

Nickel-catalyzed cross-electrophile coupling facilitated by a Co(II) co-catalyst

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Nickel-catalyzed cross-electrophile coupling (XEC) is an important method for the formation of C(sp²)-C(sp³) bonds, present in many pharmaceutical targets. To improve control over catalysis, prior work has used co-catalysts to generate the alkyl radical that can then be captured by the nickel species and coupled with the aryl substrate. Since the nickel and co-catalyst cycles are relatively independent of each other, such systems can be optimized by tuning the catalyst loadings to match the rates of intermediate steps. In this project, we aim to use a Co(salen-Me) co-catalyst to couple aryl halides with secondary alkyl chlorides. We have studied the substrate scope, optimized the catalyst system for a variety of aryl and alkyl halide substrates, and quantified yields by ¹H-NMR spectroscopy. Additional work has been done towards obtaining isolated yields and to synthesize hypothesized intermediate species for use in mechanistic studies.

Biochemical reconstitution and structural characterization of the *Alvinella pompejana* inner ring complex of the nuclear pore complex

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Nuclear pore complexes (NPCs) are the sole gateways facilitating selective, bidirectional transport of folded proteins and ribonucleic acids across the nuclear envelope. Obstacles arise in structural studies of the NPC due to the extensive intrinsically disordered regions and high flexibility within the inner ring complex (IRC). In this project, we leverage the thermophilic annelid *Alvinella pompejana* as a model organism for IRC reconstitution because of its adaptations to increase the thermostability of its proteins. We successfully biochemically reconstituted full-length *A. pompejana* inner ring nucleoporins, CNT•Nup93, *in vitro*. This involved the expression and purification of full-length homologs of the CNT and Nup93 in *E. coli* and testing whether they formed defined multimeric complexes. In addition, we biochemically validated current Cryo-EM structures of the Nup205•Nup93R2 complex via 5-Alanine scanning. By mutating various residues in Nup93 with alanine, we were able to determine residue regions of mutants A1, A3, A4, and A5 play a role in this key scaffold interaction. Future steps include specific mutations of hydrophobic and electrostatic residues in these regions to observe any changes in interaction. Another focus would be the purification and reconstitution of other *A. pompejana* inner ring homologs, to achieve a complete reconstitution of the IRC.

Elucidating the molecular mechanisms of DDX19 nucleocytoplasmic trafficking

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The export of mRNA from the nucleus to the cytoplasm is a vital step in eukaryotic protein production. DDX19, a protein involved in mRNA export, ensures directionality of this process by removing proteins bound to mRNAs as they exit the nucleus at the cytoplasmic face of the nuclear pore. Interestingly, studies have found that DDX19 translocates into the nucleus in response to DNA damage and clears harmful RNA-DNA hybrids. However, the mechanisms through which DDX19 may be transported into the nucleus remain unclear. Additionally, the interplay between its role in mRNA export and its nuclear role, including how DDX19 activity modulators impact its transport and vice versa, is unknown. In this work, we confirm and structurally characterize the interaction between DDX19 and the nuclear transport factor TNPO3 via size-exclusion chromatography with multi-angle light scattering (SEC-MALS) and single-particle cryo-electron microscopy (cryo-EM). We also explore the effect of DDX19 activity modulators on DDX19•TNPO3 complex formation. Our findings reveal that TNPO3 binds to the C-terminal domain of DDX19 through multiple interfaces, including some necessary for activity modulator binding, in a predominantly electrostatics-based interaction. Altogether, these results support that DDX19 nuclear import is mediated by TNPO3 and likely interrupts its cytoplasmic activity, contributing an additional perspective to regulation of mRNA export by the nuclear pore complex.

Mechanistic and kinetic characterization of a vanadium deprotono-metallacyclobutadiene catalyst for cyclic polyalkyne synthesis

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Cyclic polyalkynes are a family of conjugated polymers notable for their diverse physical properties, such as superior electrical conductivity and flexibility, presenting potential applications in a variety of materials-related fields. Current catalysts often display uncontrolled kinetic behavior leading to mechanistic intractability or utilize expensive and impractical 4d and 5d metals. In this study, we present the analysis of a vanadium deprotono-metallacyclobutadiene catalyst that operates via a ring-expansion pathway. The catalyst demonstrates broad alkyne substrate scope, including monomers with aryl halide-, anisole-, polycyclic aryl-, and heterocycle- substituents. NMR analysis and the synthesis of a catalytically active intermediate have allowed for an extensive kinetic study, providing insight into the reaction mechanism. Together, these studies provide a detailed mechanistic understanding of vanadium-catalyzed cyclic polyalkyne synthesis, establishing wide functional group tolerance on an economically efficient metal and allowing for focused optimization of the reaction.

