINE C: A SUBTYPE SELECTIVE PPAR AGONIST

Alexis M. Stoorza, SK Abu Saleh, Ziwei Hu, and Adam S. Duerfeldt*

Department of Medicinal Chemistry, University of Minnesota, Minneapolis, Minnesota, USA
stoor002@umn.edu

Diabetic retinopathy (DR) is the leading cause of blindness and vision impairment in the working class (ages 20-65) and the second most common complication of diabetes. Current treatments for DR are invasive, lack optimal efficacy, and are associated with severe adverse effects. Thus, novel DR treatments are needed. Small molecule agonists targeting PPARα are known to exhibit a therapeutic effect on DR. Known PPARα agonists suffer from selectivity issues, dose-limiting off-target toxicities, and/or physicochemical liabilities, and new agonistic chemotypes are sought after[1]. The natural product Picrasidine C, isolated from the root wood of *Picrasma quassioides*, was found to selectively activate peroxisome proliferator-activated receptor alpha (PPARα) over PPARγ or PPARβ/δ isoforms[2]. Interestingly, Picrasidine C lacks the characteristic carboxylic acid pharmacophore of other PPARα agonists such as FDA-approved Fenofibrate (Triglide). This poster will describe our progress towards the total synthesis of Picrasidine C and related derivatives. Highlighted chemistry includes C4 benzylic oxidation using 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ), one-pot aromatization and methylation using trimethoxymethane, Pictet-Spengler couplings to attach the asymmetric β-carbolines to the linker forming the pseudo-dimer, and late-stage oxidation to install the α-alkoxyl group followed by chiral separation. The synthesis of Picrasidine C and related congeners lays the foundation for the characterization of biological activity, future SAR, and structural biology initiatives.



Picrasidine C

(1) Dou, X.; Duerfeldt, A. S. Small-Molecule Modulation of PPARs for the Treatment of Prevalent Vascular Retinal Diseases. *Int. J. Mol. Sci.* **2020**, *21* (23), 9251. https://doi.org/10.3390/ijms21239251.

(2) Zhao, S.; Kanno, Y.; Li, W.; Sasaki, T.; Zhang, X.; Wang, J.; Cheng, M.; Koike, K.; Nemoto, K.; Li, H. Identification of Picrasidine C as a Subtype-Selective PPARα Agonist. *J. Nat. Prod.* **2016**, *79* (12), 3127–3133. https://doi.org/10.1021/acs.jnatprod.6b00883.

Poster 68

Synthesis of highly functionalized 4-iodo-7-azaindazoles via condensation/diels–alder/retro-diels–alder cyclization of iodoalkynones and 2-hydrazineylpyrimidines

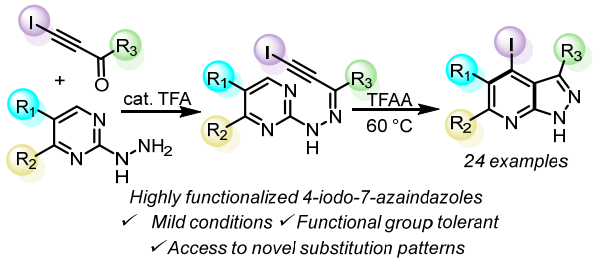
Elizabeth C. Swift,† Zachary S. Sales,† Dongpei Wu,‡ Anastassia Matviitsuk,† Daniel J. Pippel,† Terry P. Lebold‡

†Discovery Process Research, Janssen R&D, San Diego, California 92121, United States

‡Discovery Chemistry, Janssen R&D, San Diego, California 92121, United States

eswift1@its.jnj.com

Abstract: A method for the preparation of highly functionalized 4-iodo-7-azaindazoles is presented. These valuable heterocycles are synthesized via condensation of 2-hydrazineylpyrimidines with various iodoalkynones followed by Diels–Alder/retro-Diels–Alder cyclization. The method is general to the formation of products with a variety of C3, C5 and C6 substituents while preserving the C4 iodide functional handle for further late-stage functionalization. The utility of this transformation is demonstrated through the rapid synthesis of several bioactive azaindazole targets.



