

Department Research Symposium Summer 2023

August 4, 2023. CENT 192

Abstracts of Presentations

Introduction and Snacks

8:45 am: Allen Schoffstall

Understanding the Molecular Interactions of a Lupus Therapeutic

9:00 am: Camden Trent

Systemic Lupus Erythematosus, or SLE, is an inflammatory autoimmune disease and presents in about 14,000 new cases every year. The current treatment plans only focus on the symptoms of the disease and not the underlying biochemical levels. The complement system is a target for therapeutic treatments of SLE, given the production of auto-antibodies from mature B cells. Along with our collaborators, we have identified two antibodies that have been shown to halt and reverse the effects of Lupus in mouse models. This therapeutic approach stems from engineering a single chain variable fragment (scFv). The expression of one of these, 3d29, in mammalian cells resulted in high levels of pure protein after purification. The binding affinities of this protein have been studied and a model that offers a potential novel therapeutic treatment for SLE.

Reduction of 3,5-disubstituted isoxazoles

9:15 am: Brandon Shull

The synthesis of 3-phenyl-5-trimethylsilylisoxazole was accomplished using 1,3-dipolar cycloaddition methodology. Reaction of benzaldehyde oxime with NCS and then with base gave a nitrile oxide, which underwent cycloaddition with trimethylsilylacetylene to give a 3,5-disubstituted isoxazole. This synthesis was followed by a series of transfer hydrogenation reactions in attempts to reduce the isoxazole to a β -enaminone. Transfer hydrogenation reactions were attempted utilizing a variety of metallic catalysts and hydrogen donating species in both the microwave and standard reflux conditions. None of the microwave reactions tested were successful at breaking the isoxazole N-O bond or gave an incomplete reaction with a mixture of products. One standard reflux reaction that was successful in reduction of the isoxazole utilized hydrazobenzene as a proton source and a copper on iron catalyst dissolved in DMF at 100 °C overnight. These reductions still need optimization due to over reduction of the enaminone to a terminal alcohol.

Stepwise building block Os(II) complexes for potential use in photodynamic therapy

9:30 am: Alissa Ervin

Photodynamic therapy (PDT) is an area of research that aims to incorporate photosensitizing agents into cancer treatment to provide a less invasive treatment and improve patients' quality of life. Similar to past research with ruthenium complexes, osmium metal-ligand complexes have shown promising opportunity in PDT. The proximal and distal $[\text{Os}(\text{dpop}')(\text{3,6-dppn})(\text{Cl})]^+$ isomers were synthesized, separated, purified, and characterized in order to develop a preparative method for future complexes capable of binding $\text{Pt}(\text{Cl})_2$ for potential use in PDT. The complexes were purified through column chromatography using a Sephadex LH-20 column. Characterization of the complexes through ^1H , ^{13}C NMR and COSY and HSQC NMR, and HRMS verified the successful syntheses of proximal and distal $[\text{Os}(\text{dpop}')(\text{3,6-dppn})(\text{Cl})]^+$ isomers. Quantitative UV-Vis spectra showed that the metal-to-ligand charge transfer transitions in both isomers are compatible with the wavelength of light necessary to penetrate the skin.

Preparation and reaction of a tricyclic enamine

9:45 am: Kaleb Fekade and Hunter Redmon

This project is aimed at preparing tricyclic enamines for the purpose of conversion to other heterocycles. Starting with propargylated salicylaldehyde oxime, the reaction for creating a tricyclic isoxazole, 4H-chromeno[4,3-c][1,2]oxazole, using NaOCl was optimized to prepare enough tricyclic isoxazole by intramolecular cycloaddition for reducing and opening the isoxazole ring to form an enamine. Reduction of the isoxazole ring utilized methods involving either 1. diphenyl hydrazine and CuFe, 2. Raney nickel and hydrogen gas, or 3. NiSO_4 and NaBH_4 . Although all of these methods successfully consumed the starting isoxazole and broke open the isoxazole ring, only the $\text{NiSO}_4/\text{NaBH}_4$ method created the intended enamine product with high purity and yield.

Learning General Chemistry in-person, remote, online or hyflex: Which is best?