Activating cobaltocenes for electrocatalytic CO₂ reduction to formate at low overpotential by proton-coupled electron transfer mediators

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This project focuses on developing new catalytic systems for selective electrocatalytic reduction of carbon dioxide into value-added chemical products, specifically formate. In this study, a series of cobaltocene derivatives, (MenCoCp₂, n = 0, 2, 4, 6, 8, 10), serve as the homogeneous catalysts, while the piano-stool complex [CpCo(depe)H][PF₆] (Cp = cyclopentadienyl; depe = 1,2-bis(diethylphosphino)ethane) acts as a proton-coupled electron transfer (PCET) mediator. Together, these components enable the reduction of CO₂ to formate at low overpotentials with high selectivity. These cobaltocene derivatives were first synthesized and characterized and further studied through cyclic voltammetry and bulk electrolysis for formate production. Under optimized conditions, a Faradaic efficiency for formate of up to 94% was achieved at an overpotential of only 280 mV, placing this system among the best-performing organometallic catalysts in terms of both selectivity and overpotential. The mechanisms of these catalytic systems were further analyzed through UV-Vis kinetics and stoichiometric studies.

Soft ionic polymers for stretchable ionic circuits

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Wearable bioelectronics need thin-film circuits that stretch with the body, which requires an elastic, ionically conductive material between their rigid components. In this project, we develop a non-swelling, non-brittle, tough, elastic, and stretchable hydrogel for a glass capillary setup used to probe the electrical properties of the ionic circuit. An initial polyacrylamide hydrogel proved too brittle under tensile testing. We later evaluated four alternative formulations: a poly(vinyl alcohol)/zwitterionic monomer double network, a copolymer of a zwitterionic monomer with acrylamide, and a concentrated, single-monomer zwitterionic gel. The first two failed through spontaneous precipitation and excessive swelling. The zwitterionic copolymer polymerized only partially, suggesting that the initiator needs to be changed. We attribute the incomplete cure to a photoinitiator different from the one in its literature basis. We predict that the concentrated zwitterionic gel offers the most promising result with the highest toughness and greatest elasticity while preserving swelling. Remaining work includes repeating that formulation with the intended photoinitiator, switching to a redox initiator for the copolymer route, and falling back to two other monomer combinations if neither succeeds.

Tuning counteractions in molecular qubits to illuminate the effect of spin-phonon coupling and covalency on low temperature T₁

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In recent years, paramagnetic transition metal complexes have emerged as promising candidates for quantum sensing applications due to their small size and structural tunability. By monitoring electron spin decoherence data of the qubit candidates, high spatial and temporal resolution may be gleaned about the local chemical microenvironment, including the dynamics of electric and magnetic fields, the proximity of nearby ions, and the behavior of paramagnetic nuclei. Such applications, however, rely on a robust mechanistic understanding of how molecular structure and environmental factors contribute to spin decoherence. Our focus in this paper was to further understand the contributions of delocalized phonon modes and local molecular covalency, independent of other electronic factors, on spin relaxation. We honed a previous theoretical model for the decomposition spin-orbit coupling along the progression of phonon modes by allowing for reduced assumptions of anisotropy in orbital overlap and spin-relaxation. This was performed by using magnetically dilute single crystal complexes, controlling for phonon modes through counterion selection, to perform variable-temperature variable-field electron paramagnetic resonance spectroscopy to perfectly quantify the spin relaxation tensor. The technique was then applied by varying covalency while holding electronic and vibronic structure approximately constant to similarly detune the contribution of covalency to spin relaxation.

All-optical electron spin coherence in an axial tungsten complex of relevance to tungstoenzymes

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Molecules with unpaired electrons possess angular momentum via spin, an inherently quantum-mechanical degree of freedom. These paramagnetic molecules thus constitute spatially precise, structurally and functionally tunable platforms for quantum sensing. Ultrafast pump-probe optical spectroscopy offers a platform to examine spin dynamics with temporal resolution five orders of magnitude greater than traditional spin initialization and readout methods. However, such spectroscopies require substantive coupling of electron spins to light, which is governed by a complex array of electronic structure factors. In this work, room-temperature, ultrafast all-optical spin coherence is demonstrated in a low-symmetry $S = 1/2$ tungsten complex. The electronic structure of this system was probed with absorption, magnetic circular dichroism, resonance Raman, and continuous-wave/pulse electron paramagnetic resonance spectroscopies, as well as quantum-chemical calculations. Ultrafast spin dynamics and contributions to spin decoherence in room-temperature solutions were investigated with time-resolved Faraday rotation. This work both expands the library of optically addressable molecular spin qubits and elucidates contributions to spin decoherence in a system relevant to the active sites of tungstoenzymes, with potential implications for native biological quantum sensing and the electronic design elements required for optical spin-addressability in low-symmetry systems.

Generalizing blue copper proteins as biomolecular spin qubits via room-temperature electron spin coherences in azurin

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Molecular qubits can act as quantum sensors by exploiting the sensitivity of electron spin coherences to external perturbations. These systems can be rationally designed to display a desirable electronic structure and spin dynamics that enable interrogation of specific environments. Bio molecular qubits offer a promising platform for quantum sensing through native or recombinant expression of molecular quantum sensors that permit study of biological processes, especially those occurring at localized and interfacial regions in cells. Using time-resolved Faraday ellipticity/rotation (TRFE/R) spectroscopy, which enables all-optical measurement of electron spin decoherence at room temperature and in solution, this project establishes electron spin coherence in the type 1 blue copper protein azurin. This protein enables investigations into whether the reduction potential of this system correlates with its

electron spin decoherence time. Such a relationship would provide a design principle for tuning biomolecular quantum sensors and insight into a potential link between spin coherence and electron transfer driving force.