

2015 Western Regional Meeting 1

Forest fire arson: Linking field investigative data to potential sources

Detlef A. Birkholz, birkholz@ualberta.ca. Pharmacy and Pharmaceutical Sciences, University of Alberta, Edmonton, Alberta, Canada

We have been involved in the investigation of many forest fires in order to determine whether arson was the determining cause. Of particular interest was to research whether evidence of arson could be gathered well after an event was reported. Furthermore, we wanted to know whether field data collected after an investigation could be correlated to potential sources. Samples of gasoline were collected from nine service stations. These were analyzed using gas chromatography/mass spectrometry (GC/MS) using a PONA capillary column and employing both split and passive headspace analysis. Synthetic adsorbent was prepared by mixing Celite with AX-21 carbon in the ratio of 4.5:1. This adsorbent was fortified with gasoline samples and allowed to weather in a fume hood for 165 h. Measurements of alkylated benzenes revealed > 95% of the gasoline was removed. Evidence for the presence of gasoline after such extreme weathering was undeniable and correlated well with field studies where samples collected years after a forest fire revealed the presence of accelerant. Highly weathered fortified adsorbent samples could not be correlated with source gasoline, however, passive analysis of gasoline could be correlated with fuel analyzed using split GC/MS, suggesting, a strong signal obtained from a field sample may be correlated with a source. Chemometric analysis of data obtained for alkylated benzenes was most productive, however, data transformation procedures were critical

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Marijuana extraction labs: Assessing the explosion dangers

Dean Kirby¹, dean.a.kirby@usdoj.gov, Layne Higgins¹, Todd Burton². (1) Southwest Laboratory, Drug Enforcement Administration, Vista, California, United States (2) Hazardous Incident Response Team, San Diego County, San Diego, California, United States

The emergence of clandestine marijuana extraction laboratories (often referred to as butane honey oil labs) has been rapidly spreading across the United States and Canada, particularly along the west coast. The damage caused by butane gas explosions connected to clandestine extraction labs has been extensive. This study was designed to evaluate the conditions leading up to a butane explosion and then to systematically characterize those parameters by conducting controlled simulations. Phase One of the study demonstrated the heat produced and size and power of the fireball resulting from the ignition of increasing amounts of butane released in a small room. Phase Two of the study demonstrated the effects of various ignition sources and their ability to trigger an explosion. Finally, Phase Three simulated the results of a butane gas explosion that resulted from using typical clandestine extraction conditions in a small apartment room.



Butane ignition

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Experimental observation of large mass-independent isotopic anomalies from diffusion of H₂O

Gerardo Dominguez, aerogelman@gmail.com. Department of Chemistry and Biochemistry, California State University-San Marcos, San Marcos, California, United States

Understanding how the ratios of minor to major isotopes of elements change in nature is important for understanding the history of formation and alteration of natural systems. Changes in these ratios are generally classified into mass-dependent and mass-independent fractionations, with mass-independent shifts typically being associated with non-equilibrium processes. Here, using a UHV vacuum line and cavity ringdown spectrometer capable of quantifying H₂O isotopologues (H₂¹⁶O, H₂¹⁷O, H₂¹⁸O, and HD¹⁶O), we show how a non-equilibrium diffusive process can produce large mass-independent isotopic fractionations in the laboratory. We model and discuss possible causes of the observed isotopic anomalies and their implications for isotope geochemistry at large.

2015 Western Regional Meeting 4

Self-healing corrosion resistant coatings: An enabling technology for the use of alternate waters for cooling

Ganesh Rajagopalan, RGanesh@kennedyjenks.com. Kennedy/Jenks Consultants, Irvine, California, United States

Use of reclaimed water for power plant and industrial cooling requires pre-treatment to lower ammonia and dissolved salt concentration for corrosion protection, which is often cost

prohibitive. This presentation describes a new self-healing coating that can protect against ammonia and salt corrosion while not compromising heat transfer efficiency of condensers.

ACS Western Regional Meeting 2015

Self-healing Corrosion Resistant Coatings: An Enabling Technology for the Use of Alternate Waters for Cooling

Ganesh Rajagopalan^{1*}, Gaurang Bhargava², Ganesh Skandan², Paul Puckorius³

1. Kennedy/Jenks Consultants, 3210 El Camino Real, Irvine, CA 92602

2. NEE Corporation, 400 Appar Drive, Suite E, Somerset, NJ 08873

3. Puckorius & Associates, Inc., 6621 W 56th Avenue, #200, Arvada, CO 80002

* - Corresponding Author: rganesh@kennedyjenks.com

ABSTRACT

The projected population growth and limited availability of fresh water sources have imparted significant strain on the nation's fresh water use. There is a large supply of alternate waters (e.g. municipal wastewater, mine pool water, oil and gas field produced water) that could be put to beneficial use. On the demand side, power plants, industrial facilities and commercial institutions are seeking alternate waters for cooling applications.

Notwithstanding the demand, cooling systems employing waters from these sources experience significant corrosion issues due to dissolved salts and ammonia. Pretreatment to remove ammonia and dissolved salts often render use of alternate waters for cooling cost prohibitive.

The project team adopted a novel approach to address this issue. Rather than treating the alternate water to meet water quality requirements of cooling system condensers, a nanomaterial-based corrosion resistant self-healing coating was developed. The proposed technology offers a thin, self-healing, nanocomposite corrosion resistant coating developed for copper alloys (inorganic) and mild steel (organic-inorganic hybrid) without affecting the heat transfer properties. Self-healing functionality is derived from the coating matrix that has a unique molecular structure facilitating the incorporation of corrosion inhibitors, which are released "on demand" at defect sites.

Bench-scale studies were performed using copper alloys (Cu, Cu-Ni), mild steel, stainless steel and galvanized iron coupons. Salt spray tests as well as static and dynamic corrosion coupon tests using reclaimed waters were performed. Further, heat transfer resistances of the coated and uncoated tubes were tested using a modified ASTM D4778 protocol. Reclaimed waters for this study were obtained from West Basin Municipal Water District, El Segundo, CA and Boeing facility (King County Wastewater treatment plant effluent) at Long Acres, WA.

Bare and nanomaterial coated Cu and Cu-Ni coupons were subjected to dynamic corrosion testing using the reclaimed water spiked with 200 mg/L of ammonia at 120 °F. After 22 days significant corrosion were observed in bare copper coupons, as evidenced by darkening of the exposed region (corresponding to the formation of surface oxides). In addition, blue corrosion products corresponding to the formation of Cu(OH)₂ and Cu(NH₃)₄²⁺ were clearly visible. Compared to bare copper coupons, Cu-Ni coupons exhibited less corrosion effects. However, metal coupons coated with the self-healing

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corrosion resistant coating showed significant protection with no signs of corrosion. Modified ASTM D4778 tests performed to compare HTR at flow velocities of 2 to 4 m/sec showed identical values, indicating no loss of heat transfer efficiency due to the application of self-healing coating.

Static immersion tests using mild steel coupons showed corrosion rate of 18.4 and 4 mpy for bare coupons in West Basin MWD and Boeing water, respectively after 240 hours. The corrosion rates for the coupons with self-healing coatings were 0.61 and 0.03 mpy, respectively, after 240 hours.

Crevice corrosion tests were performed using 304 and 316 stainless steel coupons as per ASTM G48-11 protocol. The panels were bolted with TFE-fluorocarbon segmented washers and immersed in Ferric Chloride (FeCl₃) solution for 24 hours. Uncoated stainless steel panels showed extensive crevice formation. Self-healing coating provided enhanced corrosion protection with no crevice formation.

Galvanized steel is often used in cooling towers, and they readily form white and red rust upon exposure to moisture. Salt spray tests performed on bare and self-healing coating applied coupons showed significant differences in corrosion resistant characteristics. For example, uncoated coupons showed red rust formation after 2 weeks (336 hours) of salt spray testing. However, coupons with self-healing coatings showed significant corrosion protection against white and red rust formation.

Finally, economic evaluations were performed for compare use of reclaimed water for cooling by conventional treatment to remove ammonia and the self-healing coating developed in this study. The water treatment costs were obtained from published data from actual treatment facilities. Based on preliminary analyses (using conservative coating life and production cost), the proposed coating technique can lower the cost of using alternate water by up to 80% for cooling.

Summary

Use of reclaimed water for power plant and industrial cooling requires pre-treatment to lower ammonia and dissolved salt concentration for corrosion protection, which is often cost prohibitive. This presentation describes a new self-healing coating that can protect against ammonia and salt corrosion while not compromising heat transfer efficiency of condensers.

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Standard heats of oxidation for characterized soils in the remediation of chemically-contaminated groundwater

Nicole Moulton², *nicole.a.moulton@gmail.com*, **Stephen P. Mezyk**¹. (1) Ca State Univ, Long Beach, California, United States (2) Department of Chemistry and Biochemistry, California State University- Long Beach, Long Beach, California, United States

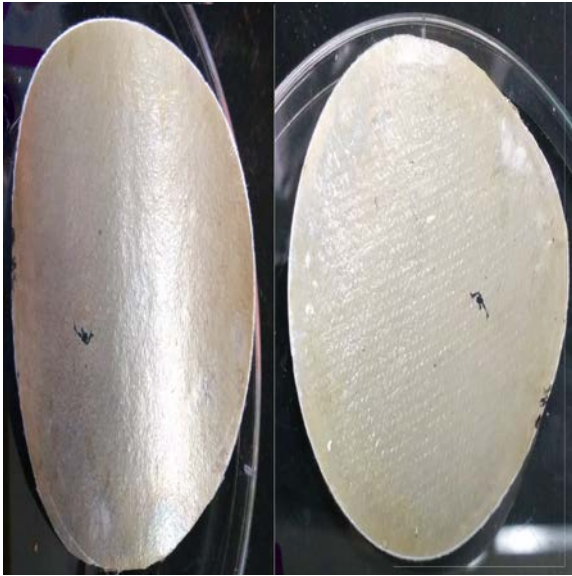
A common limitation when treating chemically-contaminated groundwaters by In-Situ Chemical Oxidization (ISCO) is knowledge of an efficient delivery of the oxidant to all the contaminant. Efficient ISCO sweeping of the impacted zones is impeded by high permeability thief zones, low permeability diffusion sinks, or mineral precipitation during treatment. Currently, there is no real-time method for assuring that the oxidant reaches the contamination. As such, we are creating a real-time continuous monitoring tool for ISCO treatment in heterogeneous groundwater. The technology utilizes the heats of reaction generated from oxidation of natural organic material and contaminants to locate ISCO delivery. Temperature changes are measured continuously using *in-situ* fiber optic distributed sensing, which provides a 0.02°C resolution. However, standard heats of ISCO oxidation of soils still need to be established. Here we determined these heats for a variety of soil standards, and correlated these values to standard soil characterizations.

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Synthesis and characterization of a graphene desalination membrane

Nanetta Pon, *npon@ucla.edu*, **Jaime Torres**, **Xinwei Huang**, **Richard B. Kaner**. Dept of Chem Biochem, Box 951569, Univ of California, Los Angeles, California, United States

We examine the feasibility of a proposed graphene desalination membrane. Graphene has been shown theoretically to be an excellent reverse osmosis membrane material due to its strength, atomic thinness, and the potential selectivity of functionalized nanopores. However, a practical graphene membrane has still never been produced. For this project, the salt rejection of large-area graphene with intrinsic defects was measured. Few-layer graphene was synthesized by chemical vapor deposition (CVD) onto nickel and copper catalysts. A method was developed to produce large-area graphene-polymer composite membranes by freeing from the growth substrate graphene sheets up to 50 cm² in area, and transferring them onto a polymer filter. The membranes were tested in a stop-flow cell with a 2 g/L NaCl solution (brackish water) at 150 psi. The composite membranes survived high-pressure conditions over several hours, and salt rejection rates of 20% were achieved. This performance supports graphene's promise as a desalination material for real-world applications.



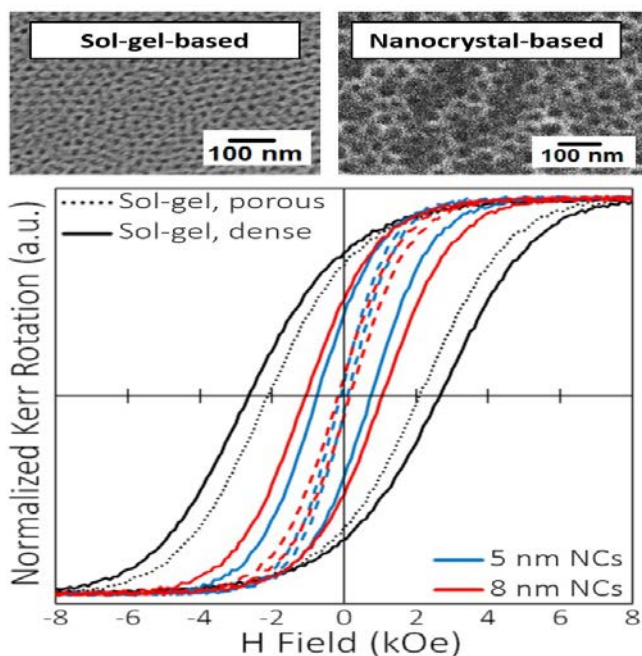
Graphene-on-PTFE membrane, before and after stop-flow testing.