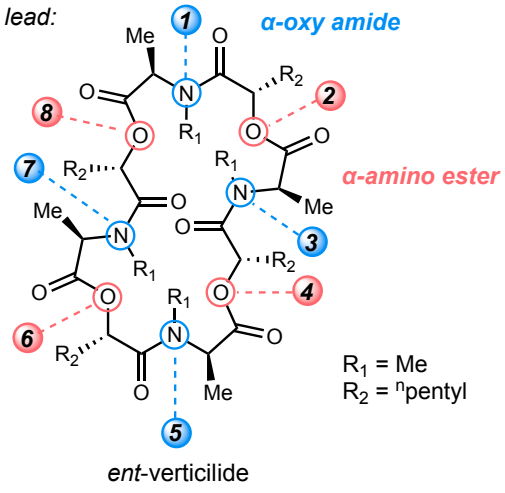
Poster 69

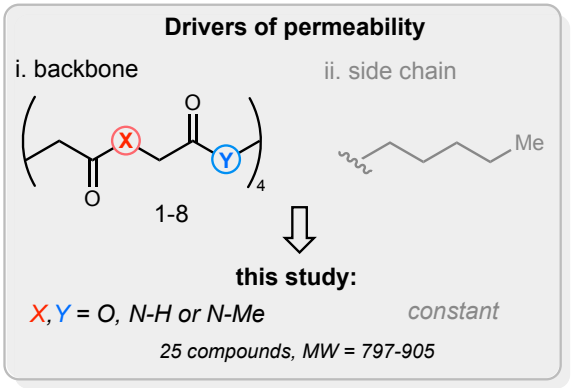
The Backbone Constitution Drives Passive Permeability Independent of Side Chains in Depsipeptide and Peptide Macrocycles Inspired by *ent*-Verticilide

Madelaine P. Thorpe and Jeffrey N. Johnston*

Department of Chemistry and Vanderbilt Institute of Chemical Biology, Vanderbilt University, Nashville, TN 37235, madelaine.p.thorpe@vanderbilt.edu

The number of peptide-like scaffolds found in late-stage drug development is increasing, but a critical unanswered question in the field is whether substituents (side chains) or the backbone drive passive permeability. Five series of macrocyclic peptidic compounds were prepared, with a focus on backbone constitution. Their passive permeability was determined (PAMPA, Caco-2), to delineate structure-permeability relationships. Each series was based on the cell-permeable antiarrhythmic compound *ent*-verticilide, a cyclic oligomeric depsipeptide (COD) containing repeating ester/*N*-Me amide didepsipeptide monomers. The combination of ester and amide functional groups in the *ent*-verticilide backbone provides a unique opportunity to further probe the hypothesis that backbone modifications can substantially affect passive permeability *independent of side chain modification*. Furthermore, the oligomeric nature of ent-verticilide provides an additional angle to query to what extent these effects might be additive. We report herein the first outline of common bioisostere interconversions, and correlation of these structural changes with passive permeability. The macrocyclic nature of these depsipeptides and peptides, and their relationship to a cell-permeable antiarrhythmic, broadens the relevance of these findings, increasing the possibility that similar correlations will be identified for use in bRo5 drug development.[1]





[1] Over B, *et al. Nat. Chem. Biol.* **2016**, *12*, 1065-1074.

Poster 70

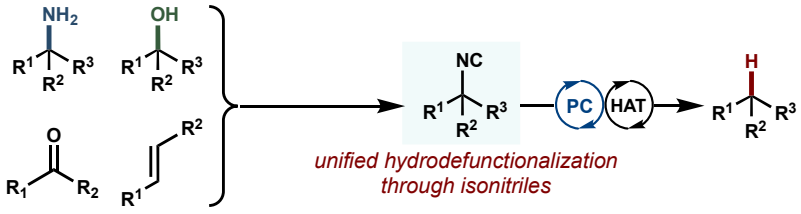
UNIFIED APPROACH TO DEAMINATION AND DEOXYGENATION THROUGH ISONITRILE HYDRODECYANATION: COMPUTATIONAL AND EXPERIMENTAL STUDIES

