

Posters Arranged by Breakout Room Number

1. Cross-Electrophile Coupling of Unactivated Alkyl and Aryl Chlorides.

Holt Sakai, David MacMillan, Princeton University.

Alkyl chlorides are bench-stable chemical feedstocks that remain among the most underutilized electrophile classes in transition metal catalysis. Overcoming intrinsic limitations of C(sp³)-Cl bond activation, we report the development of a novel organosilane reagent that can participate in chlorine atom abstraction under mild photocatalytic conditions. In particular, we describe the application of this mechanism to a dual nickel/photoredox catalytic protocol that enables the first general cross-electrophile coupling of unactivated alkyl chlorides and aryl chlorides. Employing these low-toxicity, abundant, and commercially available organochloride building blocks, this methodology allows access to a broad array of highly functionalized C(sp²)-C(sp³) coupled adducts, including numerous drug analogues.

2. Photoredox-catalyzed bioconjugation reactions (C-terminus, methionine, and tyrosine).

Beryl Li, David MacMillan, Princeton University

Bioconjugation is an important tool in a wide variety of chemical biology applications, such as tracking protein distribution in cells, probing enzymatic functions, or targeted drug delivery. Photoredox catalysis is a privileged platform for protein bioconjugation because it can selectively target redox-active amino acid residues under mild, biologically compatible conditions. Under our photoredox manifold, we can enable C-terminus-selective bioconjugation of peptides and proteins via a photoredox-catalyzed decarboxylative Michael addition. In addition, we have also recently developed additional novel bioconjugation strategies, including tyrosine-specific and methionine-specific conjugation reactions. These methods combine to showcase the versatility of photoredox catalysis in biological contexts.

3. Creating multi-responsive symmetric and asymmetric tetraarylazadipyrrin chromophores: synthesis and characterization.

Matthew Furry, Barry Pemberton, Stockton University

The development and possible applications of near-infrared (NIR) emitting chromophores have garnered considerable interest in the last decade. These chromophores have a wide variety of applications from bioimaging¹ to solar cells². We have synthesized 2-pyrene, 4-tolyl, pyrrole and 1,7-pyrene, 3,5-tolyl, bis-azadipyrrin; and are in the process of synthesizing a series of symmetrical and asymmetrical tetraarylazadipyrrin chromophores, including some with multi-responsive emission properties accessed via selective excitation wavelengths. We believe these molecules rely on three factors to provide multifunctional emission properties, including pre-orientation, rigidification, and electronic decoupling of chromophore units. Herein this presentation, we will discuss the synthesis of these molecules which proceeds through well-established chemistry, including aldol condensations, Michael additions, and heterocyclic ring closures. An essential step for the synthesis of asymmetrical intermediates involves synthesizing 2,4 di-aryl pyrroles. Finally, we will explore the steady-state and time-resolved photophysical properties of these chromophores. The goal of this research is to expand the functionality of tetraarylazadipyrrins and to understand the role large aromatic substituents play in the multi-emissive properties within these chromophores.

References

(1) Yang, Y.; Zhao, Q.; Feng, W.; Li, F. Luminescent Chemodosimeters for Bioimaging. *Chem. Rev.* 2013, 113 (1), 192–270. <https://doi.org/10.1021/cr2004103>.

(2) Loudet, A.; Burgess, K. BODIPY Dyes and Their Derivatives: Syntheses and Spectroscopic Properties. *Chem. Rev.* 2007, 107 (11), 4891–4932. <https://doi.org/10.1021/cr078381n>.

4. Carbon–Nitrogen Cross-Coupling via Metallaphotoredox Catalysis

Amy Chan, David MacMillan, Princeton University

Carbon–nitrogen (C–N) bonds are ubiquitous bond connections in a broad range of organic molecules, including pharmaceutical compounds, natural products, and organic materials. Its prevalence indicates the importance of the development of methods to access a wide diversity of C–N bonds. Herein, we report a novel photo-induced metal-catalyzed carbon–nitrogen cross-coupling protocol proceeding in high yields with excellent selectivity and functional group tolerance. The utility of this synthetic transformation stems from the abundance of readily available and bench-stable coupling partners, the biological importance of C–N bond-containing functional groups, as well as the mild and practical reaction conditions.