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Fine tuning the magnetic properties of cobalt ferrite thin films by controlling the nanoscale structure

Shauna Robbennolt, srobbennolt@hotmail.com, Abraham Buditama, Hyeyeon Kang, Paul Nordeen, Greg Carman, Sarah H. Tolbert. UCLA, Los Angeles, California, United States

Advances in nanoscience have allowed us to tune material properties by controlling the nanoscale architecture. Here, we report that by controlling film porosity, annealing temperature and building blocks (i.e. nanocrystals and sol-gel precursors) we are able to tune the static magnetic properties of cobalt ferrite (CoFe_2O_4) thin films over a wide range. Bulk cobalt ferrite is a magnetically hard material with a coercivity around 3600 Oe. However, its coercivity can be lowered by making it nanocrystalline, mesoporous or both. Furthermore, the magnetic properties can be fine-tuned by varying the annealing temperature of the films. By combining these methods, we have shown that thin films of cobalt ferrite can be made with coercivities ranging from 3200 Oe down into the superparamagnetic regime. Finally, we find that despite the large change in static properties, the dynamic properties, as probed by ferromagnetic resonance (FMR) studies, remain unchanged over the measureable samples. These results suggest that by precisely controlling the nanoscale structure, the magnetic properties of thin films can be easily tuned and tailored toward a variety of device applications



Top-view SEM images of thin films made from both sol-gel (top left) and nanocrystal (top right) precursors. (Bottom) Magnetic hysteresis loops from a subset of samples showing the range over which the magnetic properties of cobalt ferrite thin films can be tuned.

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Preparation of fluorescent magnetic nanomaterials

Lijie Dong, dong@whut.edu.cn. School of Material Science and Engineering, Wuhan University of Technology, Wuhan, China

Multifunctional magnetic fluorescent nanomaterials have made great progress in a variety of areas, ranging from drug delivery and biosensing, dynamic sealing and cell labeling, to multi mode imaging. Fe₃O₄ magnetic nanoparticles surface protonated by 3-aminopropyltriethoxysilanes was assembled with multi-core/shell quantum dots ligand exchanged by mercaptopropionic acid to obtain hydrophilic fluorescent magnetic nanoparticles with super-paramagnetic properties at room temperature. Such bifunctional fluorescent magnetic nanoparticles were obtained by directly assembling hydrophobic quantum dots onto the surface of magnetic nanoparticles through the strong coordination interactions between zinc atoms and thiol groups, which the ultimate size was around 40 nm and the quantum dots were densely attached on the magnetic cores. The electrostatic interaction was also used to fabricate the fluorescent magnetic nanobowls by using hollow magnetic nanobowls with negative charges and quantum dots with positive charges as building blocks, which made fluorescent magnet nanobowls with rapid magnetic response and well-kept luminescent properties. Nanomaterials with outstanding luminescent and super-paramagnetic properties will serve as a new multifunctional probe for simultaneous fluorescent detection and magnetic separation of biomolecules and cells.

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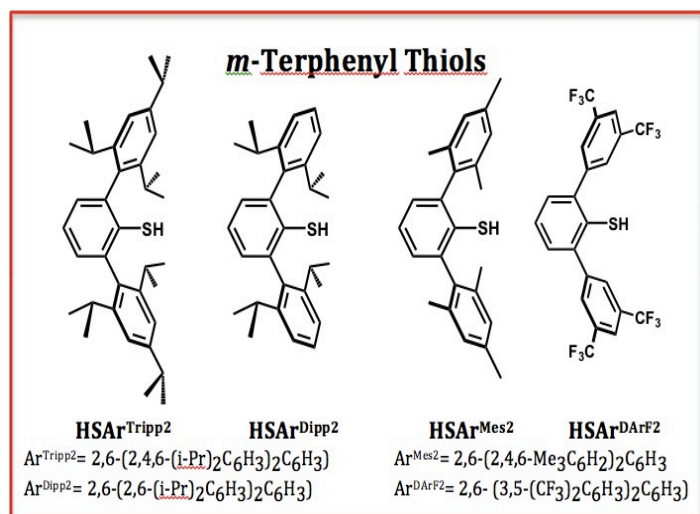
Using bulky terphenyl thiolates as capping ligands for gold thiolate nanoclusters

Noah Mendelson^{1,2}, noahmendelson52@gmail.com. (1) Chemistry and Biochemistry, University of California San Diego, Oakland, California, United States (2) Chemistry, Iowa State University, Ames, Iowa, United States

Abstract: Gold thiolate nanoclusters have aroused interest for their propensity, through chemical manipulation, to form monodisperse clusters of a defined chemical formula and structure. The most well-studied of these clusters is Au₂₅SR₁₈ (SR= 2-phenylethanethiolate). Our work in the Figueroa Group has been focused on the use of terphenylthiolates (Figure 1) as alternative passivating ligands in the synthesis of monodisperse clusters. It is our goal that by doing so we will be able to investigate alternative synthetic methodologies for the synthesis of monodisperse nanoclusters, and additionally to isolate a series of novel nanocluster sizes to illuminate structural and reactivity trends.

Synthesis: A series on gold thiolate nanoclusters (Figure 1) that are only distinguishable by steric considerations, may allow us to probe the role played by sterics in determining the compositions, sizes, and reactivities of clusters. Both the electronic and steric factors that contribute to, and ultimately determine, cluster size remain poorly understood.

Synthetic Methodology: One distinct advantage of these bulky terphenylthiolates is that these molecules are all solids. Almost all previous literature in the field invokes the use of stinky and toxic liquid mercaptans. While solid-state thiols possesses obvious synthetic benefits when compared to their volatile counterparts, this also requires slight modifications of standard synthetic techniques.



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Computational studies of states of carboranedithiols on Au{111}

Olivia Irving¹, irving@chem.ucla.edu, John Thomas⁴, Andrew Serino¹, Dominic Goronzy¹, Elisa J. Izal¹, Jonny Dadras⁵, Anastassia Alexandrova³, Paul S. Weiss², tomas base⁶, Harshan Auluck¹. (1) Chemistry and Biochemistry, UCLA, Los Angeles, California, United States (2) MC 722710, California NanoSystems Inst. UCLA, Los Angeles, California, United States (3) Chemistry and Biochemistry, University of California, Los Angeles, Los Angeles, California,

United States (5) Division of Chemistry and Chemical Engineering, Cal Tech, Los Angeles, California, United States (6) Institute of Inorganic Chemistry, Academy of Sciences of the Czech Republic, Husinec-Rez, Czech Republic

Self-assembly, defined as the spontaneous organization of a disordered molecular system, has proven to be a viable route for bottom-up design approaches in nanotechnology. Recently, carboranethiols have been shown to assemble on Au{111} substrates and to form two-dimensional monolayers made rigid through intermolecular dipole-dipole interactions. Because of molecular symmetry and the resultant reduction in types of defects, these assemblies are simpler than the prototypical and well-studied *n*-alkanethiols on Au{111}, which have multitude of distinguishable domains and defects. Within this new family of molecules, *ortho* carboranedithiols display two different binding modes – doubly and singly bound – after adsorption. We investigated surfaces have been studied and explored with scanning tunneling microscopy and infrared (IR) spectroscopy. Plane-wave density functional theory code is employed to elucidate the energetics of different binding sites on stoichiometric gold; binding energies of the local minima of both binding modalities are obtained. Experimental evidence supports majority control of the singly (dual) bound moieties with acid or base, shown on the local and ensemble scales, which is further supported by ground-state calculations and binding energies. Visualization of charge distributions of the surface and cage are provided as well as Natural Bond Order orbitals analysis of the combined system. This allows for a synergy of experiments and theory, through analysis of binding in non-periodic and periodic conditions. While finding that a radical and di-radical bind most strongly to the surface, it is an interesting question regarding mechanistic details that allow for these surface bound moiety.

2015 Western Regional Meeting 11

Synthesis and characterization of PtSn bimetallic nanoparticles: Comparison between two synthesis strategies

Ricardo Morales, rmorales@laverne.edu. Department of Chemistry, University of La Verne, La Verne, California, United States

In this report, we explore the effect of varying the metal-to-metal atomic ratio on the physical properties of SiO₂-supported PtSn bimetallic nanoparticles. This type of bimetallic system has important applications in a variety of heterogeneous catalytic processes, including oxidation, reduction, selective hydrogenation of double bonds, among others. Many previous reports have dealt with the synthesis of PtSn alloy and Pt@Sn core-shell nanostructures, and the study of them in several types of reactions. However, a few of them have studied how the size of the nanoparticles is affected by the metal ratio of Pt and Sn and what type of interaction can exist between the two metals depending on the way the bimetallic is formed (alloy or core-shell structure). This is the objective of this report: study the size dependence on the metallic ratio of Pt and Sn and study the type of interaction that can exist between these two metals if a Pt-Sn alloy or a Pt@Sn core-shell structure is formed.

2015 Western Regional Meeting 12

The culture and chemistry of chocolate

Jacqueline A. Trischman, *trischma@csusm.edu*. Chemistry & Biochemistry, California State Univ San Marcos, San Diego, California, United States

In a society that likes to take everything to extremes, chocolate has recently been declared a health food. Find out why as this presentation frames the debate. Details provided will include the nutritional values of various types of chocolates, the importance of fats in the growth of the chocolate plant and in the processed chocolate that we eat, how chocolate has been prepared across the centuries, and why some processing methods are healthier than others. A brief history of the cultivation and consumption of chocolate, first as a beverage then as a bar, is followed by some interesting chemical aspects of both cultivation and processing. The chemistry of chocolate can be used to engage a class in discussions of topics like functional groups, polarity, acidity, and saponification or simply to put your knowledge of chemistry to good use as a chocolate consumer. And, naturally, samples will be provided.

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Efficacy of highly antioxidative aqueous extract of olive leave as cargo in nano-vesicular emulsion system

Zee Haque¹, *zh5@msstate.edu*, **Ahmad C. Saddam**², **Xue Zhang**². (1) Food Science, Nutrition and Health Promotion, Mississippi State University, Mississippi State, Mississippi, United States (2) Department of Food Science, Nutrition and Health Promotion, Department of Food Science, Nutrition and Health Promotion. Mississippi State University, Mississippi State, MS 39762., Mississippi State, Mississippi, United States

Olive (*Olea europaea*) leaves reportedly have medicinal properties. This study investigated the aqueous extraction of hydrophilic antioxidative components from the leaves for use as cargo in nano-vesicular emulsion systems (NVES). Dried, crushed leaves were extracted with deionized water (1:5 ratio w/v) containing 0.1% (v/v) of hydrophilic surfactant, polysorbate 20 at pH 7.0 (22°C) to yield an extract (OLE) with 5% and 0.33 % (w/w leaves), respectively, of total phenolic compounds and protein (by Bradford). The primary constituent (40% of total proteins) of the soluble protein extract, as determined by SDS-PAGE, was a small molecular weight (~1 kDa). Nano-vesicular emulsion system was fabrication and stabilized with and without the OLE by ultra-high pressure homogenization (UHPH). Stable NVES, with mean diameter (d_{vs}) of 212 nm, were generated at 210 MPa (single pass) when dispersed-phase fraction was 0.05 and the interface was stabilized using a ternary system consisting of Edam whey protein concentrate (WPC)(2.0% w/v) and a combination of two surfactants; non-ionic Triton X-100 (10 % w/w WPC) and zwitterionic sulfobetaine 3-10-SB3-10 (n-decyl-N,N-dimethyl-3-ammonio-1-propanesulfonate) (7.5 % w/w WPC). Different WPC to OLE ratios 1:10 were combined prior to UHPH by sonication. This did not change the periodic structure of the proteins in WPC, as reflected circular dichroism, and resulted on UHPH in similar globular size distribution (d_{vs} =188 nm) though the zeta potential decreased from -46 to -35.8 indicating increased tendency for instability. The free radical quenching ability of the OLE and loaded NVES against peroxy and alkoxyl radicals, pre-generated by pyrolysis of 2,2'-Azobis (2-methylpropionamidine) dihydrochloride (ABAP), and cationic radicals of 2,2'-azino-bis (3-ethylbenzthiazoline-6-sulfonic acid) of diammonium salt (ABTS•+) was dramatically high in terms of activity and persistence and was higher than Trolox, the standard antioxidant.