Jiao,[1] Kyle T. Jaunich,‡[1] Thomas Tao,‡[2] Olivia Gottschall,[2] Maxwell M. Hughes,[1] Aneta Turlik,*[2] Alexander W. Schuppe*[1]

[1] Department of Chemistry, Vanderbilt University, 1234 Stevenson Center Ln, Nashville, TN, 37240
[2] Department of Chemistry, Skidmore College, 815 North Broadway, Saratoga Springs, NY, 12866

aturlik@skidmore.edu

A general strategy was developed to hydrodefunctionalize alcohols and amines through a common isonitrile intermediate.[1] Dual hydrogen atom transfer (HAT) and photoredox catalysis was used to cleave the relatively inert C–NC bond in order to generate a nucleophilic boryl radical. This radical leads to formation of an imidoyl radical intermediate from the isonitrile, followed by β-scission to accomplish defunctionalization. Both experimental and computational studies demonstrate a facile β-scission of the imidoyl radical and reconcile differences in reactivity between nitriles and isonitriles. Density functional theory (DFT) calculations elucidated the increased reactivity of isonitriles compared to nitriles, as well as the increased reactivity of substrates with adjacent electron-withdrawing groups compared to aliphatic substrates, allowing us to further extend the scope of our hydrodecyanation reaction to alkyl nitriles.



---

[1] Jiao, Z.; Jaunich, K. T.;† Tao, T.;† Gottschall, O.; Hughes, M. M.; **Turlik, A.***; Schuppe, A. W.* “Unified Approach to Deamination and Deoxygenation Through Isonitrile Hydrodecyanation: A Combined Experimental and Computational Investigation.” *Angew. Chem. Int. Ed.* **2024**, *Accepted*. DOI: 10.1002/anie.202405779

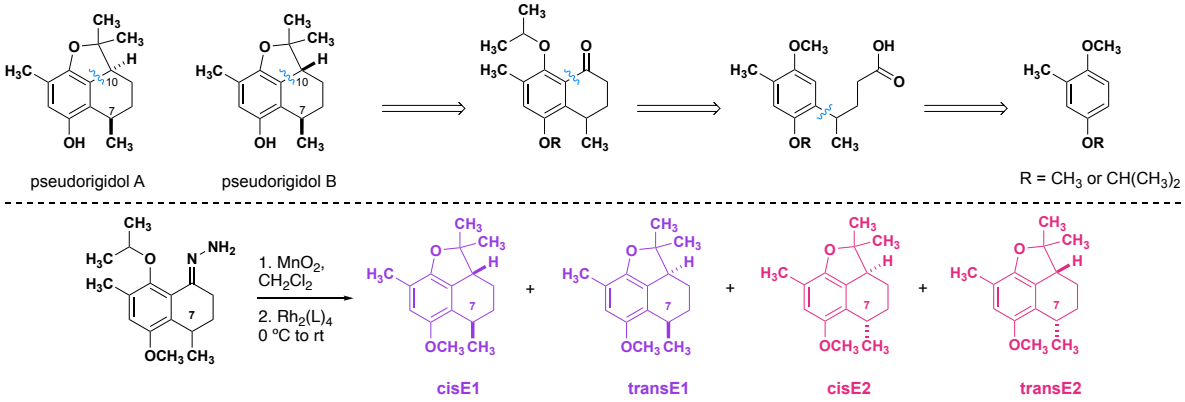
Poster 71

ELUCIDATING THE INFLUENCE OF REMOTE STEREOCENTERS ON DONOR/DONOR C–H INSERTIONS TO FACILITATE THE ASYMMETRIC ASSEMBLY OF CADINANE NATURAL PRODUCTS

Linda Ung, Sarah N. Dishman, Jared T. Shaw*

Department of Chemistry, University of California, Davis, Davis, California, USA
lung@ucdavis.edu

Intramolecular C–H insertion reactions using donor/donor dirhodium carbenes have proven useful in synthesizing molecules with high enantio- and/or diastereoselectivity.[1-3] This method can provide asymmetric access to a variety of natural products containing a benzodihydrofuran ring, including pseudorigidol A and pseudorigidol B. To assemble these cadinane natural products, the starting material contains a remote stereocenter. The aim of this research is 1) to complete the first total syntheses of pseudorigidols A and B, and 2) to investigate the influence of remote stereocenters on donor/donor C–H insertion reactions, studies on which have yet to be reported in the literature. Progress towards pseudorigidol A and pseudorigidol B, along with the dirhodium catalyst screen results, will be presented.