10:00 am: Kailene Black:

Over the previous three years, there have been multiple publications discussing the difference between course modes in Chemistry courses. The pandemic rushed many faculty to move completely remote for multiple semesters and there is a national discussion about whether students can succeed in a remote class. However, recent literature suggests little to no difference in student performance between an in-person and remote approach. Here, we present results from General Chemistry I & II student performances over the span of 9 semesters in in-person, remote, online, and hyflex course modes. Additionally, we will also discuss current projects, including introducing Learning Assistants into STEM courses across the CU system; specifically comparing a General Chemistry II section with Learning Assistants and another section taught normally. The focus will be the difference between retention, not just in information, but also in students at the university and in the Chemistry program; as well as their sense of belonging and inclusivity. Finally, we will also discuss a project delving into the relationship between STEM faculty and STEM teacher education.

Synthesis of bis-triazole diacids and derived polymers

10:15 am: Alexander Ruiz

The syntheses of two bis 1,4-disubstituted triazoles were optimized. These bis 1,4-disubstituted triazoles have carboxylic acid functionality that can be used for the synthesis of polyesters. Polytriazole-based polymers have potential applications as self-healing polymers, adhesives, and polymer carriers for drugs. Mild methods for these bis-1,4-disubstituted triazole diacids were needed due to decarboxylation seen at high temperatures. Investigations into polymerization have been done through the formation/reaction of an diacid chloride before reacting with a diol.

Synthesis and optimization of 3,5-disubstituted isoxazoles and transfer hydrogenation with hydrazobenzene

10:45 am: Nicole Beitle

A one-pot procedure for the preparation of 3,5-disubstituted isoxazoles was utilized. This reaction involved cycloaddition of hydroximoyl chlorides with acetylenes in the presence of base. Two novel isoxazoles were synthesized through this method. The reduction of model isoxazoles was tested through a transfer hydrogenation method. The transfer hydrogenation utilized hydrazo-benzene in the presence of a copper on iron catalyst. This reaction is being optimized to perform the reductive ring opening of isoxazoles to enaminones. Experimentation showed that the excess hydrazobenzene over-reduced a ketone to an alcohol instead of giving the desired enaminone. This reaction is being optimized in different solvents, various molar equivalents, and different transfer hydrogenation reagents.

A Study of External Electric Field Effects using Gradient Path Curvatures

11:00 am: Niko Hughes:

Many chemical reactions produce toxic or unwanted byproducts that could be released into the environment. These byproducts of multi-step reactions could be reduced by utilizing external electric fields. Electric field influence in chemical reactions is an emerging field of study

focused on identifying electric field interactions as catalysts and/or reactive selectivity agents. Predicting electric field effects on chemical reactions has been challenging due to a lack of theoretical understanding; however, current promising electric field experimentation work will help validate methods of prediction. This presentation highlights an encouraging, less expensive, way of calculating and observing the effects of electric fields by analyzing the curvature of gradient paths of charge densities. In the past, gradient bundle volumes have shown correlations to chemical energetic properties such as bond energies and orbital structures when an external electric field is applied. These gradient bundle volumes are calculated through integrations of complex quantum mechanical functions which is time consuming and costly. Gradient bundles are bounded by gradient paths, with the path's curvature determining the volume of gradient bundles. The gradient path can be calculated using a finite difference method which is less expensive to calculate than integrations. Preliminary computational results using gradient path curvatures correspond well with previous studies of electron population

distribution calculations using the more expensive gradient bundle integration method. This presentation focuses on methods to improve the accuracy of gradient path curvature calculations.

Reduction of 3,5-substituted isoxazolines

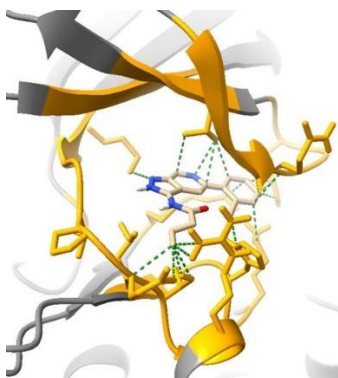
11:15 am: Jacob Cook

Isoxazolines are dihydroisoxazoles. Being non-aromatic compounds, isoxazolines are thought to be easier to reduce than isoxazoles. Numerous reduction methods were used to reduce 5-ethoxy-3-phenylisoxazoline to an enamine product. However, these methods either did not result in the formation of any new product or formed very little. Here we show the reduction methods that gave a reduction product. Raney Nickel catalyst in the presence of ethanol yielded a mixture of reduced products. Both hydrazobenzene with iron on copper catalyst and DMF as well as iron (III) chloride with aged NMP yielded reduced products.