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Investigation of antioxidant behavior of catechins from green tea extracts

Yue Zhou², yuezhou@cpp.edu, **Yan Liu**¹. (1) Department of Chemistry, Cal Poly Pomona, Pomona, California, United States (2) Department of Chemistry and Biochemistry, California State Polytechnic University Pomona, Pomona, California, United States

Green tea, a popular beverage with different varieties and flavors, is loaded with antioxidants and nutrients. It is also considered as a medicinal alternative to fight against diseases. Recently, a group of polyphenols called catechins that can eliminate free radicals inside organisms were often reported in many laboratory studies as key ingredients contributing to green tea's antioxidation benefits. To date, high performance liquid chromatography (HPLC) are employed to investigate effects of temperature and solvent on extracting green tea leaves. However, the factor from flavor supplement has not been thoroughly examined. Therefore, our project is to focus on determining the optimal extracting condition for catechins from green tea with different flavors and investigating brewing parameter affect antioxidation functionality of catechins in green tea. Green tea extracts under different brewing conditions were analyzed by a reversed-phase HPLC method using a C18 column and a mixture of methanol/water (20:80) as mobile phase with detection wavelength of 280nm. Three major catechins as Epigallocatechin (EGC), Epigallocatechin gallate(EGCG) and Epicatechin (EC) were analyzed in 15 min. The Fenton reaction assay was applied to qualify the effect from different brewing methods on antioxidant power of catechins and salicylic acid was color-developing agent which was cost-effective and nontoxic. The maximum absorb wavelength of Fenton reagent was 525nm. Preliminary data showed that the introduction of NaCl and cane sugar to green tea drinks has obvious effect on the extraction of catechins. The results from the Fenton reaction assay will be presented as well. This project is supported by California State Polytechnic University Pomona and the Goldstein Student Research Fellowship at California State Polytechnic University Pomona.

2015 Western Regional Meeting 15

Folding, unfolding, and misfolding of the RNA pseudoknot structural motif via massively parallel molecular dynamics

Khai Nguyen, nguyenkhai101@gmail.com. Independent, Anaheim, California, United States

The RNA pseudoknot is a three-dimensional structural motif that composes the catalytic core of numerous ribozymes, and can also stimulate ribosomal frameshifting. A complex topology and non-canonical hairpin-loop composition make pseudoknots an ideal structural motif with which to study the RNA folding process. Here we report our analysis of over 8,000 independent all-atom molecular dynamics simulations of the ribosomal frame-shifting Luteoviral RNA Pseudoknot. Using the Folding@Home distributed computing network and a novel Pathway Enumeration sampling method, a cumulative sampling time of over 115 μ s was achieved. K-means clustering identified 27 conformational microstates, which reached equilibrium after \sim 6 ns of ensemble sampling. The kinetics between these microstates was observed to span four orders of magnitude, with fast motions on the nanosecond timescale and slower motions on the tens-of-microseconds timescale. Multiple folding metrics were used to identify 11 macrostates participating in the folding process, including numerous previously undescribed misfolded and intermediate states, thus providing a detailed picture of pseudoknot self-assembly.

2015 Western Regional Meeting 16

Peroxyl radical formation chemistry of tobacco-specific nitrosamines

Brittany Daws, *brittanydaws@gmail.com*. Department of Chemistry and Biochemistry, California State University- Long Beach, Long Beach, California, United States

The cancer-causing action of the alkaloid-derived nitrosamines ($R_1R_2CH_2NNO$) found in unburned tobacco, tobacco smoke, and smokeless tobacco products has been investigated for many years. In the human body cytochrome P450 activation of these nitrosamine species initially occurs by catalytic reaction of this enzyme to form an α -nitrosamine radical ($R_1R_2C\cdot HN-NO$). This nitrosamine radical either combines with a hydroxyl radical ($\cdot OH$) within the catalytic site of the enzyme to form the DNA-alkylating α -hydroxynitrosamine ($R_1R_2C(OH)HN-NO$), or undergoes loss of nitric oxide. However, chemical activation of the nitrosamine can occur without P450 being involved. This alternative pathway also requires the initial formation of the α -carbon radical, by reaction of a reactive oxygen species such as the hydroxyl radical, and via a subsequent reaction with oxygen to form the nitrosamine peroxy radicals ($R_1R_2C(O_2)\cdot HN-NO$). To date, the formation of the carbon-centered α -nitrosamine radical has been well characterized. However, there has been very little study of the peroxy radical formation chemistry, particularly for the tobacco-specific nitrosamines. The measurement of these kinetic parameters for lower molecular weight nitrosamines will provide mechanistic insights into the importance of the alternative peroxy radical formation pathway for nitrosamine carcinogenesis relative to the P450 pathway.

2015 Western Regional Meeting 17

Synthesis, guest binding, and metal coordination of functionalized self-folding deep cavitands

Magi Mettry¹, *mmett001@ucr.edu*, Richard J. Hooley². (1) Chemistry, University of California Riverside, Winnetka, California, United States (2) University of California, Riverside, Riverside, California, United States

Enzymes are some of the most efficient and sophisticated catalysts known. While size and complexity give enzymes their unsurpassable catalytic activity, these properties also make enzymes impractical to synthesize. As an alternative, water-soluble synthetic receptors with catalytic functions are an attractive target. Chemists have studied functionalized cyclodextrins, cyclophanes, and crown ethers due to their abilities to bind guests in a cavity and hold the guest in place by weak forces.[1] These macrocycles are limited to a narrow field of shapes and functional groups. Many binding sites are too small to be useful, and the selection of compatible substrates is limited. Rather than designing a highly specific receptor that is only compatible with a small group of substrates, we propose a broad-scope template of water-soluble synthetic receptors for which the size and shape can be altered to meet the requirements of a particular reaction.[2]

Cavitands have the potential to provide an environment similar to the active site of an enzyme. They have been successfully used as synthetic receptors that are able to bind a variety of guests in water due to the hydrophobic nature of the cavity that is formed upon folding. In order to function as a host, the cavity must fold.

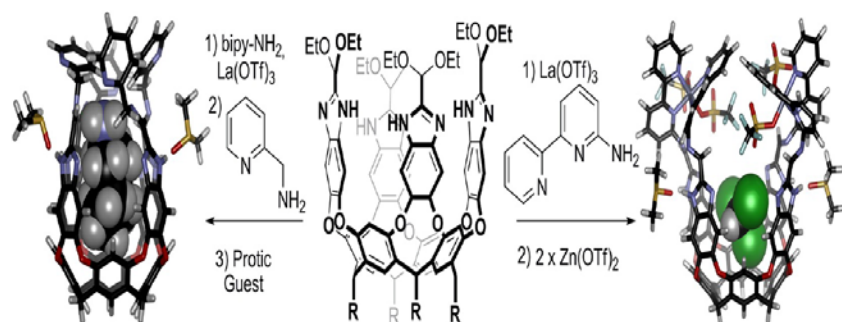
We show a new cavitand scaffold with simple method for the introduction of donor functionality to the upper rim of flexible deep cavitands which act as better hosts and analyzed the effect on self-folding, metal coordination and guest binding. The upper rim imine species provide a handle for controlled non-covalent binding of suitably sized guest species via both self-complementary

hydrogen bonding and space-filling interactions. Metal-mediated self-folding can be applied if a sufficiently strong coordinator is added to the upper rim coordinates with two zinc (II) ions above the cavity for future oxidation.[3]

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Fluorescent cytidine analogues for the study of nucleic acids

Dillon D. Burns, dillon-b@hotmail.com, Raymond Lee, Byron W. Purse. Department of Chemistry and Biochemistry, San Diego State University, San Diego, California, United States

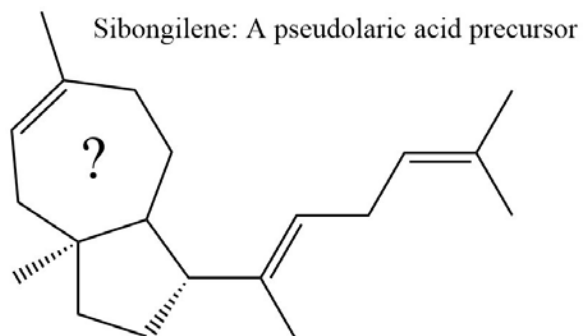
Fluorescent nucleotides have shown to be useful molecular probes as well as fluorescent labels and play a critical role in the study of biophysical processes involving nucleic acids. Recent work by our group and others has shown that the tricyclic cytidine family of compounds can closely mimic cytidine triphosphates when used as substrates for DNA and RNA polymerases and maintain bright fluorescence in duplex DNA, a context where most fluorescent nucleobase analogues are quenched by neighboring bases. This project examines the development of new fluorescent cytidine analogues with improved photophysical properties, while seeking an understanding of the structure-photophysics relationships, in the context of oligonucleotides. We hypothesize that the results will inform the rational design of the next generation of fluorescent nucleobase analogues. Using these modified oligonucleotides, we are conducting fluorescence studies to assess how the new fluorescent cytidine analogues behave in both single stranded and double stranded DNA. For RNA studies, we are testing the fluorescence of the modified oligonucleotides in an RNA hairpin and the modulation of those fluorescent properties by peptide binding to the RNA. The data will be used to determine the best fluorescent cytidine analogues using criteria of minimally perturbing the natural structure of RNA or DNA, offering fluorescence properties useful for labeling, or for probing the conformation of RNA and the binding of small molecules (e.g. prospective drug leads).

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Assigning the structure of sibongilene: A pseudolaric acid precursor

Teresa Palazzo², tapalazzo@ucdavis.edu, **Sibongile Mafu**¹, **Bronwyn Harrod**², **Dean J. Tantillo**², **Philipp Zerbe**¹. (1) Plant Biology, University of California, Davis, Davis, California, United States (2) Chemistry, University of California, Davis, Davis, California, United States

Pseudolaric acid (a naturally occurring diterpene isolated from *Pseudolarix amabilis*) has shown efficacy as a chemotherapeutic through its ability to destabilize microtubule formation and its ability to circumvent multi-drug resistance. An intermediate along the biosynthetic pathway to Pseudolaric Acid (Sibongilene) has been isolated for the first time. The structure of this isolate has been assigned using experimental and quantum chemical computational methods.



2015 Western Regional Meeting 20

Nucleophile, radical trap, or both? The role of alkenes in the intramolecular reactions of oxime and oxime ether radical cations

Nicholas Armada², narmada@csu.fullerton.edu, **Peter De Lijser**¹. (1) Chemistry Biochemistry, California State University Fullerton, Fullerton, California, United States (2) Chemistry and Biochemistry, California State University Fullerton, Chino Hills, California, United States

Oxidative processes often lead to the formation of reactive intermediates such as radicals and radical ions. Oxidation of oximes and oxime ethers yields iminoxyl radicals and oxime ether radical cations, which when formed in cells may cause damage to tissues and DNA. The reactivity of these intermediates is largely unexplored and to learn about the fundamental reactivity of iminoxyl radicals and oxime ether radical cations, we have begun an investigation on intramolecular reactions of oximes and oxime ethers using built-in alkenes as a potential nucleophile or radical trap. Previously, built-in alkynes and aromatic rings were explored as radical traps or nucleophiles. Alkyne compounds were found to react as radical traps because they only cyclized with the oximes, which is indicative of an iminoxyl radical intermediate. Compounds with built-in aromatic rings were found to react exclusively with the oxime ethers, which is indicative of a radical ion intermediate with the aromatic ring acting as the nucleophile. This project explores the reactivity of alkene functional groups under similar oxidative conditions. We hypothesize that the alkene may act as both a nucleophile and as a radical trap to form a cyclized product. Photolysis of the substrate in the presence of a sensitizer leads to the formation of the intermediate that can cyclize. Preliminary results suggest that cyclization occurs with both 2-vinylbenzaloxime and 2-vinylbenzaloxime methyl ether. NMR analysis of both reaction mixtures shows the presence of new products. These results are similar to the

reactions of the molecules with built-in aromatics and alkynes, suggesting a potential dual-reactivity with the built-in alkenes.

2015 Western Regional Meeting 21

***In situ* formation and reactions of benzylic diazo compounds**

Richard Squitieri¹, rasquitieri@ucdavis.edu, Kellan N. Lamb¹, Galen Shearn-Nance¹, Cristian Soldi¹, Jason Hein³, Jared T. Shaw². (1) Chemistry, UC Davis, Davis, California, United States (2) Dept Chemistry, UC Davis, Davis, California, United States (3) School of Natural Sciences, University of California, Merced, Merced, California, United States

Diazo compounds are well-known precursors for C–H insertion reactions and have been applied as versatile building blocks in C–C and C-heteroatom bond forming reactions. We recently developed the first examples of asymmetric intramolecular C–H insertion reactions of diaryl diazo compounds. The diazo compounds can be formed *in situ* through the MnO₂ oxidation of various hydrazones. This method was found to work in high yields (68-99 %) for a wide variety of substrates, providing high diastereoselectivity, enantioselectivity, and functional group tolerance. Additionally, it is known that diaryl diazo compounds can be successfully trapped by carboxylic acids to form esters. Using our methodology for diazo compound formation, we were able to convert a broad scope of acids into their corresponding esters through a one-pot, two transformation method (52-97 %). Utilizing ReactIR we were able to demonstrate that there is no buildup of the potentially explosive diazo compound throughout the progress of the reaction.

