Montana Local ACS Spring Conference

Saturday April 13th, 2019
Carroll College

Campus Center – lower level
1601 N. Benton Avenue
Helena, MT 59625
Schedule of Events:

All events are located in the lower level of the Campus Center (Cube).

9:00-9:25 am  Registration and poster set-up

9:30-9:45 am  Opening remarks
*Dr. David Hitt, Carroll College*

9:45-10:45 am  Poster session with light breakfast

11:00-12:00 pm  Keynote Address
*Dr. Richard Bridges, Regents Professor, University of Montana*

12:00-1:00 pm  Catered Lunch

1:00-1:15 pm  ACS History and Membership Benefits
*Dr. John Hartman, Helena College*

1:15-2:45 pm  Oral Presentations
*Moderated by Dr. Julie Kessler, Carroll College*

2:45-3:00 pm  Break

3:00-3:15 pm  Travel Award Presentations
*Steve Rowley, MT ACS chair, Division by Zero Development Labs*

Closing remarks
*Dr. Julie Kessler, Carroll College*

3:15-4:30 pm  MT ACS Board Meeting
Keynote Presentation

From Neuropharmacology to Cancer, the Serendipity of Medicinal Chemistry

Dr. Richard Bridges

University of Montana

Richard J. Bridges is a Regents Professor of Pharmacology and Toxicology at The University of Montana, where he has been on the faculty of the Skaggs School of Pharmacy since 1993. After completing an undergraduate degree in Biochemistry at the University of California at Davis, Bridges received a Ph.D. in Biochemistry from Cornell Medical College in 1984. Following postdoctoral and faculty positions at the University of California at Irvine, he moved to the University of Montana as an Associate Professor in 1993. Bridges served for 8 years as the founding Director of the NIH-COBRE Center for Structural and Functional Neuroscience. He was also a founding member of the Montana BioScience Alliance and the Montana Neuroscience Institute, where he served for several years as Chairman of the Board. Bridges also served as the Chair of the Department of Biomedical & Pharmaceutical Sciences within the Skaggs School of Pharmacy from 2008 until 2015. He has recently returned to his role as Director of UM’s Center for Structural & Functional Neuroscience.

Research in the Bridges lab group focuses on the molecular pharmacology of membrane transport proteins that regulate the movement of signaling molecules into and out of cells within the brain and spinal cord. Emerging evidence suggests that these systems, as well as the novel drugs that regulate their activities, are relevant to a wide range of CNS diseases and insults, including: ALS, traumatic injury, drug addiction, epilepsy and brain tumors.
An Exploration of Benzene, Coronene, and Similar Structures using MOPAC and DFTB Calculations and the Potential of Zeolite-Templated Carbons

Rylan Rowsey, Erin Hanson, Robert K. Szilagyi, Nicholas P. Stadie

Montana State University

Molecular Orbital PACkage (MOPAC) and Density Functional Tight Binding (DFTB) are two computational chemistry packages that can optimize molecular structures based on molecular orbitals and density functional theory, respectively. These are classified as semi-empirical methods, which implies the use of some level of empirical parameterization. Due to the differences in how these calculations are performed, it is necessary to use both in conjunction to develop an experimentally sound structural model. Several different structures including benzene, coronene, and similar molecules, were first analyzed as a benchmark molecular study. The results from these calculations show that no individual method alone can provide an energetically sound picture, but they must be carried out in conjunction with each other in order to ensure accuracy. The same methods were then also used to explore a molecular model of zeolite-templated carbon (ZTC) in a periodic boundary model. ZTCs are porous carbon framework solids with a three-dimensional network of micropores ~1.2 nm in width. The development of a quantum chemically sound model will aid in gaining a new understanding of the structure and properties of this important technological material. A second practical application of these calculations is heteroatom doping (e.g., boron) within ZTCs, shedding light on a new class of CB\textsubscript{x} porous solids. Using MOPAC and DFTB calculations the structure can be optimized and tested for energetic stability. The heteroatom doped structure can then be investigated for hydrogen adsorption and compared to pure carbon ZTCs.
Oral 2