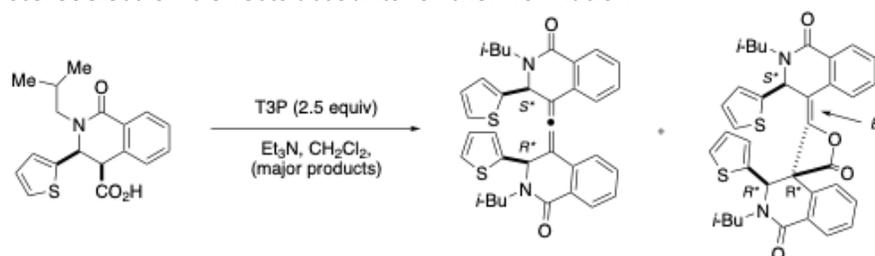
5. Stereochemical features of a complex ketene dimerization reaction

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The amidation reaction of a tetrahydroisoquinoline-4-carboxylic acid is a key step in the multi-kilogram scale preparation of the antimalarial drug SJ733, now in phase 2 clinical trials. In the course of investigating THIQ carboxamidations, we found that propanephosphonic acid anhydride (T3P) is an effective reagent, although yield and byproducts varied with the nature and quantity of the base. As a control, the T3P reaction was performed in the absence of the amine, and the products were characterized: major among them are the allene and the lactone shown. A ketene dimerization process subject to subtle steric and stereoelectronic effects accounts for their formation.



6. Functionalization and Heterogenization of Fluorine Rich Photosensitizers

Mary Chioma Okorie, Sergiu M. Gorun Seton Hall University

Phthalocyanines (Pcs) are a class of photosensitizers that generate singlet oxygen (1O_2) using visible light. Singlet-oxygen decays to form reactive oxygen species (ROS), including hydroxyl ($HO\cdot$) and superoxide ($O_2\cdot^-$) radicals. These radicals target non-specific C–H bonds. Organic photosensitizers self-destruction hinders their applications as catalysts, photodynamic therapy agents, etc, but ring fluorination enhances their robustness. While perfluorination ensures Pc macrocycle binding on supports only via van der Waals bonds, functionalized Pcs may offer opportunities for stronger catalyst/support binding. We report that

an aqueous suspension of a heavily fluorinated Pc, $F_{48}H_7(COOH)PcZn$ supported on Al_2O_3 degrades methyl orange, a model dye without catalyst decomposition. Additional, supported photocatalytic materials are envisioned.

7. New applications of halogen abstraction-radical capture (HARC) mechanisms: a copper metallaphotoredox platform for N-alkylation

Nathan W. Dow, David MacMillan, Princeton University

The catalytic union of amides, sulfonamides, anilines, imines, or N-heterocycles with a broad spectrum of electronically and sterically diverse alkyl bromides has been achieved via a visible-light-induced metallaphotoredox platform. The use of a halogen abstraction-radical capture (HARC) mechanism allows for room temperature coupling of C(sp³)-bromides using simple Cu(II) salts, effectively bypassing the prohibitively high barriers typically associated with thermally induced SN₂ or SN₁ N-alkylation. This regio- and chemoselective protocol is compatible with >10 classes of medicinally relevant N-nucleophiles, including established pharmaceutical agents, in addition to structurally diverse primary, secondary, and tertiary alkyl bromides. Furthermore, the capacity of HARC methodologies to engage conventionally inert coupling partners is highlighted via the union of N-nucleophiles with cyclopropyl bromides and unactivated alkyl chlorides, substrates that are incompatible with nucleophilic substitution pathways. Preliminary mechanistic experiments validate the dual catalytic, open-shell nature of this platform, which enables reactivity previously unattainable in traditional halide-based N-alkylation systems."