Determining necessary active site model for drug design utilizing TbGSK

11:30 am: Jen Burrows

Human African Trypanosomiasis (HAT), also known as African Sleeping Sickness, is a disease that affects sub-Saharan Africa's rural populations and is carried by the parasite *Trypanosoma brucei* (Tb). HAT causes severe physiological and neurological symptoms and is fatal if treatment is not pursued. Inhibition of Tb's glycogen synthase kinase (GSK) enzyme, which is essential for cell growth, would lead to parasitic death. This project uses computational methods to understand ligand binding within the GSK enzyme and identify the appropriate system size of the active site in order to propose novel inhibitors. Indirubin derivatives, experimentally determined inhibitors of TbGSK with known IC₅₀ values, were docked using HADDOCK. After docking, an increasing radius method was used to create smaller systems of residues within the docked enzyme-ligand complex. These active site systems were imported into Amsterdam Density Functional to calculate the system energetics using density functional theory and identify types of bonding interactions between similar ligands. The data will be used to determine the correct size of the GSK active site necessary for calculating accurate binding energies to compare with experimental IC₅₀ values. Fig 1. Indirubin drug candidate docked in GSK



Synthesis of isoxazoles and oxime derivatives

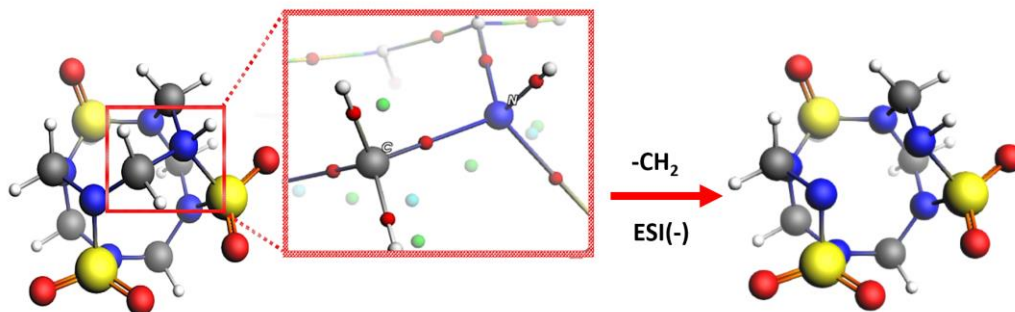
11:45 am: Hetal Mewada

Isoxazole derivatives are five-membered heterocycles which contain adjacent nitrogen and oxygen atoms. Isoxazoles have diverse applications in the medicinal industry as anti-cancer and anti-fungal agents. To synthesize isoxazoles, first an aldehyde is converted to an oxime, and the oxime chlorinated with NCS. The chlorinated oxime was converted to a nitrile oxide, which underwent a nitrile oxide-alkyne cycloaddition in the presence of a terminal alkyne. Some of our novel isoxazoles were synthesized in low yield or purity in the past. To improve the yield and purity of these novel products, two bases were tested in an attempt to increase the yield and purity of the novel isoxazoles. The final crude products were purified via flash column chromatography. Future work with these isoxazole products should include reactions with hydrazine and phenylhydrazine to form pyrazoles.

Tetramine Dimer In-Source Electro spray Ionization Fragmentation Analysis using Density Functional Theory

12:00 noon: Jon Gertner

Since the first reported publication in 1984, electrospray ionization (ESI) has become a quintessential 'soft' ionization technique in the acquisition of quasi molecular ions with identities $[M \pm H] \pm 1$ for liquid chromatography tandem mass spectrometry (LC-MS) analysis. This expected outcome, however, is not observed in previous reported analyses of the compound tetramine, a now globally banned neurotoxic rodenticide. Instead, the application of negative ion mode ESI to tetramine results in a pseudo dimerization reaction preceding the scarcely observed phenomena of in-source fragmentation (ISF) yielding a $[M - 13]^-$ molecular ion. This work therefore seeks to apply ab initio density functional theory (DFT) calculations to examine the unique energetic and structural properties of tetramine, its dimer, and related compounds that motivates the resulting atypical ion fragmentation demonstrated in previous works. Data presented has been obtained by using the fragmentation, Quantum Theory of Atoms in Molecules (QTAIM), and Interacting Quantum Atoms (IQA) computational analysis methods. These results may elucidate thermodynamic justification(s) and broader trends regarding the stability of the tetramine dimer fragmentation, thus highlighting rationalizations for future instances of ISF observed using LC-ESI-MS applications.



End of Symposium: Adjourn for a Group Photo