**Isoxazolo[3,4-d]pyridazinones positively modulate the metabotropic glutamate subtypes 2 and 4**

Christina Gates, Nick Natale

*University of Montana*

The seven transmembrane (7TM) superfamily, also known as G-protein coupled receptors (GPCR), are one of the largest superfamilies in the human genome. With approximately 30% of marketed drugs targeting the GPCRs, these proteins are among the most successful as therapeutic targets. Within the GPCR receptor family there is a subgroup called the metabotropic glutamate receptors (mGluR). Compounds that target mGluRs are important for the treatment of a variety of central nervous system (CNS) disorders, as well as cancer. The mGluR₂ subtype is a target for treatment of anxiety and schizophrenia. Activation of mGluR₄ helps to ease the symptoms of Parkinson’s disease and may even slow progress of the disease. Additionally, both of these receptors have been implicated in the treatment of variety of cancers such as glioma, medulloblastoma, or colorectal carcinoma, presenting another target to overcome these diseases. Selectively targeting the mGluRs are difficult due to the high sequence similarities. This difficulty can be overcome by targeting the allosteric site, which is located in the 7TM. Our isoxazolo[3,4-d]pyridazinones compounds were tested and found to have selective activity at mGluR 2 and 4. This selectivity, along with other tests, imply binding may not be at the venus flytrap domain (where glutamate binds), but rather at the allosteric site as positive allosteric modulators (PAMs). Further modifications of our compounds will be developed to optimize selectivity and activity, based on structural drug design and modeling at the allosteric site. Our progress on the new synthesis and biological evaluation will be presented.
Dechlorination of carbon tetrachloride by Cu(PDTC)X under environmental conditions

Tayler Songer, and Matthew Queen

Montana State University Billings

Carbon tetrachloride is a known carcinogen that is dechlorinated by Cytochrome P450, located in the human liver. Environmental reduction of carbon tetrachloride proceeds via trichloromethyl radical mechanism, which results in lesser chlorinated intermediates which can be even more harmful to living organisms. It has been shown that [Cu(PDTC)L]X dechlorinates carbon tetrachloride directly to environmentally safe CO₂ and chloride. This study investigates the dechlorination kinetics of carbon tetrachloride by [Cu(PDTC)Br]²⁺ in simulated environmentally relevant conditions found in aquifers. We created simulated Hanford ground water samples featuring Fe³⁺/²⁺, Ca²⁺, and Mg²⁺ SO₄⁻² salts. Data suggests that the rate of dechlorination of carbon tetrachloride by [Cu(PDTC)Br]²⁺ is unaffected in the presence of the aforementioned ions.
Oral 4

Analysis of Atomic Deformation Behavior under Compressive Loading at Different Strain Rates in a Simple Aluminum and Copper Cubic System

Md Salah Uddin, Brahmananda Pramanik

Montana Technological University

We studied a simple aluminum (Al) and copper (Cu) system deformed at a range of strain rates under compression at room temperature and ambient pressure. Al and Cu are important elements for aerospace grade aluminum (Al) alloys. Aluminum alloys are light metal alloys which have high demand in aerospace and automotive industries. Most of the aerospace grade Al alloys has copper composition ranges from 1.2 – 6.8%. In engineering applications, functional parts are designed for over a broad range of strain rates and temperatures. We performed a numerical simulation under compressive loading at lower strain rates to ultra-high strain rates on the Al and Cu system. The cell boundary temperature and pressure for the simulation of the material deformation were at room temperature and ambient pressure, respectively. We used a many-body interatomic potential function as modified-embedded-atom-method which is a widely used atomic level semi-empirical model for metals and impurities. The potential function was applied to five thousands of atoms in periodic boundary conditions. The talk will describe the atomic analysis of strain rate dependent material deformation under compression.
Mass Spectrometry of Radical SAM Maquettes