8. Photoacid Catalyzed C–C and C–O Bond-Formation

Jason Saway, Joseph J. Badillo, Seton Hall University

The development of new catalytic processes is essential for organic synthesis. In this presentation, we will discuss a visible-light-induced, thiourea catalyzed C–C bond-forming reaction. Specifically, Schreiner's thiourea [(N,N'-bis[3,5-bis(trifluoromethyl)phenyl]-thiourea] functions as a photoacid to facilitate the double Friedel-Crafts addition of indoles to aldehydes and isatins to form the corresponding triarylmethanes and 3,3'-diarylindolin-2-ones. We demonstrate that this protocol applies to a variety of aldehyde and isatin electrophiles and a range of electronically diverse indoles. Furthermore, this mild light-facilitated reaction is chemoselective for 1,2-addition to aldehydes over ketones and 1,4-conjugated systems. Mechanistic studies show that light is required for the reaction to be initiated. We have also shown that 6-bromo-2-naphthol catalyzes the formation of C–O bonds. Using 10 mol% photoacid catalyst enables the photo-induced acetalization of aldehydes with a range of alcohols. This presentation will also discuss the synthesis and optimization of a variety of triazole containing triarylmethanes and 3,3'-diaryloxindoles using copper-catalyzed azide-alkyne cycloaddition (CuAAC) chemistry in order to evaluate their anti-cancer properties.

9. Benzylic Functionalization Electrochemical Oxidation

Kevin Lee, Yalan Xing, William Paterson University

Compared to traditional reagent-based transformations, synthetic organic electrochemistry provides approaches with high functional group tolerance, mild conditions, and high sustainability. A new methodology for the electrochemically promoted benzylic functionalization under mild conditions has recently been developed. Benzylic-Tempo reagents were first prepared in good yields; a variety of nucleophiles can be utilized to react with the benzylic-Tempo reagents under electrochemical conditions to furnish desired the benzylic functionalization products. Oxygen, nitrogen, and carbon nucleophiles will

be screened for the formation of benzylic C-O, C-N and C-C bonds. This approach features mild reaction condition, high efficiency, and excellent functional group compatibility.

10. Photoredox autocatalytic Chan Lam coupling of free diaryl sulfoximines

Lucille Wells, Marisa Kozlowski, University of Pennsylvania

Sulfoximines are promising compounds in both organic synthesis and drug development. An area of interest in sulfoximine chemistry is the formation of N-arylated sulfoximines. Previous approaches either require strong oxidizing agents to oxidize species such as sulfilimines or had limited scope for direct N-H arylation. A photoredox dehydrogenative Chan-Lam coupling of free diaryl sulfoximines and arylboronic acids has been shown to have a good diversity of functional groups on both the sulfoximines and arylboronic acid as well as to not require an external oxidant. Mechanistic investigations and DFT calculations give insight into this coupling. Initially, a stoichiometric phase occurs converting the copper(II) to copper(I). The N-arylated sulfoximine product and the NH-sulfoximine substrate are able to serve as ligands for the produced copper(I). The ligated copper complex is a photocatalyst, which is able to reduce NH-sulfoximine by a single electron transfer, circumventing the need for an oxidant. The thermodynamic cycle between possible photocatalysts was explored. Following the oxidation of the copper, the NH-sulfoximine is deprotonated forming hydrogen gas in the process. Possible pathways were probed for the formation of the H₂ gas. These mechanistic insights provide a basis for future designs of systems for the formation of C-N bonds.

11. Lignin Valorization via Microscopic Reverse Biosynthesis

Mason Chin, Tianning Diao, New York University

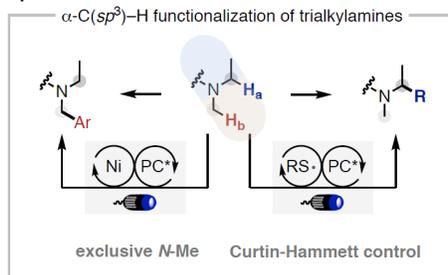
A standing challenge in biomass conversion is the valorization of lignin, an irregular polymer representing the largest renewable source of aromatic building blocks in nature. Lignin originates from phenylpropanoid building blocks, which polymerize through a sequence of oxidative radical coupling reactions to construct a complex mixture of different bonds and linkages. A new lignin depolymerization strategy based on the microscopic reverse biosynthesis converges the complex structural units to phenylpropanoid monomers using a titanium catalyst at room temperature within a few hours. The low molecular weight monomers retain important functionality and can be readily isolated in high yields as essential ingredients in fragrance, pesticides, and pharmaceutical precursors. Mechanistic studies preclude the commonly proposed titanium-mediated C–O bond homolysis in alcohol activation. Instead, the reaction is proposed to be promoted by Lewis-acid mediated carbocation formation, followed by reduction to generate a radical that proceeds to β -scission.