- *"Match/mismatch" effects observed between substrate and chiral catalysts*
- *Synergistic substrate and catalyst control*
- *Pseudorigidol A and pseudorigidol B can be accessed with high diastereoselectivity*

---

[1] Soldi, C.; Lamb, K. N.; Squitieri, R. A.; González-López, M.; Di Maso, M. J.; Shaw, J. T. *J. Am. Chem. Soc.* **2014**, *136*, 15142-15145.

[2] Lamb, K. N.; Squitieri, R. A.; Chintala, S. R.; Kwong, A. J.; Balmond, E. I.; Soldi, C.; Dmitenko, O.; Castiñeira Reis, M.; Chung, R.; Addison, J. B.; Fettinger, J. C.; Hein, J. E.; Tantillo, D. J.; Fox, J. M.; Shaw, J. T. *Chem. Eur. J.* **2017**, *23*, 11843–11855.

[3] Dishman, S. N.; Laconsay, C. J.; Fettinger, J. C.; Tantillo, D. J.; Shaw, J. T. *Chem. Sci.* **2022**, *13*, 1030-1036.

Poster 72

The Development of a 1,2-Aminoarylation Reaction via Photocatalytic Aryl Radical Generation

Oniya Valencia

The Scheidt Research Group, Northwestern University

The formation of C–C and C–N bonds is central to the construction of privileged structures in organic chemistry. Alkene difunctionalization is an efficient method to construct these two bonds in tandem and access these desired molecular scaffolds. Photoredox catalysis has become a thriving field in organic synthesis within the past two decades as a way to access new reactivities through single-electron chemistry instead of traditional two-electron chemistry. Applying strategies from photoredox catalysis to alkene difunctionalization will allow for the construction of two new bonds in a single step with mild reaction conditions. A number of highly reactive aryl radical precursors, such as aryl diazonium salts or hypervalent organoiodine compounds, have been utilized in photocatalytic alkene difunctionalization. However, aryl radicals from abundant, bench stable aryl halides have yet to be explored in these three-component systems. We hypothesized that an aryl radical can be accessed from the photocatalytic reduction of aryl halides which would then undergo radical addition to styrene to generate a stabilized benzylic radical. This corresponding benzylic radical would then undergo single electron oxidation by the photocatalyst to yield a carbocation which could then be trapped by a nitrogen-based nucleophile. We have begun to investigate the reactivity of this system and have synthesized our desired product in moderate yields. We are currently working to expand the scope of nucleophiles and improve the efficiency of this reaction by collecting mechanistic insight through control experiments.

Poster 73

PROGRESS TOWARDS THE TOTAL SYNTHESIS OF GLADIOLIIN

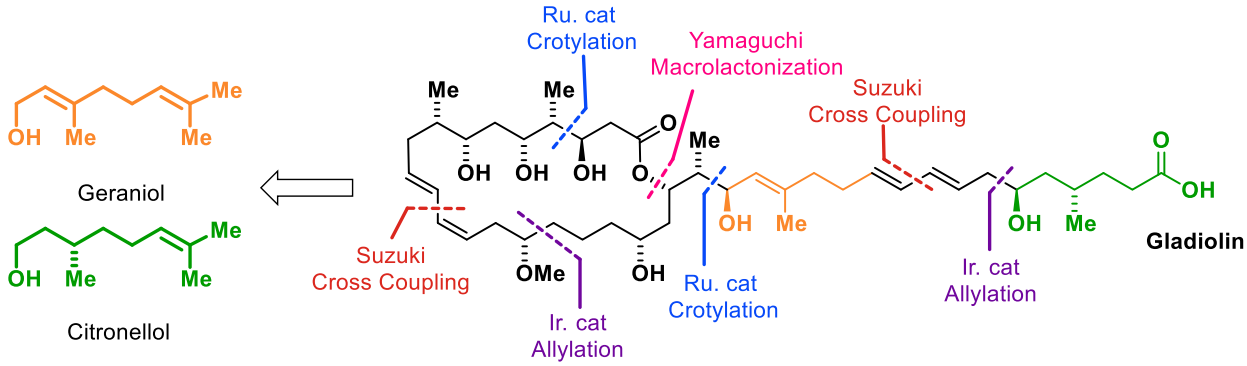
Katherine L. Verboom, Yoon Cho, Michael J. Krische*

