

Synthesis of a Novel Imidazopyrimidine-based Macrocyclic Ligand

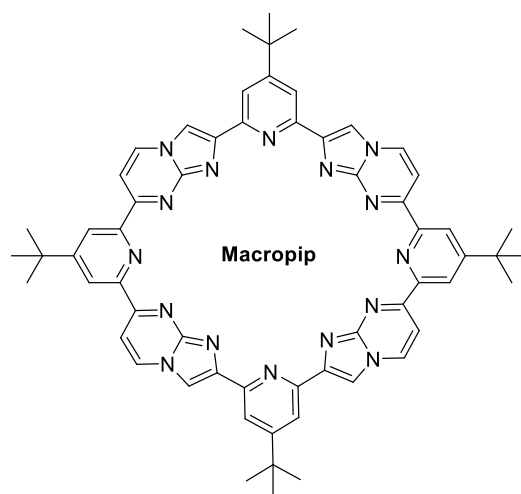
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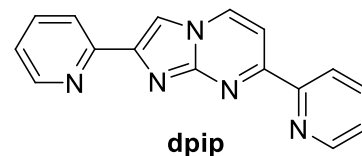
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Macrocycles are large compounds featuring a cyclic organic framework with 12 or more atoms while coordinating with one or more metal centers.¹ Such complexes offer significant advantages, as their rigid, preorganized structure often exhibits a higher affinity and reaction selectivity compared to the ring-opened analogues.² Additionally, conventional monometallic complexes have been extensively studied due to a wide range of robust and easily accessible ligands. In recent years, multimetallic complexes have attracted an increasing attention in transition-metal catalysis due to their enhanced selectivity and reactivity over monometallic analogues.³ This project aims to integrate macrocycles and multimetallic complexes together by developing a robust, high-yield synthesis of an imidazopyrimidine-based macrocyclic ligand capable of forming homo- and heterotetrametallic complexes. Following the successful synthesis and characterization of the ligand, several metal candidates—such as Cu, Fe, Pt, and Pd—could be tested for coordination into this macrocyclic ligand.



A potential synthetic approach to this designed ligand, **macropip**, have been proposed, with the half-cyclized intermediate successfully isolated and identified. A previous study on the bimetallic ligand analogue of this macrocyclic ligand, **dpip**, is shown to have unsymmetric coordination sites and strong electronic communication between the metal centers.⁴ Several heterobimetallic complexes has been reported. Therefore, we expect this designed macrocyclic ligand would further enhance these properties and offer examples of new macrocyclic heterotetrametallic complexes. This would represents a valuable contribution to the largely underexplored field of multimetallic macrocyclic complexes, offering new opportunities for structural and functional innovation.



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Toward *In Vivo* Olefin Metathesis: Targeted Catalyst Delivery via a Protein-Catalyst Conjugate

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Olefin metathesis, as an exceptionally versatile method for building carbon-carbon bonds, has enormous potential as a tool in chemical and cell biology. At the frontier of such efforts is *in vivo* olefin metathesis, in which metathesis takes place within the environment of the living cell. Examples include ring-closing metathesis (RCM) in bacteria by a metalloenzyme containing biotinylated Ru,^[1] and, more recently, metathesis of unsaturated fatty acids in living algae for the production of olefins from sunlight and CO₂.^[2] A limitation in the latter ambitious goal is the reliance on passive, affinity-labelling means to transport the lipophilic catalyst into the cellular compartments (the lipid droplets, LDs) in which the metathetical production of 1-olefins is planned to occur. Poor specificity arising from diffusion of an affinity-tagged catalyst results in accumulation of catalyst in lipid-rich areas outside these target organelles.

Here we describe a union of these approaches to enable *targeted* catalyst transport into the LDs. The catalyst is conjugated to the Major Lipid Droplet Protein, a protein which, as the name suggests, localizes to the LD (Figure 1). This approach is designed to limit non-specific interactions, to shield the catalyst from the cellular environment during transport, and to aid catalyst localization and retention in the LD, hence improving metathesis productivity and reducing cell toxicity. Advances toward this goal will be described.