12. Late-stage α -C(sp³)-H Functionalization of Trialkylamine-containing

Yangyang Shen, Tomislav Rovis, Columbia University

Trialkylamines are functional linker widely presented in numerous natural alkaloids and marketed pharmaceuticals. The direct α -C(sp³)-H functionalization of such unit would offer new opportunities to rapidly build-up structurally complex amine architecture, even in the context of late-stage functionalization.¹ Currently, the vast majority of catalytic methods undergo selective late-stage alkylation

of less substituted α -C(sp³)-H bonds (mainly N-Me group) of complex trialkylamines. Despite these advances realized, the design of catalytic late-stage N-Me selective arylation or functionalization at more substituted position remains largely under explored. We have recently discovered the means to promote late-stage N-Me selective arylation² and alkylation at more crowded α -position³ of trialkylamine-containing pharmaceuticals under photoredox conditions.



References:

1. A. Trowbridge, S. M. Walton, M. J. Gaunt, New strategies for the transition-metal catalyzed synthesis of aliphatic amines. *Chem. Rev.* 2020, 120, 2613-2692.
2. Yangyang Shen, Tomislav Rovis*. Late-stage N-Me Selective Arylation of Trialkylamines Enabled by Ni/Photoredox Dual Catalysis. under revision.
3. Yangyang Shen, Ignacio Funez-Ardoiz, Franziska Schoenebeck*, Tomislav Rovis*. Site-selective α -C-H Functionalization of Trialkylamines via Reversible Hydrogen Atom Transfer Catalysis. under revision.

13. Mechanism of Nickel-Catalyzed Cross-Electrophile Coupling Reactions

Qiao Lin, Tianning Diao, New York University

Nickel-catalyzed cross-electrophile coupling reactions have emerged as appealing methods for constructing organic molecules while circumventing the use of stoichiometric organometallic reagents. A combination of kinetic, spectroscopic, and organometallic studies reveals that a (1,10-phenanthroline)nickel-catalyzed cross-electrophile reaction proceeds via a sequential reduction mechanism. The reduction of nickel(II) intermediates by zinc is the turnover-limiting step. In contrast to a commonly speculated scenario, zinc is only sufficient to reduce (phen)Ni(II) intermediates to Ni(I) species. The chemo-selectivity of cross-electrophile coupling as opposed to homo-coupling is attributed to the activation of C(sp²) and C(sp³) electrophiles separately by (phen)Ni(I)Br and (phen)Ni(I)Ar species, respectively. An electroanalytical method elucidates that (phen)Ni(I)Ar-mediated alkyl halide activation proceeds through a concerted halogen atom abstraction mechanism. The reactivity exhibits a linear free-energy relationship with the bond dissociation energy of the electrophile, which accounts for the observed reactivity of different electrophiles in catalytic reactions.

14. Electrochemical and spectroelectrochemical properties of symmetric and asymmetric tetraarylazadipyrrin chromophores

Amira Padilla, Barry Pemberton, Stockton University

Tetraarylazadipyrrin chromophores are precursors to aza-bodipy dyes which have been of considerable interest as visible to near-infrared emitting dyes in the last decade. These chromophores are intensely blue-to-black colored molecules. We have synthesized a series of these symmetrical and asymmetrical compounds including some multi-responsive emitting molecules that are accessed via selective excitation