University of Texas at Austin
6500 Champion Grandview Way, Austin, TX, 78750
katherineverboom@utexas.edu

Gladiolin, a potent antibacterial polyketide isolated from the bacterium *Burkholderia gladioli*, exhibits remarkable activity against various strains of *Mycobacterium tuberculosis* while maintaining low mammalian cytotoxicity. Notably, it demonstrates efficacy against *M. tuberculosis* CHUV80037024, a strain resistant to isoniazid and rifampicin, which are frontline treatments for tuberculosis. Herein, we present advancements towards the first total synthesis of gladiolin, achieved in an estimated 17 steps (longest linear sequence) commencing from readily available starting materials, notably, citronellol and geraniol.

Central to our synthetic strategy are two pivotal iridium-catalyzed allylations employing allyl acetate and two ruthenium-catalyzed crotylations utilizing butadiene. These transformations, featuring a hydrogen-auto transfer process, proceed directly from the alcohol oxidation state, obviating the necessity for discrete oxidation steps. Additionally, our synthesis entails stereoselective aldol additions, Suzuki cross-coupling reactions, and a Yamaguchi macrolactonization strategy, pivotal in forging the requisite carbon-carbon bonds.

Our approach not only addresses the synthetic challenges inherent in assembling the complex framework of gladiolin but also showcases the strategic application of modern catalytic methods. The successful completion of this total synthesis holds promise for the elucidation of gladiolin's structure-activity relationship and underscores its potential as a lead compound in the development of novel antibacterial agents targeting drug-resistant tuberculosis strains.



Poster 74

SYNTHESIS AND DERIVATIZATION OF VANCOMYCIN LINEAR HEPTAPEPTIDE

Autumn Vossler, Rashanique Quarels*

Department of Chemistry and Biochemistry, Rowan University, Glassboro, New Jersey, USA
201 Mullica Hill Road, Glassboro, NJ, 08028 vossle57@rowan.edu

Antibiotic resistance occurs when bacteria develop the ability to evade the effects of antibiotic treatment. This phenomenon has been identified as a major health concern by the World Health Organization in 2018. One specific antibiotic that has been susceptible to such occurrence is vancomycin. Vancomycin is a last resort antibiotic that is used to treat bacterial infections in the intestines and the colon. Since its approval by the FDA in 1958, there have been reports of numerous bacterial strains developing resistance toward vancomycin, resulting in limited effectiveness of the antibiotic. The goal of this project is to design new glycopeptides using traditional peptide coupling and umpolung amide synthesis. The long-term goal of this project would be to test the new glycopeptides as potential therapeutics to combat drug resistant bacterial strains. Herein, we report our progress toward the synthesis of intermediates to develop vancomycin derivatives.

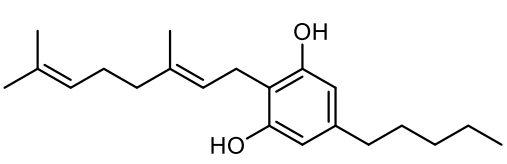
Poster 75

SYNTHESIS AND EVALUATION OF CANNABIGEROL-INSPIRED ANTIMICROBIAL COMPOUNDS

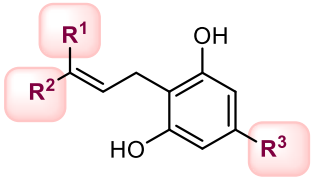
Eleanor Wong, Nicholas Jentsch, Xiong Zhang, Omar El-Halfawy, Eric Brown, Jakob Magolan*