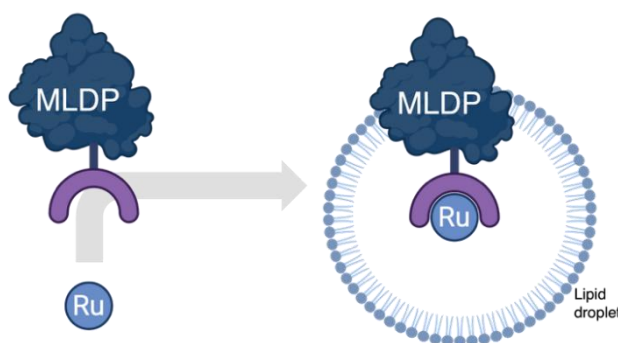


Figure 1. Targeted catalyst transport into lipid droplets enabled via Major Lipid Droplet Protein (MLDP)-catalyst conjugation

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Rational Design of a Main Group Catalyst for Suzuki Cross-Coupling Reactions with Esters

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Catalysis is a pillar of green chemistry because it allows to reduce the amount of waste generated and the energy input required for chemical transformations. The 20th century advent of transition metal coordination chemistry has enabled an explosion of catalytic processes.¹ In recent years, there has been growing interest in exploring the potential of more earth-abundant, non-metallic elements in catalysis.² This prospect would allow chemists to benefit from new, unique or previously underdeveloped reaction mechanisms and methods and cheaper catalysts. In this context, this research seeks to design a catalyst independent from precious metals to be applied for the coupling of small organic molecules into larger chemicals in a similar process to palladium-catalyzed technologies known as cross-coupling, which were honored with the 2010 Nobel Prize for Chemistry.³ This project makes use of the powerful predictive capability of computational chemistry to design a catalytic pathway for metal-free cross coupling reactions where the catalyst backbone is based on boron atoms as well as nitrogen and carbon atoms. Specifically, we experimentally tackle the cross-coupling of esters, a common organic functional group, which are traditionally inert towards metal catalysts. This metal-free approach provides alternatives to metal-based paradigms and expands the current scope of cross-coupling reactions, thus allowing the development of complementary synthetic methods and routes.

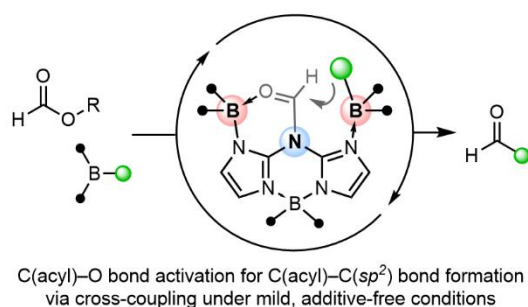


Figure 1. A metal-free catalyst for the cross-coupling of esters and organoboranes.

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2-Alkylphosphino-1-boraadamantanes

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Main group compounds are being actively studied for applications in small molecule activation and catalysis as metal-free alternatives.¹ In contrast to transition metals, main group elements rely on Lewis-acid base interactions to fine-tune reactivity.² In this field, group 13 elements, such as boron, are of interest because of their intrinsic Lewis acidity. Coordination of a Lewis base induces geometrical changes at the boron center, making it more tetrahedral and Lewis acidic. This has led to investigations that take advantage of geometric perturbation to target enhanced or differential reactivity.³ Computations have revealed that pyramidalized, non-compliant VSEPR group 13 elements, including boranes, make stronger Lewis acids than they do in their ground state due to their reduced complexation reorganization energy.⁴ Thus, providing an additional tool for tuning Lewis acidity in group 13 elements. An example of this phenomenon is 1-boraadamantane, where the boron atom in the boracycle is forced into a 3-coordinate trigonal pyramidal geometry due to its coordination environment, enhancing its Lewis base affinity.⁵ Herein, we introduce the first examples of bifunctional boraadamantanes, their modification with pendant phosphorus groups, and our foray into the coordination chemistry of these scaffolds.⁶

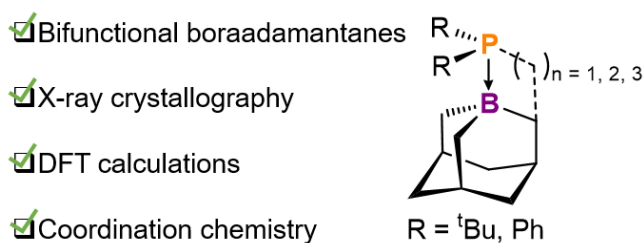


Figure 1. Boraadamantanes pertinent to this study

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C-H Activation of Azine-Type Heterocycles via Cp*Rh(PMe₃)PhH for Parahydrogen-Induced Polarization