2015 Western Regional Meeting 22

A modular approach to crowded benzoquinolines

David J. Dibble¹, djoshdibble@gmail.com, Amir Mazaheripour¹, Dylan E. Laidlaw¹, Robert Lopez¹, Mehran Umerani¹, Young Park¹, Alon A. Gorodetsky^{1,2}. (1) Department of Chemical Engineering and Material Science, University of California, Irvine, Santa Ana, California, United States (2) Department of Chemistry, University of California, Irvine, Irvine, California, United States

Quinolines and their derivatives have received much attention due to their importance as therapeutic compounds in medicinal chemistry, ligands in inorganic chemistry, and small molecular building blocks for organic electronic materials. We have demonstrated the application of the aza-Diels–Alder (Povarov) reaction for the preparation of a variety of crowded aromatic benzoquinoline derivatives with high regioselectivity and tunable electronic properties. These molecules have been characterized *via* spectroscopic, crystallographic, and electrochemical techniques, affording insight into their physical properties. Our findings hold broad implications for the synthesis of a diverse library of oligobenzoquinoline- and polybenzoquinoline-type materials for applications in nanoscale and organic electronics.

2015 Western Regional Meeting 23

Observations during prolonged sample exposure with 5N sodium hydroxide on the stability of memantine HCl internal standard in samples

*Sangita Ghosh, Cecilia Weng, **Alicia Ng**, ang@adamaspharma.com. Adamas Pharmaceuticals, Emeryville, California, United States*

Introduction: Sample preparation is often needed prior to chromatographic analysis when samples are not suitable for direct injection. The sample preparation used in this study is a liquid/liquid extraction requiring the addition of a highly basic solution, 5N NaOH, to the aqueous sample followed by an organic solvent extraction of the analyte.

Memantine HCl is used as an internal standard (ISTD) to account for any potential loss of the analyte during sample preparation. A constant amount of memantine solution is added to the samples, blank and standards followed by sample preparation. The organic solvent layer in the sample containing the extracted analyte and memantine ISTD, is injected into a chromatography column and analyzed. The peak area ratio of the analyte to memantine is used for concentration calculation.

Particular assays, such as dissolution, generates numerous samples. Analysts tend to prepare samples in a step wise fashion where each solution is added to all samples. This would increase the amount of time the sample and internal standard solution is exposed to the highly basic solution which could potentially degrade the analyte or internal standard in the samples.

Method: Memantine HCl at a fixed concentration was added to 36 samples. 5N NaOH solution was added to the standard and sample solutions in a 1:3 ratio. The samples are split into two sets, the first set was mixed promptly (within 45 minutes) with organic solvent for extraction and the second set sat for 3 hours before the addition of organic solvent for extraction. The organic solvent layer, containing the extracted analyte and memantine, is analyzed in the chromatographic system.

Results: A reduced peak area response in memantine was observed in samples mixed with internal standards and 5N NaOH that sat for 3 hours prior to organic solvent addition for extraction this resulted in high peak area ratio of the analyte/ISTD in the sample. However, once solvent was added, the extracted analyte and internal standard in the solution remained stable, no change in peak area response was observed.

Conclusion: Memantine HCl internal standard is not stable when combined with 5N NaOH for longer than 1 hour prior to organic solvent extraction procedure. Therefore, the extraction procedure should be performed immediately or approximately less than an hour as after 5N NaOH is added to the sample and reference standard solution containing the memantine internal standard to prevent alkali degradation.

2015 Western Regional Meeting 24

Synthesis of homopropargyl alcohols via three-component coupling of allenyl carbenoids, acyclic organozirconium species, and aldehydes/ketones

Jozef Stec^{1,2}, jstec@ketchum.edu, Alan R. Henderson¹, Richard J. Whitby¹. (1) School of Chemistry, University of Southampton, Southampton, United Kingdom (2) Department of Pharmaceutical Sciences, Marshall B. Ketchum University, Fullerton, California, United States

Homopropargyl alcohols represent versatile intermediates in the synthesis of various molecules of natural and synthetic origin, some of them being relevant to biology and medicine. Therefore,

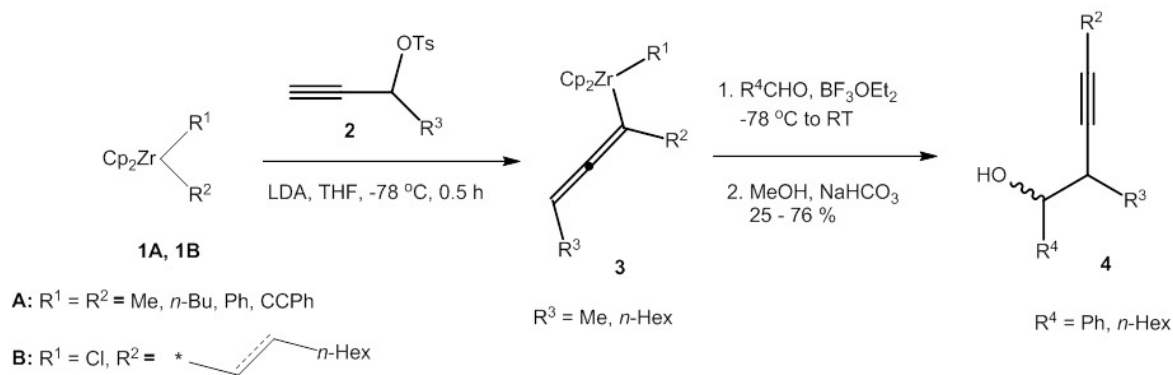
rapid access to these building blocks is of interest to a broad community of organic synthetic and medicinal chemists.

Herein we describe the synthesis of homopropargyl alcohols by using stoichiometric organozirconium chemistry.¹ Insertion of allenyl carbenoids (derived from the corresponding propargyl tosylates **2** by metallation with LDA or LTMP) into various bis-alkyl/aryl/alkynyl biscyclopentadienyl zirconium complexes **1A** and alkyl/alkenyl chlorozirconocenes **1B**, followed by 1,2-metallate rearrangement affords the corresponding allenic zirconium intermediate **3** (Scheme 1). Lewis acid promoted addition of aldehydes and ketones to the resulting allenic zirconium species gives, after protonolysis, a series of homopropargyl alcohols **4** in moderate to good yields. The secondary homopropargyl alcohols were obtained as a mixture of *anti:syn* isomers with ratios ranging from 9:1 to 2:1 and were partially separable by silica column chromatography. Asymmetric course of the reaction was investigated by insertion of the enantiomerically pure carbenoid [derived from (*S*)-but-3-yn-2-yl 4-toluenesulfonate) into **1B**. The corresponding chiral alcohols were obtained in comparable yields and moderate (62 and 71%) enantiomeric excesses.

Overall we reported the first precedent for the synthesis of homopropargyl alcohols *via* allenyl carbenoid insertion into acyclic zirconium systems and subsequent trapping of the allenyl-zirconium species with aldehydes and ketones. This protocol also showed promise for access to chiral homopropargylic alcohols; however, further improvements in yields and enantiomeric excesses are needed.

References

¹ Stec, J.; Henderson, A.; Whitby, R. J. Synthesis of Homopropargyl Alcohols via Insertion of Allenyl Carbenoids into Acyclic Organozirconium Bonds. *Tet. Lett.* **2012**, 53, 1112-1115.



Scheme 1. Zirconium-mediated synthesis of homopropargyl alcohols

2015 Western Regional Meeting 25

Progressive new methods towards the total synthesis of azaspirene and its analogs: Promising new cancer treatments

Timothy Montgomery, t_montgom@yahoo.com, **Michael J. Kelly**, **Mikael B. Bergdahl**. San Diego State University, San Diego, California, United States

Current chemotherapy treatments are often a difficult process for patients because both healthy and cancerous cells are killed simultaneously. Azaspirene, an effective angiogenesis inhibitor

recently isolated from the soil fungus *Neosartorya* sp., may be used as a milder form of chemotherapy. Instead of killing cells directly, azaspiroene and other angiogenesis inhibitors starve the tumors by blocking the unique chemical signal the tumors use to promote blood vessel growth. Azaspiroene is shown to specifically target tumor blood vessels without inhibiting normal blood vessel growth and wound repair. Azaspiroene belongs to the Pseurotin family of compounds whose members share a similar spirocycle backbone and show promise as anti-fungal and anti-bacterial agents. The supply of Azaspiroene that has been harvested from natural sources is too small to sustain further research; therefore, it is critical that an economical and efficient synthesis be established.

Our approach starts with cheap and readily available L-phenyl alanine and proceeds to azaspiroene in concise stereo-controlled reactions. The route utilizes some unique methodology including a novel copper catalyzed one-pot conjugate silyl addition to aldol product developed in our lab and the cyclization reaction used to complete the bicyclic core of the molecule. This route is both efficient and robust with high yielding reactions that are capable of being performed on the multi-gram scale.

We expect to have the total synthesis completed in the near future, and will then proceed to biological testing of azaspiroene and its derivatives. With ample amounts of compound we can begin to better characterize the biological activity of azaspiroene and its analogs through SAR, active site binding and crystal structure experiments.

Funding for this project has been provided by NIH, Pfizer and SDSU Research Foundation.

2015 Western Regional Meeting 26

Synthesis and characterization of hematite nanoparticles for mercury capture

Ji-Eun Jung, *jejung@stanford.edu*, Simona Liguori, Jennifer Wilcox. Stanford University, Stanford, California, United States

Hematite(α -Fe₂O₃) is an important mineral component of fly ash and possible noncarbon-based sorbent for mercury(Hg) capture. In order to understand factors affecting Hg adsorption of α -Fe₂O₃, nano-sized α -Fe₂O₃ particles were synthesized and characterized before and after exposure to Hg. Three α -Fe₂O₃ nanoparticles, M1, M2, and M3 have been synthesized using different precursors, i.e., Fe(NO₃)₃, Fe(ClO₄)₃, and FeCl₃, respectively. These different compositions of precursors and aging methods gave different size and morphologies of α -Fe₂O₃ which may lead to different extents of Hg adsorption.

Three α -Fe₂O₃ samples were characterized by various characterization techniques, such as x-ray diffraction (XRD), scanning electron microscope (SEM), transmission electron microscope (TEM) and x-ray photoelectron spectrometry (XPS). XRD confirmed all synthesized nanoparticles are pure α -Fe₂O₃ without other phases of iron oxides. The particle shape was varied from cubic (M1), cubic with irregular step surfaces (M2) and anhydrous (M3), with varying sizes ranging from 30 nm to 500 nm depending on precursors. The Brunauer-Emmett-Teller (BET) surface area was measured on the M2 particle, which had numerous stepped surfaces, and showed the highest surface area of 70 m²/g compared to other two particles.

Packed-bed reactor experiments were conducted to expose Hg to the nanoparticles. To investigate their sorption ability as well as adsorption behavior of the nanoparticles during the Hg exposure test, gaseous Hg was saturated onto the samples until breakthrough. The Hg exposed nanoparticles were characterized using XPS to see adsorbed Hg4f peaks onto the

particle surfaces. Results showed that a high nanoparticle surface area plays an important role in Hg adsorption rather than the size itself. Also, having a defective structure, such as a stepped surface, assists in adsorbing Hg by providing active sites for adsorption. Adsorbed Hg onto the α -Fe₂O₃ surface is in the form of oxidized Hg, such as HgCl₂.

