

MacMillan-Type Cascades Using Dendrimer Bound Catalysts

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Chemistry

We have functionalized PAMAM dendrimers with imidazolidinone catalysts. Functionalized PAMAM dendrimers were characterized by NMR analysis. We are now investigating these organocatalytic-functionalized PAMAM dendrimers for their effectiveness as catalysts in MacMillan-type cascade catalysis.

Purification of Double Mutant (C12SW49F) Protein Tyrosine Phosphatase (PTP)

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Biochemistry, Chemistry

Transcription and subsequent translation of the gene for a double mutant (C12SW49F) of human PTP were initiated by addition of the lactose analog, IPTG, to archived transformed E. Coli JMB 109 cells containing a PGEX-6P plasmid with the PTP gene linked to the gene for glutathione S-transferase (GST). A crude protein solution containing the fusion protein was obtained by lysing and centrifuging the cells. The purification of the fusion protein and double mutant PTP from the crude protein sample are reported here. The fusion protein was isolated using affinity column chromatography. The PTP-GST fusion protein bound to Pierce® Immobilized Glutathione stationary phase while the remainder of the crude protein was washed through. The fusion protein was eluted with a buffer solution containing glutathione and protein concentrations in eluted fractions were measured using the CB-X™ protein assay. Purification was monitored by polyacrylamide gel electrophoresis (PAGE). Prescission Protease was added to cleave the fusion protein to separate GST from PTP. Once cleaved, the C12SW49F PTP and the GST were separated with a column containing Pierce® Immobilized Glutathione. The double mutant PTP should have eluted through the column while the GST remained bound to the column. The fusion protein was successfully cleaved as determined by PAGE, but the double mutant PTP was not successfully purified. Multiple variations of the purification method of the double mutant PTP and the results are reported here. The ultimate goal was to determine the binding constants of various inhibitors to the double mutant PTP using tryptophane fluorescence, which required the separation and purification of PTP from the fusion protein.

Spectroscopic characterization of the protein-nanoparticle interactions under normal and oxidative stress conditions

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Biochemistry, Chemistry

The rapidly developing field of nanotechnology has dramatically increased the exposure of humans to nanoparticles and demands thorough toxicological assessments for their safe use. This research project is focused on the quantitative determination of the effects of oxidative modifications of human serum albumin (HSA) on its binding interactions with iron (III) oxide magnetic nanoparticles (MNPs). Spectroscopic techniques (UV-Vis, IR, fluorescence, and circular dichroism spectroscopy) were used to characterize the MNP-HSA binding interactions. The circular dichroism spectra suggest that the addition of MNPs increases the stability of the MNP-HSA complex. The time dependent oxidation of HSA resulted in a significant and gradual decrease in binding interactions with MNPs.

Development of Catalytic Degradation of Chlorinated Ethylenes Reaction for Upper Division Integrated Lab

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Chemistry

The CSB/SJU Chemistry Department has introduced a new curriculum for students with a 4-credit integrated lab as a required upper level chemistry course. This is a potential project for use in the integrated lab. Students will develop a method for monitoring the kinetics of the dechlorination of tetrachloroethylene (PCE) by titanium (III) citrate reducing agent and Vitamin-B12 cobalt catalyst. The students would first be required to develop their own GC experimental parameters such as column temperature, temperature ramps, and pressure to monitor PCE degradation and trichloroethylene formation. Then

the students would be able to calculate the rate constant of degradation by GC analysis by taking a gas headspace sample every 20 minutes of the dechlorination reaction. Students will also have to calculate the concentration of PCE from an original unknown solution by developing a calibration curve. This experiment allows students to develop the skills needed for quantitative analysis and proper use of the GC instrument along with comparing their rate constants with reported values from the literature.

Dental Application of Mytilus Edulis Foot Proteins

Thomas E Ortlieb

Biochemistry, Biology, Chemistry

Biological mechanisms of marine organisms, such as mussels, offer unique opportunities for innovation within modern medicine. The adhesive properties of *Mytilus Edulis* byssal proteins, utilized in underwater attachment, suggest use within dental medicine as polymer sealants and coatings. The adhesive mechanisms employed by mussels are the result of 3,4-dihydroxyphenylalanine (DOPA) containing proteins, particularly mefp-1, mefp-3, and mefp-5. These proteins are located in the mussel byssus threads secreted for aqueous attachment. The oxidation of tyrosine to DOPA yields semiquinone formation capable of both cross linkage and surface adhesion to a variety of surfaces. Utilizing atomic force microscopy and nanoindentation, researchers have shown that single DOPA molecules are capable of withstanding remarkably high retraction forces, while maintaining greater degrees of hardness and durability than traditional epoxy-resin coatings. Results support the application of DOPA-rich mussel foot proteins in the development of new, compliant dental sealants.