Agustin Pineda, Eric Shepard, Robert Szilagyi

Montana State University

Radical S-adenosyl methionine enzymes utilize a [4Fe-4S] cluster to coordinate and reductively cleave S-adenosyl methionine (SAM) into L-methionine and a highly reactive deoxyadenosyl radical. In this project, we have designed short ferrodoxin- and radical SAM - inspired oligopeptides that harbor the CX₂CX₂C and CX₃CX₂C motifs utilized by these families of enzymes. We are seeking to study the ability of these peptides to coordinate redox active [4Fe-4S] clusters (referred to as [4Fe-4S]-maquettes). The overarching goals of this project are to 1) nest site-differentiated and redox active [4Fe-4S] maquettes and 2) to probe the propensity of these [4Fe-4S] cluster to coordinate and activate small molecules. Evidence for [4Fe-4S]-maquettes has been clearly observed in the reduced (1+) state using EPR spectroscopy, and in the oxidized (2+) state using UV-vis spectroscopy. We are working on defining compositional and structural information from ESI mass spectrometry. The study of these [4Fe-4S]-maquettes provides evidence that at a fundamental level, cluster formation is thermodynamically favorable in buffered, aqueous media, and it generates cluster species with physiologically relevant reduction potentials (Eₘ = -500 – -200mV).
Oral 6

**Axial Chirality to increase selectivity of AIMs as anti-tumor agents**

Michael J. Campbell, Nicholas Natale, Matthew J. Weaver

*University of Montana*

The focus of this project is to improve the efficacy of anthracenyl isoxazolyl amides (AIMs) by adding axial chirality via strategic halogenation. AIMs are a new class of antitumor agents specially synthesized to bind and interact with G-quadruplex (G4) DNA; binding G4 DNA has been shown to repress the replication of oncogenes in cancerous tumors. By using asymmetric halogenation our goal is to introduce axial chirality into the AIMs. Many biologically active molecules are chiral and the stereoisomers often display a significant difference in activity due to interactions with chiral targets, such as DNA. Methods of over halogenation of unsubstituted anthracenes, in synthetically useful yields, have been published by Cakmak. However, with the added complexity of a substituted anthracene, the addition of halogens has been a challenge. We have successfully isolated a 1,2,3,4,10-pentabromo-anthracenyl-isoxazole-ethylester. The methods that yielded the overbrominated product require consideration of the mechanism of the reactions, in which ionic and radical intermediates are expected to predominate. The current focus is the selective reductive elimination of the overbrominated compound. The future focus will shift to selective cleavage and subsequent substitution that will afford an axially chiral final product. The benefit of stereospecific activity is that a patient may be able to take less of the chemotherapeutic agent and achieve equally beneficial results with fewer side effects. Our progress will be described.
Poster 1

**Oxidative Dimerization of 1-(2-thienyl)-pyrene and 2-methylthiophene**

Jade Combs, Audrey Yeager, Paul Wilson, John Rowley

*Carroll College*

The objective of this research was to investigate the use of thiophene containing compounds as the feedstock for photoelectrochemical solar cells that would use sunlight to form carbon-carbon bonds and thus store solar energy as a chemical fuel. Herein we discuss the synthesis of 2-(4-methylphenyl)-thiophene and 1-(2-thienyl)-pyrene via Suzuki Cross coupling reactions in the presence of a Pd$^0$ catalyst. The oxidative dimerization of 1-(2-thienyl)-pyrene to form 5,5’-bis(pyrene)-2,2’-bithiophene through electrolysis was observed at 1.5V vs. Ag/AgCl. The dimer, 5,5’-bis(pyrene)-2,2’-bithiophene was characterized using $^1$H NMR, mass spectrometry, and spectroelectrochemistry. Attempts to synthesize 5,5’-bis(pyrene)-2,2’-bithiophene using chemical oxidants, specifically molecular oxygen, H$_2$O$_2$, Ce$^{4+}$, and Ag$^+$ were unsuccessful, however compounds with nonaromatic substituents have proven to be successful in literature.

Poster 2

**Studies Towards a More Cost Effective Stereoselective Synthesis of Planar Chiral Ruthenium $\eta^6$-aryl Sandwich Complexes**