2015 Western Regional Meeting 27

3-D interconnected mesoporous tantalum nitride as a novel water splitting photocatalyst

Hyeyeon Kang, hkang@chem.ucla.edu, Sarah H. Tolbert. UCLA, Los Angeles, California, United States

The design of photocatalysts using semiconductors has been intensively studied to achieve an efficient solar-to-hydrogen conversion. Ideal photocatalysts should have a bandgap that corresponds to the visible region of the solar spectrum because 50 % of the solar output is emitted in this range. Nanostructuring photocatalysts is a good approach to improve the efficiency and rate of H₂ production through increasing the surface area, which creates significantly more active sites for the reaction to occur. Mesoporous nanoscale architectures are ideal motifs to achieve these high surface area materials. In this study, we have synthesized mesoporous Ta₃N₅ by converting sol-gel based Ta₂O₅ thin films to Ta₃N₅ via controlled ammonolysis. The bandgap of prepared Ta₃N₅ is estimated to be 2.1 eV from the absorption edge (~600 nm). The phase conversion from orthorhombic Ta₂O₅ to orthorhombic Ta₃N₅ is successfully characterized by GIWAXS shown Fig 1 (a). Ellipsometric porosimetry has been utilized to confirm that these thin films are comprised of an interconnected 3-D pore network. The pore sizes of Ta₂O₅ and Ta₃N₅ films are 14 nm and 17 nm in diameter, respectively. These results are calculated from the Kelvin equation and are in excellent agreement with the pore size estimated from the SEM images (Fig 1 (b) and (c)). Lastly, the photoelectrochemical water splitting has been carried out using a 300 W Xe lamp in 1M KOH solution. The mesoporous Ta₃N₅ catalyst shows efficient photocurrent response that is attributed to the 3-D interconnected mesoporosity.

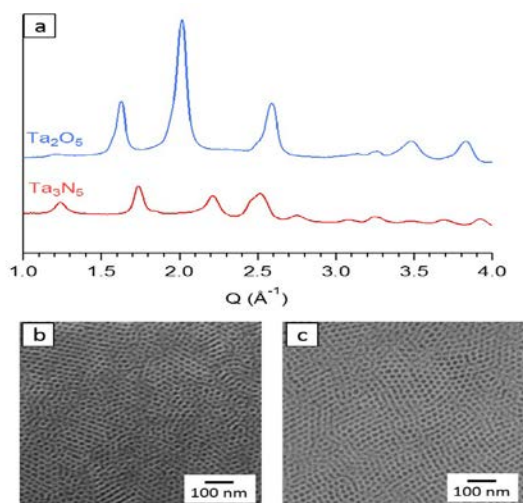


Figure 1. (a) Grazing-incidence wide-angle x-ray scattering (GIWAX) patterns of mesoporous Ta₂O₅ (blue) and Ta₃N₅ (red) film. Top view SEM images of mesoporous Ta₂O₅ (b) and Ta₃N₅ film (c).

2015 Western Regional Meeting 28

Metathesis: The versatile problem solver

John H. Phillips, *jhphillips@chemalum.berkeley.edu. Catalyst R&D, Materia Inc., Pasadena, California, United States*

Metathesis polymerization is a powerful tool for the development of new materials and polymers. Examples where metathesis polymerization has been exploited to synthesize unique materials and molecules will be discussed. This poster will focus on the utilization of metathesis for innovation within the chemical industry.

2015 Western Regional Meeting 29

Monitoring atmospheric ammonia through passive diffusion collection on California State Polytechnic University Pomona campus

Leslie Aranda¹, *leslie_aranda6@yahoo.com, Michael Torres*¹, *Yan Liu*². (1) *Cal Poly Pomona, Azusa, California, United States* (2) *Department of Chemistry, Cal Poly Pomona, Pomona, California, United States*

Ammonia is the only significant basic gas in the atmosphere and neutralizes ambient acidic species to form ammonium salts. Ammonia can be released to the atmosphere through livestock waste, fertilizer, industrial activities and natural processes in the soil. Among them, the agriculture related livestock and fertilizer are the primary source. Cal Poly Pomona is big on agriculture and there are many farmlands and livestock on campus. There is a need to monitor the sources and transport of atmospheric ammonia on campus. Air samples were collected through passive diffusion at three different locations from November 2014 to June 2015. The collected samples were extracted by DI water and analyzed utilizing the Berthelot reaction. Under basic condition ammonium ion reacts with phenol and sodium hypochlorite to form indophenol, with the assistance of cyanoferrate. Indophenol is intensely colored in blue, and its absorbance is measured by UV-VIS spectroscopy at 635nm.

It was observed that the ammonia concentration was the highest in the location by the livestock waste; and the ammonia concentration at higher elevation was slightly lower than the site by the livestock. It was also observed that the month of February had the highest concentration of ammonia for all three locations. Atmospheric ammonia at all three locations will be continuously monitored throughout the year and more results will be reported later. This project is supported by California State Polytechnic University, Pomona.

2015 Western Regional Meeting 30

Preparation of γ -aminoalcohols with pendant quinolyl moiety by reduction of ketoimines with sodium borohydride

Kevin J. Goosherst¹, *Kevin.goosherst@pepperdine.edu, David B. Green*², *Joseph M. Fritsch*¹. (1) *Chemistry, Pepperdine University, Newbury Park, California, United States* (2) *Natural Science Division, Pepperdine University, Malibu, California, United States*

A series of γ -aminoalcohols containing a pendant quinolyl moiety and electron-donating and electron-withdrawing substituents were synthesized to be used as tridentate dianionic ligands in metal complexes. Ketoimines, which have been used as tridentate monoanionic ligands, were synthesized by the Schiff base condensation of 8-aminoquinoline and 1,3-diketones with varying electron-donating or electron-withdrawing groups. The γ -aminoalcohols were prepared from the reduction of ketoimines with sodium borohydride and glacial acetic acid in THF at 0 °C. The reduction generated two stereocenters and two pairs of diastereomers which were *syn* and *anti*. The γ -aminoalcohols were isolated with column chromatography and their structures were confirmed with ^1H , ^{13}C and ^{19}F NMR and mass spectrometry.

2015 Western Regional Meeting 31

Copolymerization of L-lactide and ϵ -caprolactone by bis-ligated magnesium complexes binary catalyst systems

Reile M. Slattery, reile.slattery@pepperdine.edu, Joseph M. Fritsch. Chemistry, Pepperdine University, Newbury Park, California, United States

Bis-ligated magnesium complexes, in binary catalyst systems with 4-fluorophenol, were demonstrated to initiate the ring opening homopolymerization of L-lactide (L-LA) and ϵ -caprolactone (ϵ CL) to poly-lactic acid (PLA) and poly-caprolactone (PCL), respectively. Further, the binary catalyst systems were used to initiate the ring opening copolymerization of L-LA and ϵ CL, and the isolated polymeric materials were characterized with NMR spectroscopy and gel permeation chromatography. First, the simultaneous feeding of both monomers ($X_{\text{L-LA}} = 0.5$) resulted in the synthesis of homopolymer PLA. Polymerization experiments with sequential addition of L-LA and ϵ CL yielded surprising results. The ring opening polymerization of ϵ CL yielded PCL which with the addition of L-LA yielded a di-block copolymer of PCL and PLA. The presence of the two homopolymer blocks in the copolymer was identified with ^{13}C NMR where C=O signals corresponding to only caprolyl or lactyl linkages were observed. Reversing the order of monomer addition (L-LA followed by ϵ CL) yielded only PLA with no conversion of ϵ CL into polymer. These results were consistent with a recent report that proposed a lactide-magnesium chelate formation, which blocked ϵ CL coordination to the metal center.

2015 Western Regional Meeting 32

Nanocrystalline magnesium as an anode material for lithium-ion battery applications

Terri C. Lin², lin.tchai@gmail.com, Eric Detsi², John B. Cook³, Sarah H. Tolbert¹. (1) UCLA, Los Angeles, California, United States (2) Chemistry and Biochemistry, University of California-Los Angeles, Los Alamos, California, United States (3) Chemistry and Biochemistry, University of California, Los Angeles, Los Angeles, California, United States

This research describes the synthesis and electrochemical characterization of nanostructured Mg as a carbon-free anode for high capacity Li-ion batteries (LIBs). Nanostructured Mg can both improve kinetics by decreasing the percolation pathway and alleviate volume expansion. Alloy type anodes are attractive substitutes for graphite in LIBs for their high capacities. However, alloy anodes typically undergo a large volume change during cycling, leading to pulverization of the active material and eventual loss of contact with the carbonaceous electrode matrix. Nanostructured Mg emerges as a competitive alloying anode candidate for high electronic

conductivity, high capacity, and relatively small volume change during charge storage. In specific, Li-Mg alloys are favorable because Li-Mg forms solid-solutions from 30 to ~100 at.% Li for the Li-rich β phase. Within this broad region, no phase transformation should occur during Li insertion and extraction, which is unique as most alloy anodes undergo multiple phases during cycling. This lack of phase transformation is extremely favorable because it will decrease strain in the material, allowing the Mg framework to accommodate a continuous volume change. Mg nanoparticles are synthesized via the Rieke reaction and have been characterized by XRD, SEM and TEM. The size have been tuned from 2-10 nm by varying the amount of capping-agent as shown in Fig. 1(a) and (b). In order to understand the electrochemistry of this material better, in particular the Li-rich β phase, we used cyclic voltammetry to quantify reversibility and stability in nanoparticle based electrodes. Our preliminary studies indicate that Mg nanoparticles undergo Li insertion and deinsertion at 0.05V and 0.17V respectively. From our success in the synthesis and the preliminary electrochemistry study, Mg nanoparticles show promising potential as a next generation high capacity LIB anode.

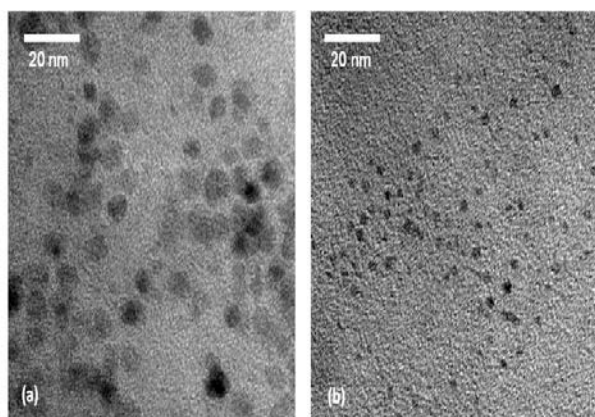


Figure 1. (a) Transmission electron microscope image of 10 nm magnesium nanoparticles (b) 2 nm magnesium nanoparticles

2015 Western Regional Meeting 33

Stress-induced lift-off silicon foil using epoxy

Hyo Sik Chang, hschang@cnu.ac.kr. Graduate school of Energy Science and Technology, Chungnam National University, Daejeon, Korea (the Republic of)

The silicon material accounts for 55% of total cost in the PV value chain. For this reason, we investigate the epoxy-induced lift-off of a (100) silicon wafer. This epoxy-induced spalling process has the advantages of reducing metal contamination and lowers the operating temperatures below 100°C. The low temperature involved in the proposed process reduce the diffusion of metal species inside the silicon bulk, improving the quality of the silicon foil as compared to the high temperature spalling of silicon. After stress-induced lift-off process, small silicon foils have been produced. The thickness of the silicon foil is between 50 μ m and 120 μ m. The surface morphology and thickness of Si foil is depend on the thickness and hardening of polymer. The PL image is used to detect defects of a silicon foil with high spatial resolution and quasi-steady-state photoconductance (QSSPC) is also used for evaluating properties.

2015 Western Regional Meeting 34

The study of spectroscopic and electrochemical properties of substituted anthraquinone in an undergraduate laboratory setting

Marco M. Allard, Jonathan D. Rojas, jroj915@lasierra.edu, Ricardo M. Morales, rmor419@lasierra.edu. Chemistry, La Sierra University, Riverside, California, United States

The overall goal of this study is to identify the spectroscopic properties of a series of substituted anthraquinones by careful examination of absorption, fluorescence and electrochemical parameters. The electrochemical potentials were assessed and correlated with DFT calculations, both in the absence or presence of water. Special attention was paid to assign an exact location within the ring for the free radicals unto the varied substituted anthraquinone moieties. It is expected that the substituents will affect the position of free radical, thus affecting some of the spectroscopic properties of these species. The study also attempted to characterize the electronic structure of the free radical containing species by means of a combination of spectroscopy and computational methods. The various substitutions included electron withdrawing and electron donating groups in order to assess their effects on the stability and electronic structure of both the parent and reduced compounds. Special care was taken to identify the actual role of water upon reduction of these species and the effect on fluorescence lifetimes on both the native and reduced states.

2015 Western Regional Meeting 35

New cellular delivery vehicles: Polymyxin B and guanidinopolymyxin B

Kristina Hamill, khamill@ucsd.edu, Lisa C. McCoy, Yitzhak Tor. Chemistry, University of California San Diego, La Jolla, California, United States

Guanidinium rich molecular transporters have been used to enable the intracellular delivery of a diverse range of biologically relevant cargos that have limited cellular uptake. Here we synthesized and investigated the uptake of biotin-functionalized derivatives of polymyxin B, a known antibiotic, and guanidylated polymyxin B as molecular transporters. At nanomolar concentrations, both carriers were able to deliver large (>300 kDa) cargo into living cells. The uptake of these two novel transporters depends exclusively on cell surface heparan sulfate. Investigation of the uptake mechanism indicated these transporters are internalized through caveolae-mediated pathways and confocal microscopy showed internalization in punctate vesicles that colocalize with the lysosomes. This suggests the possibility of using polymyxin and guanidinopolymyxin for intracellular delivery with potential as a basic research tool and novel drug delivery vehicle.