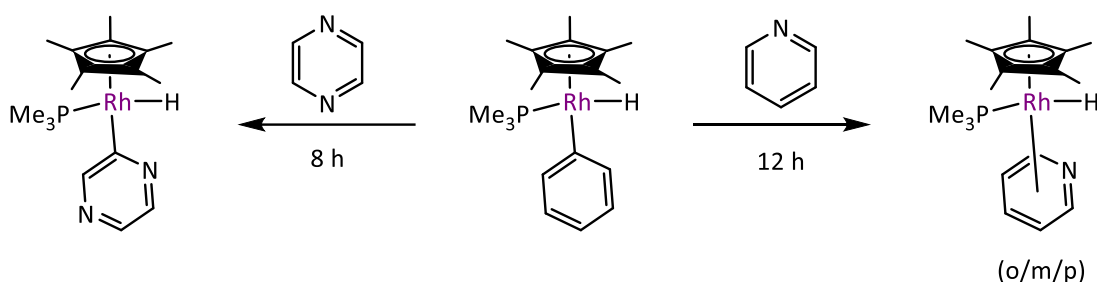
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Parahydrogen induced polarization (PHIP) is a fast, low-cost method of enhancing magnetic resonance signals. According to preliminary studies, transition metal centers have been shown to promote PHIP through the attached ligands¹. Our lab is interested in the activation of azine-type heterocyclic ligands. This class of molecules have potential uses in medicine, materials, and synthesis². This study describes the scope of polarizable ligands by synthesizing azine-type pyridinyl and pyrazinyl Cp*Rh(PMe₃)H complexes. Heating afforded pyridinyl and pyrazinyl complexes Cp*Rh(PMe₃)(py)H and Cp*Rh(PMe₃)(pz)H. While only one isomer of the pyrazinyl complex was formed, three regioisomers of the pyridinyl complex were formed, corresponding to activation at the ortho, meta, and para positions; after sustained irradiation or heating, the meta regioisomer is converted to its ortho or para analogues. These findings show potential in applications of PHIP studies on azine-type heterocycles and their derivatives.



Scheme 1. Synthesis of Cp*Rh(PMe₃)(pz)H (left) and Cp*Rh(PMe₃)(py)H (right).

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The Fabrication of Agarose/Humic Acid Persistent Luminescent Hydrogels

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In the past decade, drug-loaded hydrogels have gained popularity due to their localized release within the pathological region, thereby minimizing systemic side effects.^[1] Spatiotemporal drug release from hydrogels is commonly achieved by combining a photothermal agent with a thermoresponsive polymer during hydrogel formation.^[2] By exciting the injected hydrogel with a high-powered (e.g., 1-2 W/cm²), tissue penetrable, 808 nm laser, the heat generated by the photothermal agent can cause the gel to swell, leading to controllable drug release. However, one existing concern is the exposure duration to the laser, which can cause severe skin burns and permanent scarring.^[3] In light of this, to lessen the necessary laser exposure time for gel swelling, we incorporated a near-infrared (NIR) emitting persistent luminescence phosphor, Zn₃Ga₂GeO₈:Cr³⁺ (ZGGO), into a photothermal hydrogel. In this work, ZGGO nanoparticles, which are excitable using UV light, NIR laser, and X-rays, act as a secondary excitation source for humic acid, a photothermal agent with high photothermal conversion efficiency. In comparison to the hydrogel free of ZGGO, our thermoresponsive agarose-based hydrogel reaches desirable temperatures for gel swelling with less laser exposure time, while also maintaining higher temperatures in the absence of the laser. These preliminary findings indicate that integrating ZGGO into the hydrogel matrix enhances its potential as a suitable platform for the delivery of different therapeutics.

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Design, Synthesis, and Characterization of Multimetallic Complexes Supported by an Imidazopyrimidine-Based Trinucleating Ligand

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Homogeneous transition metal catalysis has revolutionized chemical synthesis, enabling numerous Nobel prize-winning reactions.^[1] Whilst most catalysts are monometallic, a compelling yet much underexplored area is the use of multimetallic complexes. Several studies and reviews have highlighted the beneficial effects of having multiple metal centers held in proximity.^[2,3] These sorts of systems often display improved catalytic performances over their monometallic counterparts. In terms of trimetallics, there is a paucity of ligand systems that can reliably produce a precise and controlled arrangement of the three metal centers in a way that is useful in catalysis. This is due to most relying on flexible organic frameworks tied to a symmetric node, additionally excluding them from heterometallic applications.^[4]

Herein is reported a new trinucleating ligand framework, **bpipp**, specifically designed to enforce close proximity among three metal centers upon complexation. Based on the inherently unsymmetric imidazopyrimidine backbone, a heterocycle that has previously been proven in our group to be useful in producing bimetallic complexes.^[5] The ligand features a tridentate pincer-like binding pocket with two additional bidentate binding pockets. This approach utilizes scalable synthetic methods to create a rigid ligand scaffold that precisely controls the spatial arrangement of the metals. The versatility of **bpipp** is demonstrated through the synthesis of several trimetallic complexes of Ni(II), Cu(II), Co(II); fully characterized by NMR spectroscopy, ESI-HRMS, and X-ray crystallography. Notably, our ligand design achieves short metal-metal distances ranging from 3.3–3.5 Å, significantly closer than most reported trimetallic systems. This structural feature establishes an ideal platform for investigating genuine three-metal cooperative effects in catalysis.