Austin Dobrecovich, Andrew Quinn, Orrin Dailey, David Hitt

*Carroll College*

During the 2019 Spring semester in our Organic Chemistry II lab course, we were asked to study the synthesis of planar chiral $\eta^6$-arene ruthenium(II) complexes. This study is important because ruthenium complexes can be used in therapeutics and are useful in organic synthesis as strong electron withdrawing group that can be removed easily under photolytic conditions. Uemura and coworkers have formed sandwich complexes containing aryl and cyclopentadienyl ligands stereoselectively with an ortho-
substituted arene, containing a chiral center on the benzylic position with a hydroxyl substituent. This reaction had excellent yields and diastereomeric ratios, but the reagents used for this synthesis were expensive. A later work published by Lindel and coworkers used more cost effective reagents, and is a much easier synthetic procedure to conduct, but Lindel failed to study any arenes similar to what Uemura researched. This is where our group and our fellow students have focused research for this semester. As a class, we have studied the stereoselective formation of a planar chiral ruthenium sandwich complexes using a set of arenes containing a benzylic alcohol with a chiral center in the carbinol position and a variable ortho substituent. My group has successfully synthesized a planar chiral $\eta^6$-arene ruthenium(II) complex using one of the arene structures, 1-(2-methylphenyl)ethanol, and a pentamethylcyclopentadienyl ligand, which is supported by $^1$H NMR spectral measurements.

Poster 3

**Ab Initio Study of Aqueous [Fe-S] Clusters: Computational Modelling of Stepwise FeS Cluster Building**

Luke MacHale, Rebecca Hanscam, Eric M. Shepard, Robert K. Szilagyi

*Montana State University*

Holding a key to the origins of life and chemical function of extant metalloproteins found in every domain of life, iron-sulfur (Fe-S) clusters take a central role in bioinorganic and metalloenzymology research. My use of quantum computational methods complements the experimental side of the superfamily of radical S-adenosylmethionine (SAM) enzyme research that are the focus of several experimental laboratories at Montana State University. In my work, I utilize the level of theory that was shown to be most accurate for Fe/S systems and supplement this theory with implicit solvation I previously validated for the hydration of iron and sulfur ions. These ions combine, form a cascading series of Fe-S clusters and nanoparticles before the bulk FeS (mackinawite) phase appears. Geochemical characterization of Fe-S precipitation indicates a barrier less, spontaneous cluster formation process. Utilizing a two-step computational treatment that includes corrections to
translational entropy and inclusion of empirical dispersion has the potential for reproducing experimental thermodynamic values within an order of magnitude. This validated method was used to predict specific stoichiometries for Fe-S clusters that represent deep thermodynamic wells along the spontaneous recombination processes of geochemically relevant species on the path toward the formation of site-differentiated [4Fe-4S]^{2+} clusters found in radical SAM metalloenzymes. Results from the enthalpy of step-wise addition to the [4Fe-4S]^0 was characterized into a variable matrix, through which the enthalpy was predicted for higher order clusters. A complete characterization of the coulombic interactions allows for the prediction of any neutral cluster’s enthalpy to be predicted given initial conditions.

Poster 4

**Got Phthalates? Analysis of Plasticizers in Popular Consumer Products**

Talya Vaira, Caroline Pharr

*Carroll College*

This study reports on phthalate presence in popular consumer products including macaroni and cheese powder and baby diapers. Phthalates are a group of chemicals used as plasticizers in hundreds of products. Some phthalates are classified as endocrine-disrupting chemicals. Health effects include early labor, infant hormone level imbalances, and decreased semen quality. Phthalate exposure occurs through volatilization and leaching, leading to environmental contamination and concerning levels of exposure to the general population. One primary source of exposure is by the direct contact of consumer products with plastic materials during processing, packaging, and labeling. Using solubility extraction techniques phthalate presence will be investigated via Gas Chromatography – Mass Spectrometry (GC-MS).
Ruthenium $\eta^6$-arene sandwich complexes are useful in organic synthesis because the metal acts as an electron-withdrawing group thus opening up a range of chemical reactivity not normally accessible to benzene derivatives. For example, the metal’s withdrawing ability should make an alkene attached to a ruthenium $\eta^6$-arene substituent more electron deficient and therefore more reactive as a dienophile in a Diels-Alder (DA) reaction. Several studies have shown that DA reactions using Ru-arene sandwich complex substituents are possible, but only preliminary studies by Hitt and Bains showed that Ru-sandwich complexes performed the DA reaction much faster than non-complexed arenes. These experiments, however, were conducted with a Ru-complex that was fairly expensive to prepare and required heating. Rather, we investigated the reactivity of ruthenium $\eta^6$-arene complexes using a dienophile prepared in a single synthetic operation using ethyl trans-cinnamate, 1,2,3,4,5-pentamethylcyclopentadienyl anion (Cp*), and ruthenium(III) chloride as the metal source. Furthermore, this reaction was conducted at room temperature. In our initial attempt to prepare this compound, we obtained evidence that a DA reaction occurred between the complexed dienophile and the Cp* precursor, 1,2,3,4,5-pentamethylcyclopentadiene (Cp*H) demonstrating the DA reaction does not actually require heating to occur as originally implemented by several other research groups. We are currently investigating whether varying the amount of Cp*H will stop the in situ formation of the DA adduct.
Poster 6

