

Investigation of Aromatic Amine Inhibitors of LMW-PTP

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Biochemistry, Chemistry

The goal of this investigation is to generate a combinatorial library of novel aromatic amino based inhibitors to LMW-PTP via in silico screening, synthesis of those displaying the lowest docking scores, and finally, to test their levels of inhibition in vitro. Using Maestro, Schrödinger's robust modeling program, 161 aromatic amino compounds were bound to the core molecule. Subsequently, human isoform 1XWW of LMW-PTP was exposed to the novel compounds via the Glide feature within Maestro and their docking scores were recorded. However, due to the double bond nature of the azo compounds (and the lack of Glide's compatibility with preparing a library of ligands across a double bond), many of the proposed ligands' docking scores were not calculated via Glide, but simply by building the ligand and exposing it to 1XWW individually. Four promising leads expressing the lowest docking scores from the trial were selected for synthesis. The synthesis of the inhibitors was achieved through Sandmeyer reactions and purification was performed via recrystallization. Inhibition assays were conducted according to the procedure outlined by DeSouza, Louwagie, and Seiler. The results of the inhibitory assays will be compiled into a grid containing the structure and docking score of each novel inhibitor. The overactivity of LMW-PTPases has been associated with the development of cancer and diabetes. Therefore, the importance of identifying potent inhibitors of LMW-PTP cannot be understated, as they may one day serve as effective treatments to these diseases.

The Effects of Soil Composition on Water Retention Rates

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Biochemistry, Biology, Chemistry, Environmental Studies, FoCuS, NATS, Sustainability

The increasing demands for usable water for the population creates a need for more efficient practices utilizing clean water resources. Irrigation for farmland uses a significant portion of potable water that has been declining in recent years. The changing amount of rainfall and surface water that is accessible for use in farming has created an issue regarding the use of underground water as irrigation instead of drinking water. The soil texture and structure greatly influence the water filtration, permeability, and water-holding capacity of the soil. These properties influence the efficiency of water retention for irrigated and dry-land crop production systems and the estimated efficiency is 50%. There have been attempts to increase the efficiency of the water retention in soils in order to reduce the amount of potable water used for irrigation. The attempts to increase the efficiency have used several different methods for modeling the existing water retention rates. The goal of these experiments is to improve the water retention properties of the soil in order to preserve the supply of potable water.

Copper-Nitrogen Interactions of a Ceruloplasmin Model Enzyme

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Multicopper oxidases are of great interest due to their ability to catalyze the reduction of O₂ to H₂O. An example of such a compound is ceruloplasmin, which contains three copper ions incorporated into its structure. The function of ceruloplasmin is not well understood, and part of the difficulty in studying such an enzyme is its size. To better understand the function of a multicopper oxidase such as ceruloplasmin, model enzymes can be utilized, which allow us to focus only on the active components of the enzyme. The synthesis of one arm of such a model enzyme was undertaken, in order to better understand how the copper ions are incorporated into the active site of ceruloplasmin. At this point, the model arm has been synthesized, but is not purified to the point that accurate results can be obtained from the incorporation of copper ions into the structure. When the model arm is sufficiently purified, the copper ions can be introduced, and ¹H NMR can be utilized in order to understand which nitrogen atoms interact with the copper ions. Procedures from the literature were followed and improved upon in the project. Future work on the project will include fully characterizing and purifying the model complex so that the copper ions can be added and more accurate results can be obtained.

Making, Modeling, and Biological Testing of Potential Anticancer Agents

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The objective is to synthesize an inhibitor of Low Molecular Weight Protein Tyrosine Phosphatase (LMW-PTP) that is unable to be degraded as quickly as a current known inhibitor, Pyridoxal 5'- Phosphate (PLP). LMW-PTP is a target to investigate due to it being found in high concentrations in malignant cells. Inhibition of LMW-PTP may be one way in order to treat cancer. Boronic acids are a suitable mimic for the hydrolyzable phosphate group of PLP. To make these boronic acids, we did a hydroboration of an alkene. The chemistry was developed using benzaldehyde and styrene as the model aldehyde and alkene. We started with benzaldehyde and converted it to styrene using the Wittig reaction described in Keliher. The styrene was then converted to the boronic acid using dichloroborane-dioxane and water as described in Josyula. The boronic acid analog of PLP has not yet been synthesized. Once synthesized, its inhibitory effects on LMW-PTP will be investigated