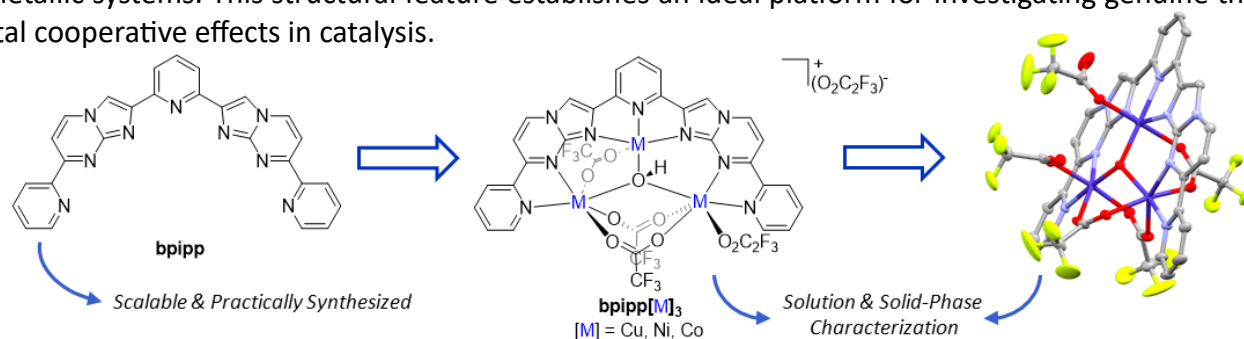


Figure 1. Design, synthesis, and characterization of homotrimetallic complexes supported by **bpipp**.

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Exciting Boron Difluoride Hydrazone (BODIHY) Dyes using Persistently Luminescent Strontium Magnesium Silicate (MSO)

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Boron difluoride hydrazone (BODIHY) dyes exhibit intense fluorescence and tunable optical properties¹, making them promising candidates for applications such as photovoltaics and bio-imaging. However, one limiting factor is their need for constant excitation, limiting their use in low-light conditions. In this study, we demonstrate a proof of concept for developing persistently luminescent (PersL) BODIHY dyes by coupling them to strontium magnesium silicate nanoparticles (MSO) in hybrid films. Films were synthesized by using the doctor blade method to apply a film of MSO and BODIHY homogenized in an acrylic medium. The properties of this hybrid film were characterized by photoluminescent spectroscopy and decay. The emission spectrum of MSO ($\lambda_{em} = 471$ nm) and UV absorption of BODIHY ($\lambda_{abs} = 554$ nm) show significant overlap, enabling efficient energy transfer. The hybrid films exhibited dual emission peaks corresponding to MSO and BODIHY, with tunable peak emission wavelengths and intensities dependent on mass ratios. Upon removing the excitation source, the emission peak of the film remains stable and the emission decays following a bi-exponential decay curve with time constants $t_1 = 21.00$ and $t_2 = 25.66$.

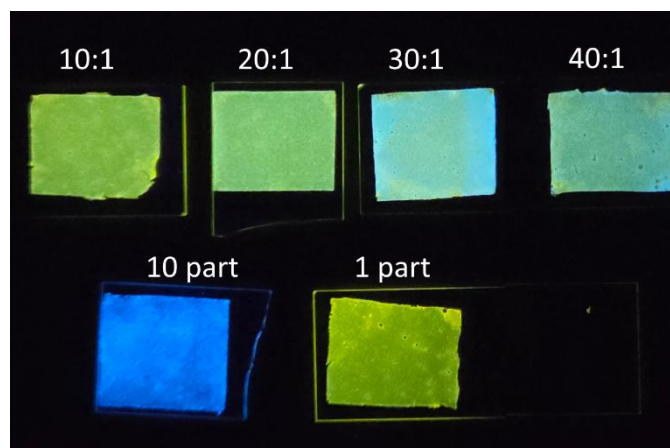


Figure 1. BODIHY and MSO films under UV excitation ($\lambda_{ex} = 365$ nm). Hybrid films were developed following 4 different mass ratios (40:1, 30:1, 20:1, and 10:1 BODIHY to MSO). Control films were 10 part MSO and 1 part BODIHY.