**Platinum(II)-Catalyzed Additions to Conjugated Alkynones**

Beau Howard, John W. Hartman

*Helena College*

Platinum(II) compounds have been previously established to efficiently catalyze the addition of water and alcohols to a variety of alkyne substrates to yield ketone and acetal products, respectively. Catalyst systems ranged from simple platinum(II) halides to complexes like Zeise’s Dimer. Unsymmetrical alkyne substrates yielded product mixtures with modest to excellent regioselectivity dependent on steric effects of both the alkyne and the catalyst ligands. We now report platinum(II)-catalyzed regiospecific addition of alcohols to conjugated alkynones to exclusively yield conjugated keto vinyl ethers. Reaction conditions, proposed mechanism, and progress towards scope and optimization will be presented.

Poster 7

**Forming Carbon-Carbon Bonds Via Photo-oxidation**

Joseph Pesa, John Rowley

*Carroll College*

1-(2-thienyl)-pyrene has been viewed to form a carbon-carbon bond when oxidized. We investigated a palladium catalyzed reaction leading to the dimerization of a furan. However, ostensibly a similar reaction can occur in the absence of palladium but the presence of a photocurrent substantial enough to push an electron to an excited state, leaving a hole in it’s previous orbital. After this occurs, this molecule can find another of the same nature and complete the desired carbon-carbon bond. In creating this bond, we will have synthesized a “solar fuel” that can store energy in a stable bond using light.
Poster 8

**Quantifying the Temperature Dependent Rate of Solventless Redox Reactions**

*Audrey Yaeger, Paul Wilson, Talya Vaira, John Rowley*

*Carroll College*

Solventless reactions are becoming increasingly popular in the chemical industry due to the dangers posed by hazardous solvents necessary to perform chemical reactions. These hazardous solvents are undesirable as they require specialized disposal due to toxicity, flammability and carcinogenic characteristics. Therefore, safely disposing of these solvents can be expensive. Solventless reactions have the potential to be advantageous if they demonstrate improved efficiency and selectivity compared to reactions carried out in solvents. As a result, chemists have begun examining the feasibility of solventless reactions. Herein we report the solventless redox reactions transforming diphenylmethanol to benzophenone and vice versa. Oxidation has been observed to occur at room temperature using infrared spectroscopy through the loss of the alcohol stretch (3200-3600 cm\(^{-1}\)) and growth of the carbonyl peak (1700 cm\(^{-1}\)). Solid state reduction of benzophenone to diphenylmethanol was also observed through the development of an alcohol stretch (3200-3600 cm\(^{-1}\)) and loss of the carbonyl peak (1700 cm\(^{-1}\)). The goal of this research is to study the rate of redox reactions at various temperatures to obtain high quality data so activation energy for the reactions can be determined.
Poster 9

Synthesis of 2-(4-ethoxycarbonylphenyl)thiophene and 5,5’-(4-ethoxycarbonylphenyl)-2,2’-bithiophene: Case Study of a Derivative Synthesis Project to Support a Hammett Analysis of an Electrochemical Oxidative Dimerization