Department of Biochemistry and Biomedical Sciences, McMaster University, Canada
wonge38@mcmaster.ca

Cannabigerol (CBG) and other cannabinoid natural products demonstrate potent antimicrobial activity.[1,2] Here we report the chemical synthesis and antimicrobial evaluation for more than forty novel synthetic derivatives of the cannabigerol scaffold. As a key step in the synthesis of these compounds we employed a newly-discovered alumina-mediated phenol geranylation reaction. This presentation will include a discussion of this chemistry and the results of the evaluation of our novel CBG-inspired compounds against methicillin-resistant Staphylococcus aureus (MRSA).



cannabigerol (CBG)



CBG analogues

---

[1] Farha, M. A.; El-Halfawy O. M., Gale, R. T.; MacNair, C. R.; Carfrae, L. A.; Zhang, X; Jentsch, N. G.; Magolan, J; Brown, E. D., Uncovering the Hidden Antibiotic Potential of Cannabis. J. Infect. Dis. 2020, 6(3), 338-46.

[2] Appendino, G.; Gibbons, S.; Giana, A.; Pagani, A.; Grassi, G.; Stavri, M.; Smith, E.; Rahman, M. M.; Antibacterial cannabinoids from Cannabis sativa: a structure-activity study. J. Nat. Prod. 2008, 71(8), 1427-30.

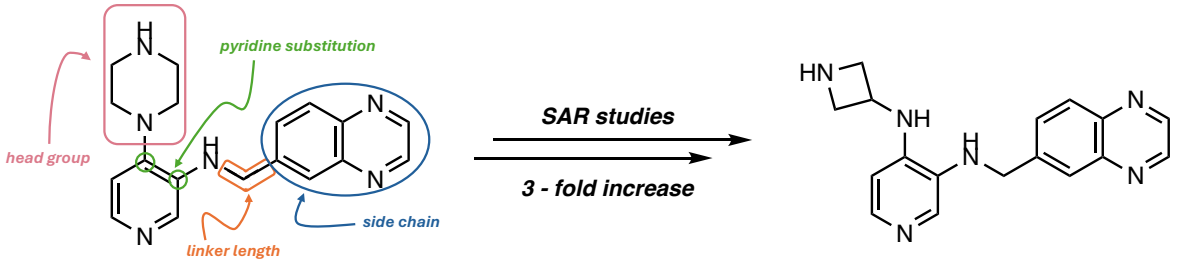
Poster 76

TARGETING THE MRNA THIAMINE PYROPHOSPHATE RIBOSWITCH WITH SMALL MOLECULES

Abigale Wood, Ahlam Armaly, Shouhong Jin, Ryan Sherrier, Kevin Weeks, Jeffrey Aubé**

Department of Chemistry, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA
awood4@unc.edu

RNA is an essential biomolecule that plays a central role in the transfer of cellular information. Despite an abundance of research implicating many RNAs in disease pathology, this macromolecule is drastically underexplored as a target for drug discovery campaigns. Recently, we published a fragment-based ligand discovery study that identified a binder to the messenger RNA thiamine pyrophosphate riboswitch with high affinity.[1] In this presentation I describe studies to optimize a small molecule – RNA binding interaction, which led to the discovery of potent nanomolar binders.