Rational Design of Low Molecular Weight Protein Tyrosine Phosphatase (LMW-PTP) Inhibitor Pyridoxal 5'-phosphonate

Christopher P Moore

Biochemistry, Chemistry

The over expression of Low Molecular Weight Protein Tyrosine Phosphatase (LMW-PTP) is connected to tumor onset and progression. Markedly high levels of LMW-PTP have been recorded in human tumor tissues including breast, colon, and neuroblastoma cancers. Past research has shown that pyridoxal 5'-phosphate (PLP), the active form of vitamin B6, tightly binds LMW-PTP as an inhibitor. In past research, PLP was used as a structural basis for synthesis of non-hydrolysable phosphonate acid analogs. The analogs of PLP were synthesized and screened for their inhibitory properties against LMW-PTP isoform B. In continuation of this research, processes were developed toward synthesis of a pyridoxal 5'-phosphonate inhibitor.

The Determination of the Capabilities of the C6 Multi-Sensor Platform and Cyclops-7 Sensors

Katherine J Kaiser

Chemistry

Oil is a toxic contaminant in marine ecosystems that can have a harmful effect on water and the environment. As components of oil have fluorescent qualities, fluorescence spectroscopy can be used to identify the presence of oil in water. The C6 Multi-Sensor Platform with the Cyclops-7 sensors is an instrument that uses fluorescence to analyze water quality. Through the use of custom designed sensors, a wide spectrum of oil mixtures can be tested as well. The instrument had six sensors, one each for chlorophyll, CDOM (colored dissolved organic matter), and turbidity and had three sensors for oil. As the instrument was custom designed, the various capabilities and parameters of the instrument were investigated. The sensor responses to CDOM, Turbidity, and oil were analyzed individually. Standard plots were created for each sensor for future use. Finally, combinations of parameters were analyzed to determine the effects they have on each other.

The Role of the Beta-Amyloid Peptide in Alzheimer's Disease

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Biochemistry, Chemistry

Alzheimer's disease is a degenerative brain disorder that is the 6th leading cause of death in the United States. Currently there is no effective cure or treatment of the disease, but over the last three decades there has been much advancement in the understanding of its causes. Beta-amyloid peptides have been shown to play a large role in the formation of senile plaques in the brain and in the killing of cells that occurs in the brains of Alzheimer's patients. This presentation provides an overview of the role of beta-amyloid peptides in Alzheimer's disease. It also explores the current research that is being done to target beta-amyloid peptides that could potentially lead to the development of an effective treatment or prevention of Alzheimer's disease

Separation and Detection of Hydroxyl Radical Oxidized (Tert-Butoxycarbonyl)-Tryptophan Using Reverse Phase HPLC-UV

Matthew M Syverson

Biochemistry, Chemistry

The free radical oxidation of amino acids by reactive oxygen species (ROS) is related to protein misfolding and aggregation leading to many pathological conditions. However, simple methods for the separation and detection of oxidized amino acids in biological samples are not widely available. In this study, we used amine protected tryptophan as our model amino acid. Tryptophan was oxidized by a free radical hydroxyl group, generated from the Fenton reaction. The structure of the oxidized compound was determined using proton and carbon nuclear magnetic resonance spectroscopy, and infra-red spectroscopy. The oxidation mixture was separated by high pressure liquid chromatograph (HPLC) with UV detection at 220 nm and 280 nm. An HPLC gradient method was developed and optimized for separation of oxidation product from non-oxidized tryptophan in less than 35 minutes.

Structure and Properties of Complexes of Nickel(II) and Salicylaldehyde Derived Schiff Base Ligands

Jonathan Wolf

Chemistry

An integrated lab developed for upper-division chemistry program incorporates organic synthesis, inorganic synthesis, and recrystallization followed by analysis using UV-Vis spectrophotometry, cyclic voltammetry, and magnetic susceptibility. The lab involves the coupling of salicylaldehyde derived Schiff bases ligands with nickel (II). Ligands were chosen based on the sterics of the amine group, which allowed for control of the geometry of the complex. Previous research has shown substitutions of the amine in N',N'-bis-(salicylidene)-diamine nickel(II) cause shifts in peak potential and λ_{max} . This lab can be used to demonstrate the basics of ligand field theory, and to have students correlate changes in cyclic volumetric, absorption peak, and magnetic susceptibility data with geometry as controlled by the ligands on the metal.

A systematic investigation of Selective Serotonin Reuptake Inhibitors

Vant Andreas J Washington

Biochemistry, Chemistry

A description of the anti-depressant drug class of Selective Serotonin Reuptake Inhibitors (SSRIs) along with their efficiency in minimizing depression related symptoms. This presentation focuses on the description of the above class of drugs' methods of action, synthesis, selectivity, specific examples of commercial products and binding affinity. This presentation also highlights precursor anti-depressant drug treatments, and the future studies of SSRIs.