Probing the Interactions of Polyethylene Glycol-Coated Magnetic Nanoparticles with Human Hemoglobin

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The interactions between polyethylene glycol (PEG)-coated magnetic nanoparticles (MNPs) and human hemoglobin (Hb) were investigated using various spectroscopic techniques. UV-Vis spectrophotometry and dynamic light scattering (DLS) indicated strong binding between Hb and MNPs. Fluorescence quenching experiments were used to determine the binding constant (K_a), enthalpy changes (ΔH^θ), entropy changes (ΔS^θ), and free energy changes (ΔG^θ). Results indicated that PEG-coated nanoparticles quenched hemoglobin fluorescence mainly by a static quenching mechanism. The binding constants (K_a) were determined as $1.12 \pm 0.18 \times 10^7 \text{ M}^{-1}$, $0.95 \pm 0.12 \times 10^7 \text{ M}^{-1}$, and $0.78 \pm 0.16 \times 10^7 \text{ M}^{-1}$ at 297, 302, and 307 K, respectively. The changes of secondary structure of hemoglobin due to binding with nanoparticles will also be investigated in the future using circular dichroism (CD) spectroscopy.

Screening of Inhibitors against Purine Nucleoside Phosphorylase

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Purine nucleoside phosphorylase (PNP) catalyzes a reversible reaction of inosine and hypoxanthine, is involved in the salvage pathway of purine metabolism, and is essential for the proliferation of T- and B-cells. Finding a suitable inhibitor for PNP is important for treating T- and B-cell problems. First, a coupled enzymatic assay was run modified from the literature.² Then several candidates were screened and monitored using UV similar to the literature.³ These new inhibitors were screened using a 96 well plate, scaling down the process from using cuvettes and requiring less material per test. Each candidate was tested at various dilutions to determine the EC50 and IC50 values. These tests were done to develop an integrated lab experience. So far, eleven candidates have been tested for their ability to bind and inhibit PNP. A good inhibitor binds to PNP, inactivating it. These inhibitors can be used to therapeutically treat T- and B-cell malignancies, gout, psoriasis, rheumatoid arthritis, and malaria. 1. Calduri, F., R.G. Silva, D.M. Dos Santos, M.S. Palma, L.A. Basso, D.S. Santos, and W.F De Azevedo. "Biological Crystallography." Structure of Human PNP Complexed with Ligands. 2005. 2. Chu, S. Y.; Cashion, P.; Jiang, M. A New Colorimetric Assay for Purine Nucleoside Phosphorylase. *Clin. Biochem.* 1989, 22, 357-362. 3. Montgomery, J. A.; Secrist, J. A. PNP Inhibitors. *Perspectives in Drug Discovery and Design* 2.1 1994, 205-20.

Paper-Based Device for Colorimetric Detection of Malondialdehyde in Biological Samples

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Oxidative stress in biological systems is known to be involved in the development of many diseases such as Alzheimer's disease, Parkinson's disease, many cancers, among numerous other disorders and diseases in patients. Oxidative stress in a biological sample is caused by the accumulation of Reactive Oxygen Species, which results in the formation of free radicals and peroxides which can damage and/or have adverse effects on cell function. Our research primarily involves the oxidative stress biomarker Malondialdehyde (MDA), one of the major products of lipid peroxidation in a cell. The goal of our research is to develop a paper-based microfluidic device that is able to colorimetrically determine levels of MDA in a biological sample, specifically in saliva. This measurable change in color

is done through the formation of a complex of MDA and Thiobarbituric acid (TBA) which absorbs light at 532nm, appearing pink. Our research has optimized this technology by adjusting variables in the preparation of the paper and addition of biological samples to achieve an optimum LOD as well as accurate and precise measurements of the analyte. This will provide a portable and affordable way to easily and accurately determine ones level of oxidative stress without the use of invasive or expensive equipment.