K_D = 152 nM

K_D = 56 nM

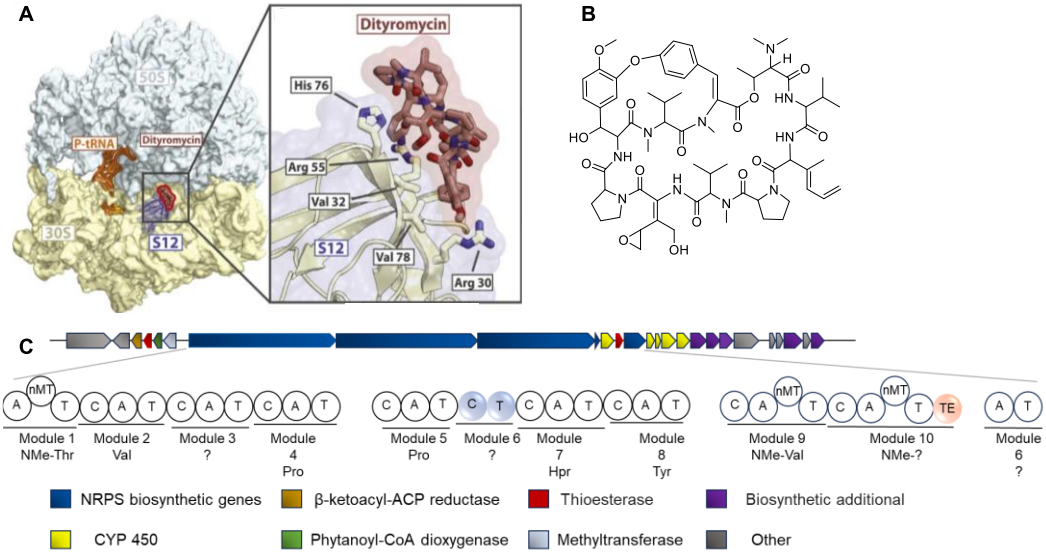
(1) Zeller, M. J.; Favorov, O.; Li, K.; Nuthanakanti, A.; Hussein, D.; Michaud, A.; Lafontaine, D. A.; Busan, S.; Serganov, A.; Aubé, J.; Weeks, K. M. *Proc. Natl. Acad. Sci. U.S.A.* **2022**, *119* (20), e2122660119.

BIOSYNTHETIC AND STRUCTURE-ACTIVITY INVESTIGATIONS ON TRANSLATION-INHIBITING CYCLIC PEPTIDE NATURAL PRODUCTS

Jia Yang, Max Crüsemann*

Institute of Pharmaceutical Biology, University of Bonn, Nussallee 6, 53115 Bonn; Germany; jyang@uni-bonn.de

Nonribosomal peptides (NRP) are a class of natural products with high structural complexity and diverse bioactivities, assembled by enzymatic machineries in a stepwise, modular fashion.[1] GE82832 and its analog Dityromycin are highly complex macrocyclic depsipeptide antibiotics targeting the protein S12 at the 30S unit of the bacterial ribosome thereby inhibiting elongation factor G-catalyzed tRNA translocation. This unique mechanism of action outlined a region of the ribosome that can be a target of future structure-based antibiotic design.[2] Through sequencing of the bacterial producers genomes, we identified the candidate biosynthetic gene clusters (BGCs) of GE82832 and Dityromycin. Detailed bioinformatic analysis revealed unconventional nonribosomal peptide synthetase assembly lines for these two antibiotics and a number of modifying enzymes for the generation of the highly modified building blocks. Latest results on the isolation, purification, and structure elucidation of GE82832, the Cas12a/Cre-lox-dependent direct cloning, as well as the optimization of heterologous expression of the candidate BGC of GE82832 will be presented.



(A) Binding site of GE82832/Dityromycin with the ribosome and their interactions with S12
(B) Chemical structure of Dityromycin
(C) Biosynthetic gene cluster of GE82832

[1] R. D. Süssmuth, A. Mainz, *Angew Chem Int Ed* **2017**, *56*, 3770.
[2] D. Bulkley, L. Brandi, Y. S. Polikanov, A. Fabbretti, M. O'Connor, C. O. Gualerzi, T. A. Steitz, *Cell Reports* **2014**, *6*, 357.