Saliva as a Diagnostic Specimen for Monitoring Oxidative Stress.

Felicia N Burns

Biochemistry, Chemistry

This research project aims to establish a functional technique for monitoring oxidative stress levels using saliva as a diagnostic specimen. Malondialdehyde (MDA) is a common biomarker for oxidative stress and naturally occurs in saliva. Most currently available methods for MDA detection are based on reaction of MDA and thiobarbituric reactive substances (TBARS) which form an adduct that can be measured spectrophotometrically. This type of assays suffer from poor selectivity because TBARS forms adducts with many other components of saliva. In this project we evaluate, the reagent dye 1-methyl-2-phenylindole as an alternative to TBARS for detection of MDA using UV-Vis spectroscopy. MDA concentrations in simulated and real saliva samples will be measured using this new method.

Rhodium Catalyzed Dehalogenation of Environmental Pollutants

Daniel M Neuburger

Chemistry

Halogenated organic compounds are known toxins and ground water pollutants. Toxicity is related to the halogen substituents, so complete dehalogenation of these pollutants effectively removes this concern. Catalytic hydrodehalogenation of chlorinated ethylenes and halobenzenes by 5 wt % rhodium on alumina catalyst in the presence of dihydrogen as the reducing agent under aqueous conditions is described. Kinetic parameters and product distribution for hydrodehalogenation reactions were determined using gas chromatography-mass spectrometry headspace analysis. The effects of various buffers on the rate of trichloroethylene hydrodechlorination were investigated. The presence of a phosphate buffer in the reaction flask was found to increase the dehalogenation rate constant. Substrate scope was explored using halogenated benzenes where the final products are cyclohexanes. The rate constants for the halogenated benzenes were found to be less than that of trichloroethylene under the same reaction conditions.

Asymmetric Aldol reaction Induced by Chiral Auxiliary

Damiene A Stewart

Chemistry

The aldol reaction is important in forming new carbon-carbon bonds and, as such, in forming molecules that may be important starting material for many pharmaceutical products. This experiment is a three –step asymmetric aldol reaction that attempts to use a ‘chiral auxiliary’ and a substrate to prepare a specific aldol product with controlled stereochemistry. The first step of the experiment is the preparation of the chiral auxiliary; the second, the coupling of the auxiliary and the substrate. The third step is performing a base catalyzed aldol condensation reaction at 0°C or lower. After each step, the product formed is purified and analyzed.

Rate of Tetracycline Photolysis

Abby J Gauer

Biochemistry, Biology, Chemistry, Environmental Studies

Kinetics of photolysis of the antibiotic tetracycline hydrochloride (TC) was investigated in three buffer solutions under a medium pressure mercury vapor lamp with wavelength ranging from 220-1400 nm. The rate of photodecomposition was measured by high performance liquid chromatography. The results verified that TC degrades by direct photolysis.

Counter Ion Effect on the Synthesis of Silver Iodide Nanoparticles in Ionic Liquids

Tyler L Gerads

Chemistry, Physics

In this experiment, an ionic liquid of either, 1-butyl-3-methylimidazolium tetrafluoroborate (BmimBF₄) or 1-butyl-3-methylimidazolium hydrogen sulfate (BmimHSO₄), was added to a water-in-oil micro emulsion to observe the effect of the ionic liquid on the rate of formation of silver iodide nanoparticles (AgI NPs) in a reverse micelle template of Polyethylene glycol tert-octylphenyl ether (Triton X-100) surfactant. A time driven UV-Vis absorbance measurement was used to approximate the relative population of nanoparticles and showed an increase in the rate of formation of the nanoparticles when ionic liquid is present up to a certain quantity. It is suspected that the viscosity and the polarizability of the ionic liquid components compete to affect the reaction rate. In an effort to determine how the ionic liquids in the synthesis is affected by other ionic species during the synthesis, a growth kinetics study using iodide precursors with different counter-cations (potassium iodide and sodium iodide) were conducted. Results show that the BmimHSO₄ ionic liquid solution shows an ionic mobility trend similar to water, but BmimBF₄ does not.

Degradation of Chloroethylenes in Lake Sagatagon

Marissa K Oram

Chemistry

Catalytic hydrodechlorination of trichloroethylene (TCE) using a 5 wt % rhodium on alumina catalyst with dihydrogen as the reducing agent is described. The reactions kinetic parameters of TCE hydrodechlorination and ethane product formation was determined using gas chromatography head space analysis. The goal was to explore the affect of water collected at different times of the year on the rate of TCE degradation by performing the reaction in deionized water, pH 7 phosphate buffer, fall lake water, and summer lake water. Both of the natural water samples behaved more closely to the pH 7 phosphate buffer system than to the deionized water system. The fall lake water had a faster rate of TCE degradation and product formation than the summer lake water, implying differences in their seasonal constituents. The natural water components did not have a clear effect on the rate of TCE degradation. The rate of ethane product formation was slowest in both of the natural water samples, indicating that natural water components have a negative effect on product formation, particularly delaying the initial rate.