Investigation of Alcohol Metabolizing Enzymes

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Biochemistry, Chemistry

Pharmacogenomics is concerned with the study of how groups of people differ in their responses to drugs due to their genetics, and its future is focused on optimizing individualized treatments for patients. One drug that causes 3.3 million deaths worldwide that differs in metabolism between racial populations and gender is alcohol consumption. The two enzymes responsible for ethanol metabolism are liver alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH). The main steps that remove ethanol from the body are ADH oxidizing ethanol to acetaldehyde and then ALDH oxidizes acetaldehyde into acetic acid. The acetic acid can then be excreted in urine or be reused by conversion into acetyl-coenzyme A. Due to the different isoforms of ADH and ALDH, certain alleles such as the ALDH2*2 and ADH2*3 cause certain ethnicities to react differently when consuming alcohol. Not only do different isoforms of alleles matter but one's gender also plays a role in how alcohol can be metabolized in the body. Within certain individuals, alcoholism tends to occur at a higher rate than others. This is due to the different isoforms of ADH and ALDH that a person has in their DNA. Disulfiram is an effective treatment for alcoholism because it is able to inhibit acetaldehyde from being used as a substrate by dehydrogenase, aldolases, and oxidases. Acamprosate is a new drug that has been proved useful in treatment of alcohol dependence as well; however, the exact mechanism is still unknown. Future research in ethanol metabolism and alcoholism treatment includes investigation into Acamprosate's mechanism of action as well as exploration of ethanol metabolism in interracial individuals. The results of these studies would be beneficial to the emerging field of pharmacogenomics and the treatment of alcoholism in people with different genetic backgrounds.

Investigations into Uncharacterized Radical S-Adenosylmethionine (SAM) Enzymes

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Biochemistry, Chemistry

Radical S-Adenosylmethionine (SAM) enzymes are a superfamily of thousands of enzymes from all kingdoms of life whose varied functions include enzyme activation, vitamin biosynthesis, DNA repair and antibiotic resistance among many others. These enzymes share a conserved cysteine motif which binds an iron sulfur cluster that plays an essential role in the reductive cleavage of SAM producing methionine and a 5' – deoxyadenosyl (dAdo) radical. This radical is responsible for the initiation of further steps in radical SAM enzyme catalysis. While there are a handful of well characterized radical SAM enzymes, there are still hypothesized subgroups of these enzymes which remain unstudied. Additional investigation of these enzymes will allow for a better understanding of how these common characteristics allow for such a diverse set of catalyzed reactions. To advance our understanding of these enzymes and their catalytic mechanisms two genes encoding for hypothetical radical SAM enzymes were selected for analysis. The Structure Function Linkage Database maintained by the University of California, San Francisco (UCSF) was used to screen subgroups of the Radical SAM superfamily for potential but unstudied enzymes. One of the selected gene products is being cloned into an expression vector by Blue Heron and the second is being cloned into a pET-14b expression vector utilizing PCR, restriction enzyme digests, and ligation reactions. Gene insertion will be verified with DNA sequencing. Once these vectors containing the gene inserts are obtained, the gene product will be over-expressed and purified using a Ni-affinity column and the Fe-S cluster reconstituted. This resulting enzyme can then be used for further experiments.

Treating Tuberculosis: Examining Shorter Regimens

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Biochemistry, Chemistry

Mycobacterium tuberculosis, the bacteria that causes tuberculosis (TB) has been a global public health concern for decades. An estimated one-third of the population carrying latent tuberculosis and millions of cases of active TB are diagnosed every year. There exists a treatment regimen that, until recently, could effectively treat TB. Tuberculosis is such an old disease and since effective treatment options exist, why is it still such a prevalent disease? Why is this regimen no longer effective? The treatment regimen is long and therefore patient compliance is difficult to maintain for the entire duration of treatment; this has led to severe drug resistance, further complicating the fight against TB. Recent TB research has focused on shortening the treatment regimen to help increase patient compliance and eliminate the creation of new drug-resistant strains of TB. This review examines some of these new shorter treatment options.