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Designing Polar Crystals by Co-crystallizing Molecular Nanodiamonds

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Polar crystals are high in demand, largely due to their piezoelectric and non-linear optical properties as seen by second harmonics generation. The polarity of the crystals also makes it a useful property for synthesizing quantum bits. As opposed to metal oxides (ceramics), which require high-temperature processes for manufacturing, polar crystals using organic molecules are a promising alternative since these can be manufactured under mild conditions. While most polar molecules crystallize into non-polar space groups, several hetero-adamantanes (molecular nanodiamonds containing heteroatoms) crystallize in the polar space group R3m. As expected, hetero-adamantane polar crystals also create second harmonics and have piezoelectric properties. We discovered that some hetero-adamantanes form crystalline solid solutions (cocrystals that are molecular alloys) with each other. Specifically, we found that Br-TAA and Cl-TAA (7-halo-1,3,5-triazaadamantanes) form solid solutions in R3m without any miscibility limits.^[1] PTA (1,3,5-triaza-7-phosphoadamantane) is a hetero-adamantane with potential to form polar crystals, yet there do currently not exist any studies about crystalline solid solutions using PTA and related molecules. We are currently investigating PTA itself, and its derivatives including its oxide, sulfide, and selenide, regarding their ability to form solid solutions among each other and with X-TAA. Our findings related to structures and physical properties of these hetero-adamantanes and crystalline solid solutions will be presented.

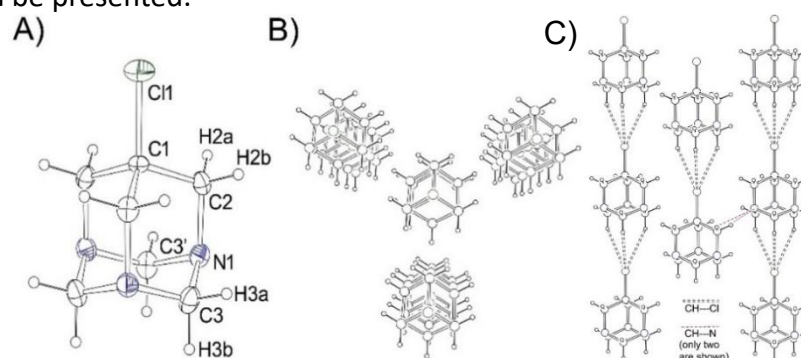


Figure 1: Crystal structure of Cl-TAA. A) view of the molecular unit. The crystallographic three-fold axis runs through Cl1 and C1 (crystallographic c-axis). Selected distances (Å) and angles (°): C1-C2, 1.526(2); C1-Cl1, 1.810(4), C2-N1, 1.469(3), C2-C1-C2', 109.64(14); C2-C1-Cl1, 109.30(14); C2-N1-C3, 108.66(14); C3-N1-C3', 107.5(3). B) Packing viewed along the c-axis. C) Packing shown with c-axis aligned vertical. CH-Cl short contacts (2.939 Å) involving H3b are shown with dashed double lines; a selected instance of two CH-N short contacts (2.738 Å) involving the same methylene is shown with dashed single lines.^[1]

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Magnesium Germanium Oxide Hydrate Nanowires with Outstanding Surface Stability for Selective Cationic Dye Removal

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Physical adsorption is one of the most promising methods for organic dye removal in wastewater. However, existing adsorbent materials lack a combination of selectivity, efficiency, stable performance over a wide pH range, and reusability after repeated regeneration. In this work, we presented a novel adsorbent, magnesium germanium oxide hydrate (MGOH) nanowires. Utilizing electrochemical and acid-base titration methods, we found that MGOH possesses a unique crystal structure that is rich in hydroxyl (-OH) groups. These -OH groups keep the surface of MGOH negatively charged over a wide pH range from 0 to 10.6, which hasn't been achieved by any adsorbent to date. Using rhodamine B (RhB) as a model cationic dye, we demonstrated that a 97.4 % removal efficiency can be achieved within 15 min in contact with MGOH at room temperature. The adsorption selectivity of MGOH toward cationic dyes was further demonstrated by effective removal of target dyes in dye mixtures. In addition, MGOH can be easily regenerated through solvent washing and thermal annealing for multiple cycles without losing its adsorption capability.



Figure 1. Graphical Abstract.

References:

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