2015 Western Regional Meeting 36

High performance liquid chromatographic determination of four biological aminothiols after microwave-enhanced derivatization with SBD-F

Morgan B. Blayney¹, morgan.blayney@pepperdine.edu, Susan E. Helm², David B. Green¹. (1) Department of Chemistry, Pepperdine University, Malibu, California, United States (2) Department of Nutritional Sciences, Pepperdine University, Malibu, California, United States

Homocysteine, cysteine, cysteinyl-glycine, and glutathione are significant aminothiols which have been implicated as risk factors in atherosclerosis and other vascular diseases. Rapid determination of these aminothiols is, thus, desirable. Following reduction of the disulfides with tri-*n*-butylphosphine, a widely used method utilizes derivatization with ammonium 7-fluorobenzo-2-oxa-1,3-diazole-4-sulfonate (SBD-F) as a fluorogenic probe prior to reversed-phase HPLC analysis. We report the results of microwave-enhanced synthesis of the fluorescent derivatives at temperatures ranging from 90-110 °C in microcentrifuge tubes. Utilizing microwave heating, we reduced the derivatization time at all temperatures from 1 h to less than 2 min. Standard solutions produced rectilinear calibration curves with correlation coefficients >0.99 for all four aminothiols. We compared the results obtained for the four aminothiols extracted from mouse plasma, kidney, heart, muscle, and urine using traditional heating and microwave heating. No statistical differences were observed for the aminothiols, except glutathione which was consistently lower with microwave heating. We also report the results of recovery experiments and differences in calibration sensitivities between the two methods.

2015 Western Regional Meeting 37

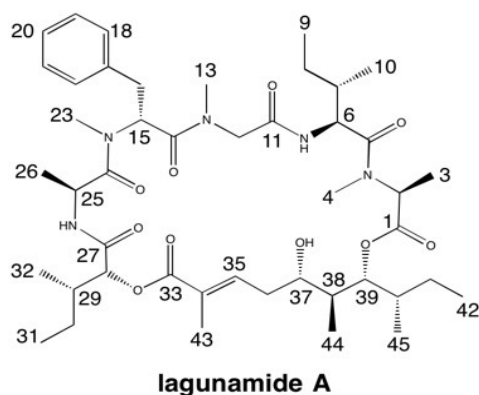
Highly stereoselective synthesis of lagunamide A: Unprecedented potential for anti-malarial and anti-cancer bioactivity

Brent Banasik, *brentbanasik@hotmail.com*, **Lee Wang**, **Arielle S. Kanner**, *kannera@gmail.com*, **Nicole Kohnen**, *kohnenicoles@gmail.com*, **Mikael B. Bergdahl**. *Chemistry and Biochemistry, San Diego State University, San Diego, California, United States*

Lagunamides are complex novel macrocyclic depsipeptides possessing high anti-malarial properties (IC₅₀ 0.19-0.91 mM), cytotoxic properties against P388 murine leukemia cell lines (IC₅₀ 6.4-20.5nM), and ileocecal colon cancer (1.6nM). The focus of this research is to develop an efficient and highly convergent strategy for the total synthesis of lagunamides. Recent experiments suggest the mode of action of the natural product as an intrinsic apoptotic pathway by cleavage of caspase-9, activating a downstream cascade that results in mitochondrial-mediated apoptosis, a popular target for therapeutics. An efficient synthetic pathway will ultimately lead to structural analogs that can be used in quantitative structure-activity relationship (SAR) studies against various cancer cell lines and treatment of malaria. Moreover, lagunamide A shows promise as an extremely powerful therapeutic agent, presenting the need for the total synthesis of the compound.

We present a new and optimized convergent strategy introducing methodologies for coupling unique *N*-methylated unnatural peptide fragments completed via solid phase synthesis to afford an advanced, functionalized pentapeptide fragment, completing the C1-C25 “northern hemisphere” of the molecule. The C27-C45 “southern hemisphere” is synthesized via a highly convergent asymmetric route to establish five of the 10 crucial stereocenters that form Lagunamide A. Specifically; the Vinylogous Mukaiyama Aldol Reaction (VMAR) was employed to establish 4 contiguous stereocenters in high yield and diastereomeric ratio. The synthesis concludes with a macro-cyclization to afford the full cyclic structure.

Advanced intermediates have been synthesized and characterized by NMR spectroscopy, X-ray crystallography, polarimetry, FTIR, HPLC and HR/LC-MS. We will present our tunable total synthesis, which enables points of diversity necessary for accessing a large and diverse molecular library.



2015 Western Regional Meeting 38

Online spectra database for undergraduate organic chemistry laboratories

Jeff Charonnat, jeff.charonnat@csun.edu, Kelly Hazen, Nazeli Paronian. Chemistry and Biochemistry, California State University, Northridge, Northridge, California, United States

An on-line spectra database has been constructed for undergraduate organic chemistry laboratories. Spectra include infrared, ^1H NMR, ^{13}C NMR, and mass spectra of starting materials and products for a number of reactions commonly run in these laboratories. Students in the laboratories access these spectra on-line and include spectral analyses as part of their laboratory reports. By doing so, they gain considerable experience in the interpretation of spectral data.

2015 Western Regional Meeting 39

Monobocylation of diamines in continuous flow

Alex Ku¹, kuafgfg@yahoo.com, Amanda C. Evans². (1) Biochemistry, California State University Fullerton, Laguna hills, California, United States (2) Chemistry & Biochemistry, California State University Fullerton, Fullerton, California, United States

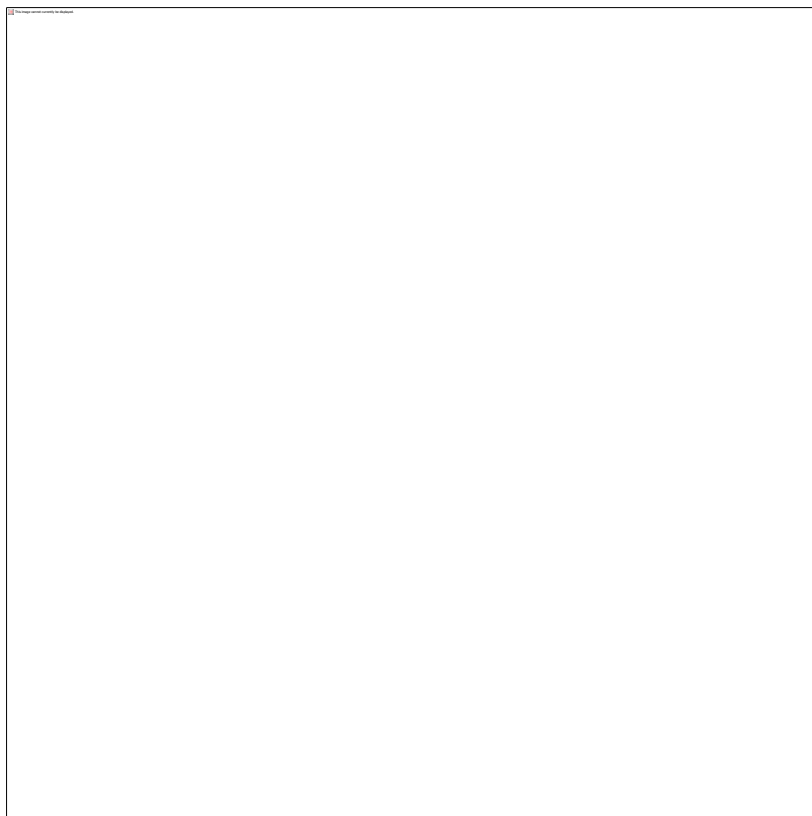
The monobocylation of 1,3-diaminopropane and other diamines have been optimized at reduced temperatures under continuous flow conditions. The optimization process, facilitated by the use of a Labtrix Start microreactor, allowed for the production of the desired carbamate in moderate to high yields at reduced temperatures. Monobocylation has now been optimized to both increase production of single protected amine and decrease production of the bis-protected amine.

2015 Western Regional Meeting 40

Towards continuous flow syntheses of levomilnacipran

Matthew Nguyen^{2,1}, monkeyhoa@gmail.com, Christian Ayoub^{2,1}, Amanda C. Evans¹, Jackson Feng^{1,2}. (1) Chemistry & Biochemistry, California State University Fullerton, Fullerton, California, United States (2) California State University, Fullerton, Santa Ana, California, United States

Cyclopropanes are interesting synthetic targets because they are used as precursors in many pharmaceuticals and are present in several bioactive molecules and insecticides. Levomilnacipran is a cyclopropane-containing selective serotonin and norepinephrine reuptake inhibitor (SNRI) used to treat the symptoms of fibromyalgia syndrome (FMS). This research investigates a continuous flow synthesis of levomilnacipran using chemical and biochemical cyclopropanation strategies.

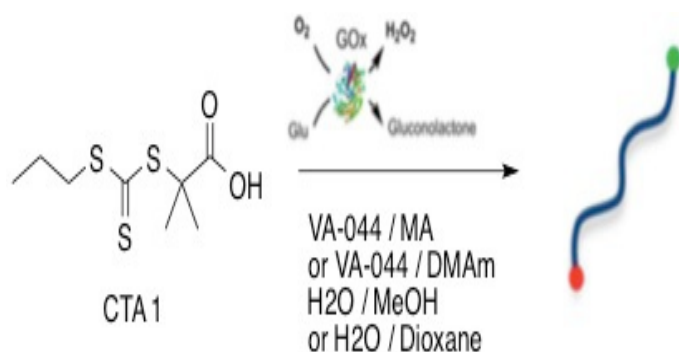


2015 Western Regional Meeting 41

Enzyme degassing for RAFT polymerization in continuous flow

Scott Matsuda², scottmatsuda17@yahoo.com, **Amanda C. Evans**¹. (1) Chemistry & Biochemistry, California State University Fullerton, Fullerton, California, United States (2) Chemistry and Biochemistry, California State University Fullerton, Newport Beach, California, United States

Controlled radical polymerization is an efficient way to synthesize polymers of a specific chain length; however ambient oxygen is an excellent radical scavenger that may interfere with the reaction. Glucose oxidase (GOx) can be used as an oxygen scavenger during reversible addition fragmentation chain transfer (enzyme facilitated RAFT, or “Enz-RAFT”) polymerization, providing sufficient degassing at low concentrations in aqueous and various water/organic solvents. In order to increase the efficiency of Enz-RAFT polymerization, Enz-RAFT has now been deployed under continuous flow conditions using methacrylic acid and *N,N*-dimethylacrylamide as monomer units.



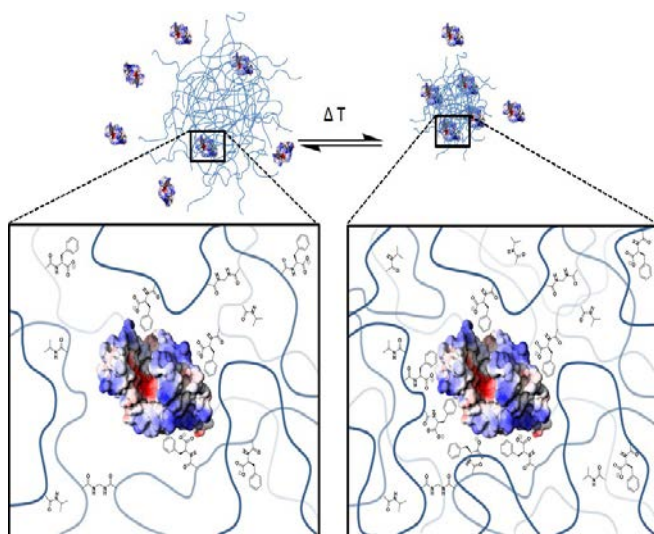
Use of Chain Transfer Agent **1** (CTA **1**) under Enz-RAFT conditions to form monodisperse polymers.

2015 Western Regional Meeting 42

Thermally controlled multivalent interactions between biomimetic polymer NPs and target biomacromolecules

Adam C. Weisman², aweisman@uci.edu, **Kenneth J. Shea**¹, **Keiichi Yoshimatsu**³. (1) Univ of California, Irvine, California, United States (2) Chemistry, University of California Irvine, Corona, California, United States (3) University of California, Irvine, Irvine, California, United States

Incorporating naturally occurring amino acids into synthetic polymer scaffolds is currently under investigation for the development of bio-inspired materials with a wide array of novel structures and useful material properties. Here we evaluate the physiochemical properties of poly-isopropylacrylamide (NIPAM) based nanoparticles (NPs) doped with amino acid derived monomers. The amount of amino acid incorporated, and the side chain hydrophobicity were observed to significantly alter the phase transition properties of the materials. The NIPAM induced phase transition was then utilized to modulate the multivalent interactions between amino acid containing NPs and a model protein. Interestingly, the physiochemical properties of NPs containing either leucine or phenylalanine were very similar, but very different behavior in binding the model protein was observed. These results highlight that NP composition may be tuned to generate materials with stimuli-responsive multivalent interactions towards biomacromolecules.