Identification of New Inhibitors of Low Molecular Weight Protein Tyrosine Phosphatase

Kyle A Richards

Biochemistry, Chemistry

Low Molecular Weight Protein Tyrosine Phosphatase (LMW-PTP) plays a vital role in both cell proliferation and intercellular communication. Over-activation of LMW-PTP has been linked to the transformation of cells in the liver, kidney, and breast. Past research has shown the National Cancer Institute's diversity set I and II both contained inhibitors targeted against LMW-PTP. Our research is focused on the identification of novel inhibitors of LMW-PTP based on the National Cancer Institute's diversity set III. Inhibitors were first identified via virtual screening using Maestro (Schrodinger LLC) before being tested through an enzymatic assay. Results of these efforts will be presented.

The Mayo Innovation Scholars Program Experience

Katharine Nystrom, Alex Hanson

Biochemistry, Biology, Chemistry, Computer Science, Exercise Science and Sport Study, Experiential Learning & Community Engagement, Mathematics, NATS, Nursing, Nutrition, Physics, Psychology

The Mayo Innovation Scholars Program pairs a team of undergraduate science and business students with an MBA project manager to assist Mayo Clinic Ventures in the assessment of new product submissions by Mayo researchers. This program provides research opportunities for undergraduate science and business students while providing leadership development and research opportunities for MBA students.

Polyurethane Synthesis using Biorenewable Monomers

Christopher P Stevermer

Chemistry

Biorenewable polymers and their properties have become a growing field of interest with the increasing price of petroleum products. Biorenewable monomers are becoming a more cost effective and viable alternative. In pursuit of this field two natural products menthone, derived from spearmint oils, and dihydrocarvone, derived from caraway oil, were transformed into the lactones menthide and dihydrocarvide using a green Baeyer-Viliger reaction utilizing Oxone and sodium bicarbonate. The lactones were purified of epoxides and excess reagent using distillation and column chromatography and confirmed using GC-MS and H-NMR. The lactones were then used as monomers in a polymerization of polyurethane

Synthesis and Characterization of A Biomimetic Model of the Tricopper Binding Site of Multicopper Oxidases

Haosen Wang

Chemistry

This research employs the principles of bioinorganic modeling, simplifying the extraneous structures of the molecule being mimicked and focusing only on the active components of the large biological molecules. Specifically, this project attempts to mimic the structure and reactivity of tri-copper active sites found in Multi-copper Oxidases, such as Laccase and Ceruloplasmin, that bind with oxygen and reduce it to water. After experimenting with various other structures that failed to mimic the active sites, we selected another potential ligand, 1,3,5-tri(2-pyridylmethyltriazole)-2,4,6-triethyl benzene, abbreviated Ltapma, to be the Cu binding scaffold for this research to bind with three Cu(I) ions and then to bind with oxygen molecules. This project devised new procedures to synthesize and purify alkyne 13 and Ltapma. Cu binding and oxygen binding were attempted, and data shows evidence of binding but more data need to be collected before we could arrive at a decisive conclusion on their binding patterns.

Testing a New Combination Therapy for Patients with Relapsed/Refractory Multiple Myeloma

Andrew T Humbert

Biology, Chemistry, Computer Science, Mathematics, NATS, Nursing

Multiple myeloma, an incurable B-cell lymphoma, is the second most prevalent hematological disorder in the U.S. It affects nearly 20,000 people annually. There has been little development of successful new treatments for patients with multiple myeloma in the past few decades which is of particular concern given the majority of patients die within 5 years of diagnosis and that many of the current treatments result in high adverse effects. Angiogenesis has proven to be an important factor in the progression of multiple myeloma, thus targeting angiogenesis is believed to improve patient outcomes. This new combination therapy looks to target agents of angiogenesis (in particular Vascular Endothelial Growth Factor (VEGF)) to prevent cancer progression. The combination treatment used in this phase II clinical trial includes two drugs currently used together, lenalidomide and dexamethasone, paired with a new drug bevacizumab. Both lenalidomide and bevacizumab have been shown to inhibit VEGF though through different mechanisms. The combination of these drugs is believed to yield greater VEGF inhibition which in turn will prevent the progression of multiple myeloma and have more successful outcomes for patients. The statistical analysis study will include basic summary statistics to describe the demographics, confidence intervals using the Wilson score method to determine response rates and toxic responses to the treatments, survival analysis to determine overall survival and progression free survival rates, and an exploratory analysis using biological endpoints (VEGF, interleukin-6, macrophage inflammatory proteins) to determine any correlations between response and survival rates with these biomarkers.