Matthew Fonte, Michael Henderson, David Hitt, John Rowley

Carroll College

In this study, we present the synthesis and characterization of 2-(4-ethoxycarbonylphenyl) thiophene. Additionally, we have spectroscopic evidence consistent with the successful synthesis of its dimer, 5,5’-(4-ethoxycarbonylphenyl)-2,2’-bithiophene. This monomer-dimer pair will be used in a Hammett Analysis study of the mechanism of an oxidative-homocoupling reaction that has potential use in a fuel-forming solar panel. The monomer was synthesized via a Suzuki cross coupling reaction between 4-ethoxycarbonylbenzeneboronic acid and 2-bromothiophene. Spectral data for the coupled product was found to be consistent with the expected monomer structure. A similar Suzuki cross coupling reaction using 5,5’-dibromo-2,2’-bithiophene was used in an attempted synthesis of the dimer. The product of the reaction had a UV-vis absorption maximum that was red shifted from the monomer at 300 nm to 370 nm. Further spectral characterization of this compound is ongoing. This study represents an example of a class project in the second semester Organic Chemistry II lab at Carroll College to synthesize and characterize a range of monomer-dimer pairs for use in studying the mechanism of the oxidative homocoupling reactions using electrochemical methods.
Limited hydrogen storage capacity is one of the primary barriers to viable hydrogen fuel cell vehicles. The DOE has specified a target of 4.5 weight percent hydrogen at ambient conditions in order to meet the requirements of a mobile passenger vehicle. Theoretical studies predict crystalline BC3 (a bulk graphite-like material) to have a much greater hydrogen storage capacity than related pure carbonaceous materials. One study predicts a reversible storage capacity of 6.1 weight percent hydrogen under near ambient conditions. The objective of this research project is to characterize the hydrogen uptake of bulk boron-doped graphitic carbon and determine its viability for hydrogen storage. A Sieverts apparatus was designed, constructed, and commissioned for hydrogen sorption measurements between temperatures from 298-400 K and pressures from 0-12 MPa. By application of the Unilan model, the absolute quantity of adsorption and the isosteric enthalpy of adsorption were determined.

Carbenes are an important class of reactive carbon used in metal catalyzed formation of new carbon-carbon bonds and are commonly found in interstellar space. Carbenes exist in either a triplet state or a singlet state. This is determined by the configuration of the electrons and each state possess different chemical reactivity. Carbenes are inherently very reactive and unstable, making studying them under standard conditions challenging. Thiophene ylides offer a method for accessing carbene intermediates without the need for extremely low temperatures and pressures. This research focuses on synthesizing a series of thiophene ylides, with the goal of identifying trends in
reactivity within a series of malonate carbene derivatives. Analysis of the reactivity is accomplished by irradiating the ylide, which will generate the carbene intermediate. This irradiation will be carried out in the presence of a trapping agent, which will react quickly with the carbene intermediate to form several stable products. These products will be analyzed and the amount of carbene consumed as well as the spin state (singlet or triplet) will be identified. Analysis of the products formed will give insight into the factors affecting carbene reactivity with potential to broaden their applications in chemistry.

Poster 12

**Synthesis of bis(2-diphenylphosphinophenyl)amine Ligand**

Zachary Brandt, Harry Green, Palmer Moylan, Julie Kessler

*Carroll College*

In this project, the air free synthesis of the bis(2-diphenylphosphinophenyl)amine ligand (BDP₃A, (4)) from 2-Iodoaniline (1) was performed. The synthetic route included an oxidative addition reaction using tetrakis(triphenylphosphine)palladium(0), (Pd(PPh₃)₄) followed by a reductive elimination reaction yielding the intermediate 2-(diphenylphosphino)benzenamine (2DPPBA, (2)). Reaction products were purified by column chromatography and analyzed via ¹H-NMR and ³¹P-NMR spectroscopy. An alternative synthesis of 2DPPBA will be explored using copper(I) iodide as an oxidizing agent. Upon formation of 2DPPBA, this structure will be combined with 2-(diphenylphosphino)benzaldehyde (3) to form the BDP₃A ligand (4). Ultimately, BDP₃A will be complexed to first and second row transition metals (such as Co, Ni, Cu, Ru, Pd, or Ag) and investigated as a catalyst for coupling reactions, or the reduction of ketones to alcohols.
Acknowledgements:

- Poster and oral presentation participants
- MT-ACS local section for funding
- MT-ACS board members for judging presentations
- Carroll College conference organizers: Drs. David Hitt, Julie Kessler, and Kyle Strode
- Sodexo Catering services
**Meeting Location:** Campus Center – Lower Level (Building 1 on map below, purple box, enter through E or S entrance). Please park in lots on SW side of campus (red boxes). No street parking!

**Campus Address:** 1601. N Benton Avenue, Helena MT, 59625.

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Main entrance to campus at stoplight. Directly across street from Brewhouse and Intrepid Credit Union.