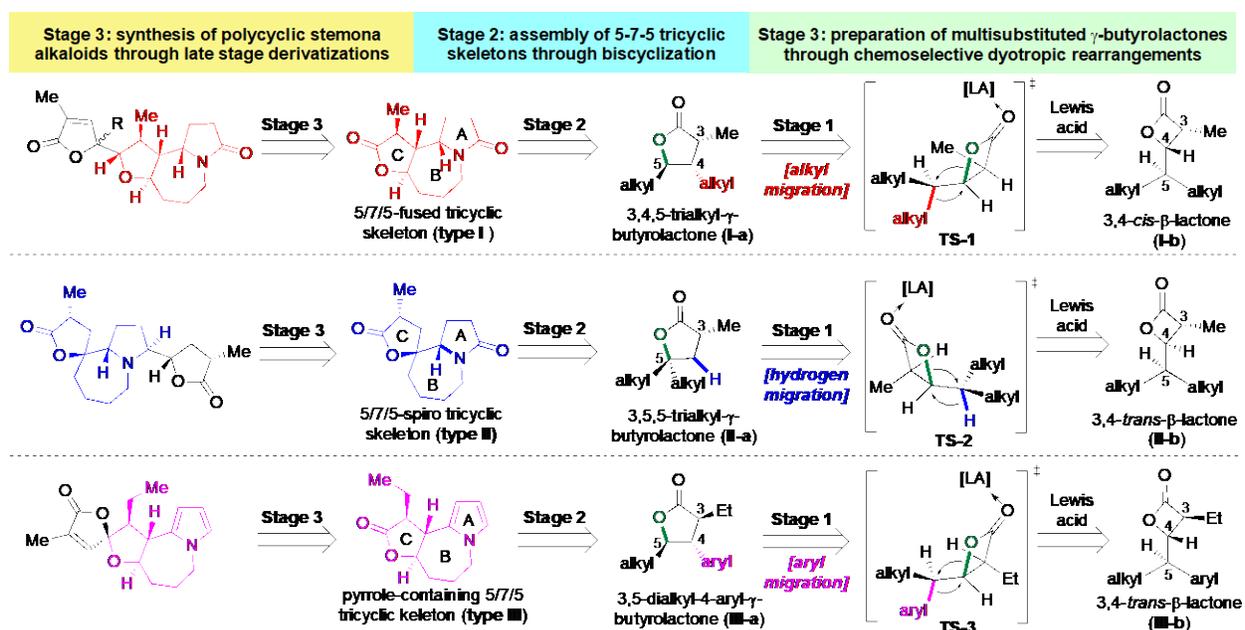
wavelengths. To afford multi-responsive emitting chromophores on a single molecule, three conditions must be met: pre-orientation of the substituents, rigidification of the structure and electronic decoupling between the chromophores. Using electrochemistry as a diagnostic tool, we can explore the electronic decoupling of these individual chromophoric units and measure the changes to their absorption via spectralelectrochemical techniques. The goal of this research to broaden our understanding of the photophysical and electrochemical behaviors when attached to dipyrin backbones to create more efficient multi-responsive chromophores.

15. Divergent Synthesis of Stemona Alkaloids through Chemoselective Dyotropic Rearrangement of β -Lactones"

Zhen Guo¹, Ruiyang Bao^{1,2}, Yuanhe Li¹, Jingyang Zhang¹, and Yefeng Tang^{1*}

¹Tsinghua University, Beijing, China, ²New York University, USA

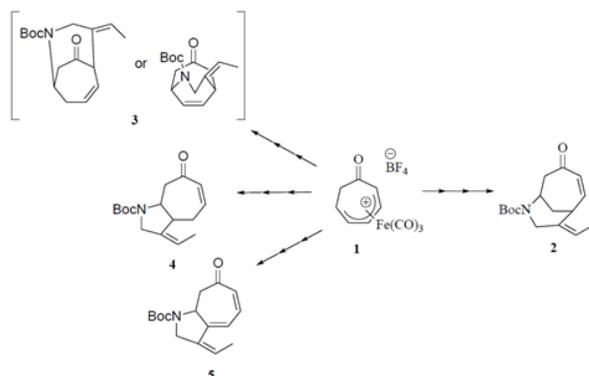
Stemona alkaloids, primarily isolated from the Stemonaceae plants, constitute a salient class of natural products displaying remarkable structural and biological diversity. So far, more than 200 Stemona alkaloids have been identified, and they have emerged as popular synthetic targets for decades. Our interest in Stemona alkaloids was motivated by the mechanistically interesting and practically useful dyotropic rearrangement of β -Lactones. Through judicious manipulation of the substrate structures, a various kind of multisubstituted γ -butyrolactone moieties, which are rich in Stemona alkaloids, can be obtained. Specifically, three typical 5/7/5 tricyclic skeletons associated with stemoamide, tuberostemospiriline and parvistemonine were first accessed through chemoselective alkyl-, hydrogen-, and aryl-migration dyotropic rearrangements of β -lactones, respectively. Furthermore, several polycyclic Stemona alkaloids including saxorumamide, isosaxorumamide, stemonine and bisdehydroneostemoninine were obtained from the aforementioned tricyclic skeletons through late-stage derivatization. Our effort results in the divergent synthesis of seven Stemona alkaloids, through a unified strategy.