Quantification of Epoxides from their Carbamate Derivatives: Environmental Applications

Gabriel Amon
Chemistry

This project focuses on developing a method to quantify epoxides in atmospheric organic aerosol samples. In the atmosphere, there are copious environmental contaminants present that can affect people's health as well as climate and one particular class of compounds of growing interest are epoxides. Epoxides are formed in the atmosphere through oxidations of volatile organic compounds, but there is little information on their ambient concentrations due to their high reactivity. Previous research has been done to quantify epoxides in biological and water samples, but there are few methods to quantify in atmospheric aerosol samples. Various model epoxide compounds are derivatized with sodium diethylcarbamodithioate (DTC) and the concentration of the resulting carbamate is measured at 278 nm. Calibration curves for 6 model epoxides have been measured with a linear dynamic range of 2.5- 50 μ M. An HPLC method has also been developed to separate derivatized epoxides from the aerosol mixture for identification using electrospray mass spectrometry. Finally, these methods are used to quantify epoxides formed from the reaction of m-xylene with hydroxyl radicals in an environmental chamber. These methods allow for quantification, identification, and structure elucidation of epoxide compounds in organic atmospheric aerosol.

Asymmetric Aldol Reaction Induced by Chiral Auxiliary

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Chemistry, Undergraduate Research

The principal objective is to allow undergraduate students to examine asymmetric reactions in three steps: synthesis of the chiral auxiliary, attachment of the chiral auxiliary to the aldol substrate, and the aldol reaction via in situ formation of the corresponding boron enolate. The purchased chiral auxiliary, (S)-4-Benzyl-2-Oxazolidinone, was successfully attached to the aldol substrate and the aldol reaction completed. ^1H and ^{13}C NMRs were used for structural analysis. The experiment is very feasible for an undergraduate laboratory as each step takes approximately 3-4 hours each.

Dihydrocarvone-Based Polyurethanes

Levi Salzl
Chemistry

In order to continue exploring the field of renewable polyurethanes, monomer and polymer syntheses were explored using the bio-renewable feedstocks, dihydrocarvone and menthone. Polymer synthesis can be derived from lactone polymerization, but a green synthetic approach to lactones from these sources required a Bayer-Villiger reaction catalyzed by Oxone®. Addition of catalytic Dess-Martin periodinane resulted in a promising increase in yield of this reaction, producing dihydrocarvone. Co-polymerization took place with benzyl alcohol or 1,4-butanediol as initiator and diethylzinc as catalyst. NMR studies of the co-polymer showed a good degree of control over the product using menthene/dihydrocarvone ratios of 3:15, 4:14, 5:13, and 6:12. Post-polymerization modification of the co-polymer to make polyamines was attempted through a thiol-ene addition of cysteamine hydrochloride to pendant alkenes.

Pure Epoxides

Emmanuel G Freeman

Chemistry

In an attempt to prepare phosphonate sugars, our research group has struggled to purify the phosphonate epoxide product in (scheme 1). An alternate approach to synthesizing and purifying this compound was developed (Scheme 2). An Arbuzov reaction was used to make the diethyl cinnamoylphosphonate. The reaction was then followed by silica gel chromatography. NMR and the IR spectroscopy were used to determine the product structure. Progress is being made to complete the second scheme. Once completed, we will evaluate the effectiveness of the two approaches by calculating the percent recovery and purity. Scheme 1 Scheme 2

Redox Potential of Metal Complexes: Development of a Laboratory Project

Timothy J Doyle

Chemistry

The goal of this project is to investigate the binding of various cobalt metal complexes with DNA using cyclic voltammetry (CV). The water-soluble metal complex, tris (1, 10-phenanthroline) cobalt (III) was first synthesized prior to characterization. Initial trials showed no binding of the metal complexes with DNA. This is due to the high concentration of proteins present in the DNA solution. Further trials investigated the binding of the metal complexes with bovine serum albumin (BSA). The BSA trials also showed no binding of the metal complex with the DNA. Binding with another strain of DNA and purified DNA will be discussed. The project will be used in integrated laboratory and would give students experience using a CV, synthesizing a metal complex, and investigating binding mechanisms.