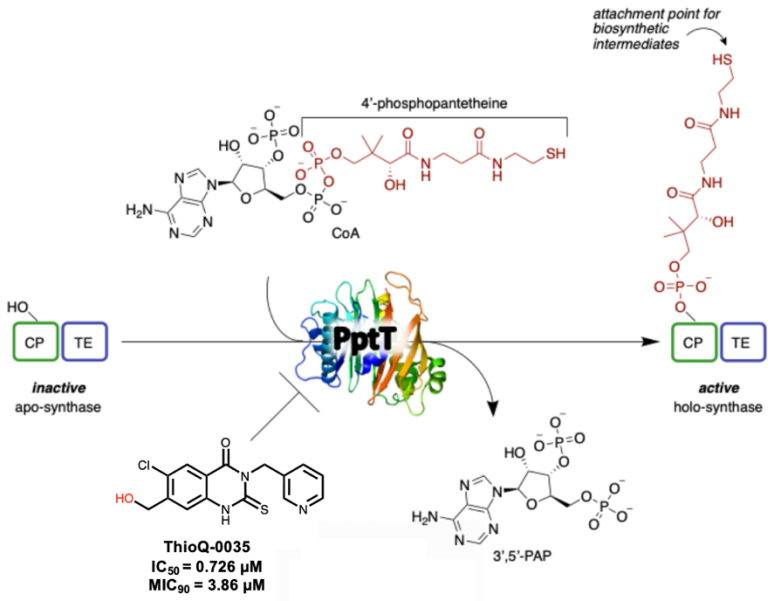
Poster 78

THIOQUINAZOLINONES AS ANTITUBERCULOSIS AGENTS TARGETING PHOSPHOPANTHETHIENYL TRANSFERASE

Cindy Zhang[1], Logan Zwerneman[1], Amrita Singh[2], Takushi Kaneko[3], Andrew Perkowski[1], David Zhang[2], James C. Sacchettini[4], Nader Fotouhi[3], Jeffrey Aubé[1]*, Carl F. Nathan[2]**

[1]Division of Chemical Biology and Medicinal Chemistry, UNC Eshelman School of Pharmacy, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina 27599, USA, xzhang2@unc.edu; [2]Department of Microbiology & Immunology, Weill Cornell Medicine, New York, New York 10021, USA; [3]Global Alliance for TB Drug Development, New York, New York, USA; [4]Department of Biochemistry and Biophysics, Texas Agricultural and Mechanical University, College Station, Texas 77843, USA.

Tuberculosis (TB) is the most lethal infectious disease in world history and is annually responsible for the deaths of an estimated 1.5 million people. An ever-increasing instance of multi-drug- and extensively-drug-resistant strains of TB's causative agent, *Mycobacterium tuberculosis* (*Mtb*), emphasize the need for new drug targets. Phosphopantethienyl transferase (PptT) has emerged as a viable drug target for treatment against *Mycobacterium tuberculosis* due to its critical role in cell wall biosynthesis. This work describes the structure-activity relationships of a new class of PptT inhibitor, the benzothioxoquinazolinone (ThioQ), that was initially identified in a high-throughput screen. These studies indicate that while the ThioQs' heterocyclic core is critical for PptT inhibition, improvements to biological activity relative to many previously reported PptT inhibitors may be made via two primary means: increasing biochemical potency through the introduction of polar functional groups to the pyridine ring, or increasing on-target whole-cell activity by hydroxymethylating the 7-position or by introducing a hydroxymethyl-based prodrug. Preliminary pharmacokinetic (PK) data show that, while many ThioQs exhibit suitable Caco-2 permeability, microsomal stability, and hERG inhibition, many of the more whole-cell active ThioQs have poor kinetic solubility and oral bioavailability. Studies focused on balancing cellular potency with structural features that lead to favorable PK data are ongoing.



Poster 79

STEREOCONTROLLED SYNTHESIS OF FUNCTIONALIZED TRICYCLIC O-HETEROCYCLES

Patrycia Zybura, Alison J. Frontier*

University of Rochester
Department of Chemistry, Rochester, NY, 14620, United States

Patrycia Zybura: pzybura@ur.rochester.edu
Alison J. Frontier*: frontier@chem.rochester.edu

The *halo*-Prins/*halo*-Nazarov reaction sequence has emerged as a versatile approach for synthesizing complex ring systems from simple starting materials. Here, I will introduce the development of a *halo*-Prins/*halo*-Nazarov cationic cascade as a powerful method for the synthesis of cyclopenta[b]benzofurans. This methodology enables the rapid formation of three contiguous stereocenters, four new bonds, and two new rings. Furthermore, the resulting products exhibit diverse functionalities, facilitating subsequent derivatization. The optimization of reaction conditions, functional group tolerance, and broad applicability of this methodology will be discussed.