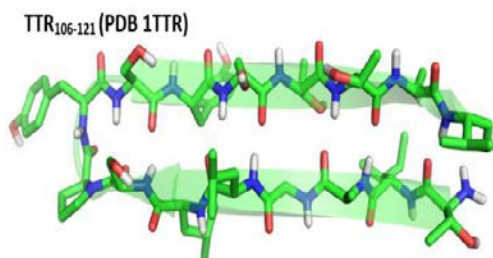


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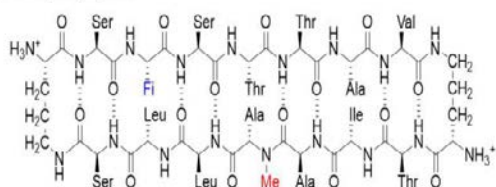
A β -hairpin peptide derived from transthyretin 106-121 that forms square hydrophobic channels

Stan Yoo³, yoostan@gmail.com, Nicholas Truex¹, Adam Kreutzer⁴, James S. Nowick². (1) Chemistry, UC Irvine, Irvine, California, United States (2) University of California, Irvine, California, United States (3) Chemistry, University of California - Irvine, Irvine, California, United States (4) Chemistry, University of California Irvine, Irvine, California, United States

Transthyretin tetramers dissociate into monomers that aggregate to form toxic oligomers and fibrils in several amyloid diseases. Elucidating the structure of these aggregates is critical to understanding these and other amyloid diseases. This presentation describes the X-ray crystallographic structure of a β -hairpin peptide derived from a region of TTR that is important in aggregation, TTR₁₀₆₋₁₂₁. The peptide crystallizes to form square hydrophobic channels that have not previously been observed. The design, structure, and assembly of the TTR-derived peptide will be described and the implications for amyloid diseases will be discussed.



β -hairpin peptide

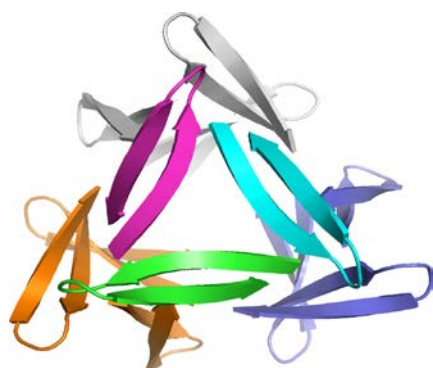


2015 Western Regional Meeting 44

X-ray crystallographic structures of amyloid oligomers: A dodecamer of A β ₁₇₋₃₆ that forms an annular pore

Adam Kreutz², akreutze@uci.edu, Imane L. Hamza², James S. Nowick¹. (1) University of California, Irvine, California, United States (2) Chemistry, University of California Irvine, Irvine, California, United States

Amyloidogenic peptides and proteins form porelike assemblies of oligomers that are thought to be important in neurodegeneration [Quart. Rev. Biophys. **2006**, 39, 167]. The structures of these assemblies are not known at atomic resolution. The absence of high-resolution structures of these assemblies constitutes an important gap in understanding Alzheimer's disease, Parkinson's disease, and other amyloid diseases. Our research group recently elucidated the X-ray crystallographic structure of a dodecamer formed by a β -hairpin that comprises A β ₁₇₋₂₃ and A β ₃₀₋₃₆ [JACS **2014**, 136, 5595]. The dodecamer consists of a tetramer of trimers, each of which consists of three β -hairpins. In the current study we have incorporated A β ₂₄₋₂₉ to create a β -hairpin comprising A β ₁₇₋₃₆. Here we report the X-ray crystallographic structures of the dodecamers formed by twelve of the A β ₁₇₋₃₆ β -hairpins and an annular pore formed by five of the dodecamers.



X-ray crystallographic structure of a dodecamer derived from A β ₁₇₋₃₆ (PDB 4NTR, JACS **2014**, 136, 5595)

2015 Western Regional Meeting 45

How do undergraduate students conceptualize acid-base chemistry? Development, validation, and utilization of a learning progression-based measure

William Romine, romine.william@gmail.com, Amber Todd, Travis Clark. Department of Biological Sciences, Wright State University, Dayton, Ohio, United States

We developed and validated a new instrument, called Measuring Concept progressions in Acid-Base chemistry (MCAB), and used it to better understand the progression of undergraduate students' understandings about acid-base chemistry. Items were developed based on an existing learning progression for acid-base chemistry. We used the Rasch rating scale model for validation and to explore how students at different ability levels conceptualize the topic. We then used latent class analysis (LCA) to place students into concept classes. We found that three

concept classes were sufficient to describe students' various response patterns, and that these concept classes described a progression of understanding related to acid-base chemistry. All items fit well with the Rasch model. The final 33-item instrument measured students along a continuous scale with a reliability of 0.76, and categorized students with a precision of 0.89. All students possessed non-scientific understandings of pH and the pH scale. However, even the most novice students displayed basic scientific understandings about how acid-base indicators work and the Arrhenius model of acids and bases. Rasch and LCA procedures for analysis of learning progression-based assessments make way for simple algorithms chemistry instructors can use to diagnose students' misconceptions.

2015 Western Regional Meeting 46

Formation and stability of silver nanoparticles formed by the reduction of silver ions by humic acid

Renee Leslie, *reneeleslie96@live.com*, **David Pullman**, *Department of Chemistry, San Diego State University, San Diego, California, United States*

This study investigated the formation and stability of silver nanoparticles (AgNPs) formed from the reduction of silver ions by humic acid in the presence of UV light. The interest in AgNPs comes from an increased concentration of silver ions entering the environment and whether or not these ions can be reduced by humic acid to form stable nanoparticles. This study shows that silver nanoparticles can form in a solution of silver nitrate and humic acid in the presence of UV light. The rate of AgNP growth increased linearly as the concentration of humic acid or silver nitrate was increased. AgNP growth was monitored by UV Vis and AgNP size was monitored by dynamic light scattering. This study demonstrates the potential for silver ions to reform nanoparticles which can disrupt sensitive ecosystems.

2015 Western Regional Meeting 47

NMR characterization of ionicity and transport properties for a series of diethylmethylamine based protic ionic liquids

Forrest Thompson, *thompsonftm@gmail.com*, *Department of Chemistry and Biochemistry, Arizona State University, Tempe, Arizona, United States*

Protic ionic liquids (PILs) are the product of a proton transfer between a Brønsted acid and Brønsted base. PILs have sparked great interest due to their wide range of applications such as electrolytes in fuel cells, solvents for biocatalysis, use in protein self-assembly, and many others. The ionicity of a PIL is difficult to define due to the nature of the proton transfer reaction, in which equilibrium is created between molecular species, ion pairs, and dissociated ions where an incomplete reaction results in neutral species and ion pair aggregates. This study used ^1H and ^{15}N NMR to determine the ionicity and behavior for a variety of diethylmethylamine. Quantifying the free energy of the proton transfer between the Brønsted acid and base during PIL formation is of critical importance in understanding PIL properties. Unfortunately, the free energy, which is considered to be a measure of acid strength, is poorly understood because of the weak binding of the proton to the conjugate base of the Brønsted acid. This necessitated the development of a straightforward and quantitative measurement of acidity. These relative acidities were quantified through the N-reactions between an array of

acids and a single base, diethylmethylaniline. The strengths of the conjugate acids were then deduced by characterizing the bases through their proton attracting power, which is directly linked to the N- shift indicates a more complete transfer of the exchangeable proton to the base, and therefore, a stronger acid. Determining the ΔpK_a of superacids through traditional means, by measuring the relative acidity with respect to a standard in a non-aqueous solvent and then approximating the solvation effect of water, is also problematic because it neglects differences in the solvation energies of different species. When this N- a deviation in the trend is seen in the studied superacids, while acids of lower ΔpK_a trend together.

2015 Western Regional Meeting 48

Application of α,β -dipeptides in organocatalysis under solvent-free conditions

Claudia G. Ortiz, *gabriela@relaq.mx*. Departamento de Química, Centro de Investigación y de Estudios Avanzados, Instituto Politécnico Nacional, Mexico City, Mexico, Mexico

Organocatalysis has become a very important tool in modern organic chemistry. Particularly, solvent free processes are getting special attention from a sustainable chemistry point of view.¹ Although the organocatalytic activity of various α -amino acids and small proline-containing peptides is well known,² in this work we report the application of α,β -dipeptides 1-6 derived from primary amine amino acids in the Michael addition reaction of aldehydes to maleimides and nitroolefins (Figure 1). α,β -Dipeptides 1-6 allow the reaction to take place with good yields and high enantioselectivities under solvent free conditions.

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2015 Western Regional Meeting 49

Synthesis of imidazolium chiral ionic liquids derived from (S)-prolinamine and their application in asymmetric Michael reaction

Arturo Zuniga, *lqilaoz@relaq.mx*. Departamento de Química, Centro de Investigación y de Estudios Avanzados, Instituto Politécnico Nacional, Mexico City, Mexico

Ionic liquids are organic salts with melting points below 100 °C that have attracted the attention of the scientific community in recent years. Incorporation of chiral side chains, e.g. (S)-pyrrolidinmethyl, to these molecules has allowed their use as chiral organocatalysts in asymmetric reactions.¹ A particularly attractive feature of chiral ionic liquids is that they can usually be recovered from the product mixture to be reused. In this work, we would like to report the synthesis of two new imidazolium chiral ionic liquids (CIL-1 and CIL-2) derived from (S)-prolinamine and their application as recyclable organocatalysts in the asymmetric Michael reaction of ketones to nitroolefins under solvent free conditions (Figure 1).

2015 Western Regional Meeting 50

Alkylation of acids, alcohols, and phenols using *N*-(1)-adamantyl-*O*-isopropyl-4-nitrobenzenesulfonimide

Hiep Truong, *HiepTNguyenTruong@gmail.com. Department of Chemistry, California State University-Long Beach, Long Beach, California, United States*

SNAAP® Alkylation is a useful synthetic approach for the preparation of esters and ethers. Nucleophilic substitution of acids, alcohols and phenols (SNAAP®) with the alkylating agent *N*-(1)-adamantyl-*O*-isopropyl-4-nitrobenzenesulfonimide usually yields esters and ethers at room temperature without racemization or molecular rearrangements. An advantage of this method allows the sulfonamide byproduct to be readily recycled back into the sulfonimide. Thus research of *N*-(1)-adamantyl-*O*-isopropyl-4-nitrobenzenesulfonimide was studied to determine its potency in respect to its isopropyl functional group. To synthesize the sulfonimide, a combination of *N*-1-adamantyl-4-nitrobenzenesulfonamide, silver oxide and isopropyl iodide were stirred in refluxing methylene chloride. Alkylation reactions were conducted with a variety of acids, alcohols and phenols in room temperature. For reactions with alcohol or phenol, each substrate was combined with the sulfonimide and tetrafluoroboric acid diethyl ether complex catalyst. For reactions with acids as the substrate, only the sulfonimide was needed because acids were autocatalytic. After completion of each reaction, the byproduct sulfonamide was filtered and the filtrate was treated with sodium hydride. Sodium salts were filtered, the filtrate was concentrated and the product was obtained through kugelrohr distillation. Products were analyzed by NMR and GCMS. Future explorations will continue to focus on expanding the alkylation of other types of acids, alcohols and phenols.