Biodegradable Polymers and their Biomedical Applications

Carmen Probst

Chemistry

This project outlines the history of the field of biodegradable polymers. It focuses on the synthetic approaches to the polymers as well as their degradation mechanisms. The application of these materials within the biomedical field is also addressed.

Synthesis of 1,2-Amino Alcohols through Arbuzov Approach

Brianne Gibson

Chemistry, Undergraduate Research

This research involves the synthesis of one diethyl amino-dihydroxy butyl phosphonate which hold characteristics shown to serve as an anti-fungal and anti-microbial agent. The first step of this research involves epoxidation of the phosphonate-containing olefin made using the Arbuzov procedure with crotonaldehyde. The second step synthesizes an oxazolidone using benzyl isocyanate to open the epoxide and cyclize the compound. Hydrolysis of the oxazolidone is performed for the production of the 1, 2 amino-alcohols in the third stage. This step synthesizes the amino-phosphonates. The preparation for the first step, as well as the first step itself has been completed. Upon successful retrieval of the oxazolidones, the alcohol can be synthesized. The oxazolidone will also be manipulated to produce phosphonosugars. Throughout the exploration of these compounds, stereo-chemical manipulation on the epoxides and their resulting products will also be investigated.

Characterization of Aqueous Phase Atmospheric Reactions

Cameron Axberg

Chemistry

This project focuses on simulating aqueous phase atmospheric reactions of small molecules with hydroxyl radicals to form high molecular weight products. Aqueous phase atmospheric chemistry is becoming an increasing area of research to try and identify the products forming in our atmosphere and assess their impact. Hydroxyl radicals are a

major oxidant in the atmosphere for the formation of a variety of compounds and it is believed that many of these compounds lead to secondary formation of aerosols. Based on previous research glyoxal, acetic acid, and m-xylene are believed to be important for the formation of these oligomers and other products that lead to these organic aerosols. This research focuses on characterizing these oligomers and intermediate products in an effort to better understand the pathway for the formation of organic aerosols. The solubility of these high molecular weight products will be explored.

Synthesis of sustainable monomers for a polyurethane

Clare Johnston

Chemistry

The aim of this project was to develop a renewable polyurethane from a dihydrocarvide- and menthine-based polyamine. Synthesis of dihydrocarvide presented difficulties due to unwanted side products. Previously published procedures for the Baeyer-Villiger oxidation of dihydrocarvone to dihydrocarvide produced a mixture: 60% desired lactone and 40% epoxide. Optimal synthesis of dihydrocarvide was studied through the addition of various salts, Lewis acids, and oxidants. Superior results were ultimately obtained through the use of catalytic amounts of oxidants including sodium molybdate, potassium permanganate, and Dess-Martin periodinane. These conditions led to lactone in 96-98% purity by ¹H NMR and an isolated yield of 85%. Subsequent copolymerization of menthine and dihydrocarvide was successful with good control of polymer molar masses determined from ¹H NMR spectra. Polyamine synthesis studies are ongoing.

Carbon Sequestration, what's that?

Ian C Manion

Chemistry

The Earth's climate is currently experiencing a rapid increase in the mean global temperature of a degree higher than any previously observed natural change of temperature in Earth's history. It has been shown that rising levels of atmospheric CO₂ could lead to temperatures rising beyond what would be a manageable level for living organisms. Carbon sequestration science offers a variety of methods for decreasing atmospheric CO₂ concentrations through direct removal as well as emission reduction from industrial sources. Carbon sequestration is an essential part of society's current move toward sustainability and this talk will focus on the different strategies for reducing atmospheric CO₂ concentrations.

An Investigative Look into the Sesquiterpenes Displaying the Rare Pacifigorgiane Carbon Skeleton

Jack A Luke

Chemistry

Abstract – A number of natural products have been isolated from gorgonian soft corals found throughout the world's oceans. These natural products, which show significant biological activity, have been synthetic targets for the past few decades. Pacifigorgiol displays ichthyotoxic properties at very low concentrations while Tamariscol is noted as having a pleasant fragrance to be used as a perfume. This presentation will discuss the synthetic efforts toward these sesquiterpenes, which display the rare pacifigorgiane carbon skeleton.