16. "Tricarbonyl(tropone)iron as a versatile platform for the syntheses of diverse azapolycycles".

Aaron Shoemaker, Daniel Griffith, Lafayette College

We demonstrate the use of tricarbonyl(tropone)iron as a versatile, yet simple starting material for accessing bridged azapolycycles with a seven-membered carbocycle, a structural motif found within a number of biologically active alkaloids. In this work, the bicyclic core of ervitsine was obtained in 31% overall yield from the cationic iron complex **1** via three key reactions: (1) aza-Michael addition, (2) photo-demetallation, and (3) intramolecular Heck cyclization. The effects of variations on these reactions were investigated, including alkene position(s), halogen scope, and Heck reaction conditions. Interestingly, two additional bicyclic systems were accessed by way of a second step oxidative demetallation followed by a tandem Heck reaction-anion capture. Through the simple variation of demetallation and Heck reaction conditions, diverse azabicyclic systems—3 in this work alone—can be efficiently accessed.



17. Computational investigations on the reactions of elemental sulfur with nucleophiles

Jyoti Sharma and Pier Alexandre Champagne, New Jersey Institute of Technology.

Elemental sulfur is often used in organic synthesis as its low cost, along with high abundance, makes it a desirable source of sulfur atoms. However, sulfur's unpredictable catenation behavior poses challenges to its widespread usage as it causes difficulties in designing new reactions that can account for its multifaceted reactivity. Chemically accurate results can be obtained using modern computational approaches such as Density Functional Theory (DFT) calculations, except for the largest systems. Therefore, they are apt for probing experimentally invisible intermediates and transition structures in the complex chemical reactivity pathways of sulfur and polysulfides.

This presentation will showcase our recent efforts in two areas. First, benchmarking 12 well-known DFT functionals that include local, non-local, and hybrid methods against high-level methods for the accurate treatment of organic polysulfides, taking cyanide as a nucleophile. Our results indicate that B3LYP-D3(BJ) and M06-2X density functionals are the most accurate for calculating reaction energies, whereas MN15, MN15L, M06-2X, and ωB97X-D are the most accurate for activation energies. The second part will discuss how we applied the best method(s) to uncover the molecular mechanisms explaining how elemental sulfur and organic polysulfides react with nucleophiles. We will compare the propensity of strong

nucleophiles (CN⁻, PPh₃, sulfides, carbanions), nitrogen nucleophiles (methylamine, aniline, NDAP, DABCO), and oxygen nucleophiles (hydroxide, alkoxides, methoxy) to react with elemental sulfur. Our preliminary results indicate that several products could be possible from strong nucleophiles via inter- and intramolecular attack on polysulfides. It was also noticed that polysulfides formed from the nitrogen nucleophiles have less energetically favorable pathways than anticipated, opening new possibilities for the study of organic polysulfides in various settings.

18. Cationic porphyrins: synthesis, characterization and application.

Usha Kalra, James E. Hanson, Seton Hall University

The preparation of cationic porphyrins is important for a variety of biochemical studies. The traditional method of alkylation of tetra-pyridylporphyrin is proved to be inefficient, requiring very large excesses of alkylating agents. We have explored the use of “click chemistry” as an alternative method for the preparation of meso substituted tetracationic porphyrins. The azide-alkyne cycloaddition (AAC), has become a powerful basis for the click reactions and this has been converted into a distinctive tool for the design and synthesis of wide range of products. This cationic porphyrin is able to bind to other molecules for further studies like capable of binding to the DNA molecules and stabilizing them.