Characterization of Self-Assembled Monolayers Composed of Various Alkyl Thiols Using Scanning Tunneling Microscopy

Alexander Bramer

Chemistry

Self-assembled monolayers are the most elemental form of an organic thin film material at the nanometer scale, and form structured patterns on the gold surface so by changing the thiols arranged on the surface of gold the interfacial properties of the metal can be modified. Characterization of these respective thiols on gold thus provides information on how each of them modifies the surface differently. This research sought to characterize and compare the surface

organization of alkyl thiols with differing groups attached to the sulfur head. Monolayers of octanethiol, 2-ethylhexanethiol, and cyclohexanethiol were deposited onto gold samples using solution deposition. Scanning tunneling microscopy (STM) was used to characterize the surface structure of the formed monolayers. Matlab was then used to process the STM surface images.

Rhodium Catalyzed Hydrodehalogenation of Fluoroarenes in Mild Conditions

Anna M Luke

Chemistry, Undergraduate Research

The fate of fluoroarenes in the environment has become a concern, in part because of the higher use of fluoroarenes in pharmaceuticals and industrial processes. One way to help alleviate this environmental concern is to explore ways in which fluoroarenes are degraded to benign compounds. Fluorinated aromatic compounds are hydrodefluorinated using a heterogeneous 5 wt % rhodium on alumina catalyst under mild conditions (1 atm. H₂, 25°C). The catalytic hydrodehalogenation mechanism and substrate scope were explored by looking at a variety of substituted fluoroarenes. The effects of electron-withdrawing and electron-donating substituents as well as the position of the substituents to the fluorine atom (ortho, meta, para) were examined. The substrate degradation, subsequent intermediate(s), and product formation rates were monitored using GC/MS. The fluorophenols are the quickest to undergo degradation with an average rate of $5.0 \pm 1.1 \times 10^{-3} \text{ min}^{-1}\text{mg}^{-1} \text{ Rh/Al}_2\text{O}_3$ and the fluoronitrobenzenes, with an average degradation rate constant of $0.80 \pm 0.40 \times 10^{-3} \text{ min}^{-1}\text{mg}^{-1} \text{ Rh/Al}_2\text{O}_3$, are the slowest.

Transformation of atmospheric epoxides into their carbamate derivatives and their effect on climate change

William McCue

Chemistry

Abstract. The goal of the following paper is the quantification and qualification of epoxides derivatives to study their effect on atmospheric climate change. Epoxides were derived through the use of diethyldithiocarbamate in a hot bath at constant pressure. Samples were analyzed using high-performance liquid chromatography and ultraviolet/visible spectroscopy. Peak area and absorbance values were plotted against concentration to determine a linear relationship between the two variables. This research is novel in that it aimed to create one unique methodology which could be used for the analysis of any unknown epoxide mixture. Through the research, we were able to formulate an effective method for the six tested epoxide compounds. Future research will involve taking unknown air samples and determining the epoxides and quantities of the epoxides in the sample. This research is beneficial to the study of environmental chemistry because the quantification and qualification of epoxides within the atmosphere will allow for proper methods to be derived to combat the epoxides in the air.

The Formation of Self Assembled Monolayers using Hexyl Isothiocyanate

Joseph Cartier

Chemistry

Self-assembled monolayers (SAMs) are made by depositing compounds on a surface, which can give scientists greater control over the properties of that surface. Through this procedure, the surface can be made hydrophilic or hydrophobic. This research has focused on understanding molecule interactions with the substrate, specifically looking at the deposition of hexyl-isothiocyanate on Au(111) and comparing it to the well-studied surface made by depositing octanethiol on Au(111). Samples were prepared through a solution-based deposition and analyzed using scanning tunneling microscopy (STM). It was discovered that the hexyl-isothiocyanate formed structured domains on the surface along with areas with limited to no structure. The results obtained open the door for further investigation into the ability of all isothiocyanates as potential substrates for the creation of SAMs.