2015 Western Regional Meeting 51

Gaining structural insights into folding of the carboxyl-terminal domain of GIV using circular dichroism spectroscopy

Adam Maddox, *amadox91@yahoo.com. Department of Chemistry, California State University - Long Beach, Long Beach, California, United States*

A vast majority of cell signaling is mediated through activation of hetero-trimeric G proteins. G α -Interacting Vesicle associated protein (GIV) is a non-receptor Guanine nucleotide exchange factor (GEF), which activates Gi family of heterotrimeric G proteins downstream of activated receptor tyrosine kinases (RTKs). GIV's GEF function is mediated by a stretch of highly conserved ~20 residues, which is followed by an SH2-like domain in the C-terminus of the protein. Previous studies have shown that the C- terminal 211 amino acids of GIV (referred to as

“GIV-CT” henceforth) are capable of functioning autonomously from its recruitment to the cell surface upon activation of RTKs to promoting downstream signals by binding to and activating Gi proteins. However, despite all the functional information and computational predictions, the structural insights into how GIV-CT is able to perform all these functions is missing. Here, we have attempted to probe the structural aspects of GIV-CT using circular dichroism (CD) spectroscopy - the most commonly used method for determining the secondary structure of peptides and proteins. N-terminally His6-tagged GIV CT wild type (WT) and a phosphomimetic mutant (S1674D; binds and activates G α i better than the WT) were expressed and purified from E. coli BL21 cells using Co2+-NTA affinity chromatography. The quality and quantity of the purified proteins (dialyzed in 1X phosphate buffer pH 7.4) were determined by SDS-PAGE followed by Instant blue staining and the detergent compatible protein assay (Biorad), respectively. Our preliminary CD spectroscopy analyses showed a random coil profile for GIV CT WT as well as S1674D mutant, both of which could be induced to adopt an α -helical conformation by addition of trifluoroethanol (TFE). Together, our data suggest that although recombinant GIV-CT may be predominantly in an unstructured state, it likely has a propensity to fold into a regular secondary structure, perhaps upon interacting with another protein. Our current and future goals include obtaining and analyzing the CD spectra for GIV-CT in the presence of its binding partner(s) - a phosphorylated peptide of Epidermal growth factor receptor (EGFR) tail, His6-G α i or both. This project is supported by the CNSM Start up funds to DB and in part by the National Institute of General Medical Sciences of the National Institutes of Health under Award Number R25GM071638.

2015 Western Regional Meeting 52

Structural elucidation of the nano-bio interface: Histidine on fumed silica nanoparticles

Haley Swanson, *haleyswanson@ymail.com. Department of Chemistry and Biochemistry, San Diego State University, San Diego, California, United States*

Nanosystem development is occurring at a rapid rate and has far reaching impact in a broad range of fields including energy, medicine and nanocomposite materials. However, molecular level characterization at the interface between nanoparticles and biomolecules still requires development. The interface between L-histidine (His) and fumed silica nanoparticles was probed using a combination of solid-state nuclear magnetic resonance (SSNMR) and thermogravimetric analysis (TGA). One (1D) and two-dimensional (2D) magic angle spinning (MAS) SSNMR techniques were used to interrogate the binding of isotopically enriched ($^{13}\text{C}/^{15}\text{N}$) His on fumed silica nanoparticles at various loading levels. A battery of SSNMR methods was used including 1D ^{13}C and ^{15}N cross polarization (CP)-MAS and 2D 1 experiments. Proton-detection schemes and ultrafast MAS rates are used to increase sensitivity and resolution in the 1 on the silica nanoparticle surface. The adsorption of His on silica nanoparticle surfaces has been quite interesting with observation of unique hydrogen-bonding interactions between the His imidazole ring and the silica surface. Experimental NMR isotropic chemical shifts are compared with density functional theory (DFT) computed ones to develop models for His binding at the silica nanoparticle interface. His is one of the most ubiquitous amino acids in biological systems and it is anticipated that these results will aid other researchers in determining how peptides or proteins bind silica surfaces and advance our understanding of the nano-bio interface.

2015 Western Regional Meeting 53

Novel thermochromic compounds as sensors for high strain experiments

Joseph Sanz, *jsanzzz94@gmail.com*, **Javier R. de Alaniz**, *Department of Chemistry, University of California Santa Barbara, Santa Barbara, California, United States*

Stimuli-responsive molecules have recently emerged as ideal sensors to visualize and map the magnitude and location of stress in polymeric materials subjected to high-strain rates. Because most of the effective stimuli-responsive molecules used as sensors, such as spiropyrans, suffer from intrinsic limitations – simultaneous activation by heat, light and mechanical stress, and low stability in the highly colored form – we seek to develop a stimuli-responsive system based on new thermo- and photochromic materials recently developed in our laboratory, called donor-acceptor Stenhouse adducts (DASA). Herein we focus on synthesizing other DASAs with varying electronic properties at both the amine donor group and the acceptor group with the goal of affecting the amount of energy required to activate the small molecules and modifying the absorbance wavelength of the adducts. By integrating multiple DASAs into the same polymer system, regions of higher and lower stress can potentially be observed. This will have a significant impact on our ability to understand how polymers fail when exposed to high-strain rates; information that will be critical in the design of new polymers.

2015 Western Regional Meeting 54

Aryl di-*n*-butyl phosphates and derivatives as selective inhibitors of butyrylcholinesterase: Compounds with potential for the treatment of Alzheimer's disease

Trina Tran, *trangnha1711@yahoo.com*, *Department of Chemistry and Biochemistry, California State University - Long Beach, Long Beach, California, United States*

Acetylcholine is a major neurotransmitter in the brain and is hydrolyzed by the two sub-families of cholinesterase: butyrylcholinesterase (BChE) and acetylcholinesterase (AChE). In Alzheimer's disease (AD), concentrations of acetylcholine in the brain gradually decrease as the disease progresses, resulting in cognitive loss so characteristic with AD. Therefore, current treatment focuses on increasing the concentration of acetylcholine in the brain by inhibiting the activity of the cholinesterases. However, recent studies have shown BChE activity is found to increase in patients with Alzheimer's disease, while AChE activity remains unchanged or declines. Thus, the use of molecules that selectively inhibit BChE has attracted attention as a potential therapeutic for patients with Alzheimer's disease. Previous studies in our laboratories have demonstrated that dialkyl phenyl phosphates are novel inhibitors of BChE. In particular, di-*n*-butyl phenyl phosphate was found to be one of the most potent and selective inhibitors. In this study, we probed the effect of structural changes in the aromatic region on cholinesterase inhibition by synthesizing a library of aryl dibutyl phosphates and their analogs. These organophosphates were prepared by allowing dibutyl chlorophosphate to react with an appropriate alcohol in the presence of pyridine and DCM. Our studies established that the incorporation of alkyl groups on the aryl moiety led to better inhibitors relative to dibutyl phenyl phosphate for all inhibitors tested, but inhibition properties were dependent on the number and location of the methyl group(s). Increasing the size of the aryl substituent to a naphthyl group also led to a better inhibitor with the 2-naphthyl analog showing a 10-fold lower K_i value compared to the 1-naphthyl analog. Di-*n*-butyl 3,5-dimethylphenyl phosphate ($K_i = 1.3 \mu\text{M}$) and di-*n*-butyl 2-naphthyl phosphate ($K_i = 1.9 \mu\text{M}$) were the two most potent inhibitors. The factors responsible for the inhibitory property of our compound library were further examined through

docking studies.

2015 Western Regional Meeting 55

Binding properties of curcumin with DNA: Influence of the water network in the DNA minor groove

Asma El-Magboub, *elmagboub@gmail.com. Department of Pharmacology and Pharmaceutical Sciences, University of Southern California, Los Angeles, California, United States*

Curcumin is a pharmacologically interesting molecule that has poor aqueous solubility and stability at physiological pH. These properties and the general hydrophobicity of curcumin make it difficult to evaluate its binding characteristics with proteins and DNA. In this study, we used multiple modeling tools to evaluate binding of curcumin with DNA duplexes of different sequences. The structural features of curcumin are compatible with a typical minor groove binder. Curcumin-DNA complexes were built using an in-house program, NASDAC, or through docking with AutoDock, followed by minimization using NAMD. Solvation of the minor groove in the absence or presence of curcumin was calculated using another in-house program, WATGEN. This program places water molecules in the groove based on optimization of hydrogen bonding and minimization of steric and hydrophobic contacts. Additional software permits computation of the energy of each water molecule and comparison of these energies in the solvated free DNA and curcumin-DNA complex. Vacuum docking showed that curcumin interacts with DNA as a minor groove binder with $\Delta G = -7.7 \pm 1.3$ kcal/mol, which is more negative than values obtained experimentally (approximately -5 kcal/mol). Solvated models of curcumin-DNA complexes suggested that curcumin does not fully displace water molecules from the minor groove. The remaining water molecules in the curcumin-DNA complex may contribute unfavorably to complex formation and reduce the affinity of curcumin to the value observed experimentally.

2015 Western Regional Meeting 56

In-class and online student performance in a pharmacy problem-based learning class

Asma El-Magboub, *elmagboub@gmail.com. Department of Pharmacology and Pharmaceutical Sciences, University of Southern California, Los Angeles, California, United States*

The goal of the study was to compare the performance of students in small group discussion meetings held face-to-face (in-class) or by synchronous, real time videoconference (online). All meetings were led by a faculty facilitator and were part of a pharmaceutical sciences course taught in a problem-based learning (PBL) format. Three parameters were used for scoring: participation of students in the discussions (*Par*), quality of interactions between facilitator and student (*Fc-St*), and cooperation among students (*St-St*). Interactions during the discussion sessions were mapped as sociograms. Surveys were used to determine the students' perceptions of the discussions. Compared to face-to-face meetings, online discussions had significantly lower scores for *Par* and *St-St* ($P < 0.05$) and tended to have lower *Fc-St* ($P < 0.06$). Consistent with these findings, sociograms showed reduced interactions for discussions held synchronously by videoconference. Student feedback from surveys excluded technology barriers or student dissatisfaction as reasons for the lower interaction levels during online

sessions. Therefore, we conclude that online synchronous discussion meetings require the facilitator to promote student participation in a more active manner than that used in class.

2015 Western Regional Meeting 57

Synthesis of bivalent organothiophosphate compounds and their inhibition of butyrylcholinesterase for potential treatment of Alzheimer's disease

Ambreen Tahira, *ambreent@gmail.com*. Department of Chemistry and Biochemistry, California State University-Long Beach, Long Beach, California, United States

Alzheimer's Disease (AD) is one of the most common types of dementia accounting for 60 – 80 percent of all dementia cases. Treatment of AD is centered on inhibition of the cholinesterase enzymes: Acetylcholinesterase (AChE) and Butyrylcholinesterase (BuChE). Current research in the treatment of AD has showed that a decrease in activity of AChE through inhibition in an AD patient is combated by an increase of BuChE activity, making BuChE also significant in the treatment of AD. While majority of early research had centered on AChE in understanding AD, BuChE role in the hydrolysis of acetylcholine when AChE activity decreases in AD patients has recently gained interest in the research for AD treatment. Structural similarities of the two enzymes have led to the test of inhibition on BuChE by compounds synthesized for test on AChE inhibition. Organophosphates and organothiophosphates are a few of the leading inhibitors of AChE. Studies on the inhibition of BuChE by bivalent organophosphates connected by a junction of varying alkyl chain showed a promisingly similar inhibition as AChE. The replacement of an oxygen by sulfur to the organophosphate bivalent compounds showed lower K_i and IC_{50} in comparison to compounds without sulfur, and compounds with larger alkyl chain in comparison to a shorter alkyl chain also had lower K_i and IC_{50} values, directing the research towards testing inhibition of organothiophosphate compounds of varying alkyl group. A second variation of the organothiophosphate by the addition of carbonyl group in backbone of the phosphate while varying the alkyl chain length was also tested on BuChE inhibition and their IC_{50} and K_i values will be calculated. The results will show which alkyl chain is the new and potent inhibitors of BuChE while we simultaneously continuing the research on the physical properties of oxygen, sulfur, and carbonyl with sulfur and their interaction with BuChE that places each of them at a specific inhibition range.

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2015 Western Regional Meeting 58

Synthesis of nanoparticle polymer and testing affinity with IgG

Rishad Dalal, *dalalr@uci.edu*. Department of Chemistry, University of California, Irvine, Irvine, California, United States

IgG (Immunoglobulin G) is a workhorse protein that can be used for research, diagnostics, and therapeutic applications. IgG is the most abundant antibody isotype found in circulation, which represents approximately 75% of serum immunoglobulins in humans. Although IgG is productive and active, the protein denatures at ~60 °C. To address the problem, I am proposing the use of polymer nanoparticle (NP) hydrogels to use as artificial heat shock proteins for IgG.

These N-isopropyl acrylamide (NiPAm) based NPs have been synthesized with a range of compositions with co-monomers N-tert-butylacrylamide (tBAm), N-hexylacrylamide (Ham), N-octylacrylamide (OAm), acrylic acid (AAc), and N,N'-methylene-bis-acrylamide (Bis). The NPs were then characterized, tested for affinity, release ability, and heat protectant ability.

2015 Western Regional Meeting 59

Effects of tetra-alkyl bisphosphates on BuChE activity using HEPES as a function of pH

Kaycee Villarreal, *kgvillarreal@aol.com. Department of Chemistry and Biochemistry, California State University-Long Beach, Long Beach, California, United States*

Abstract: The development of Alzheimer's disease (AD) correlates with reciprocal changes in the level of cholinesterase activity, i.e., butyrylcholinesterase (BuChE) increase while acetylcholinesterase (AChE) decreases. The consequence is a decrease in the level of acetylcholine and loss of cognitive function. As such, butyrylcholinesterase inhibitors are potential therapeutics to relieve the symptoms of AD. Bisphosphates were synthesized with varying internal alkyl linkers and external alkyl groups and were evaluated for their inhibitory effects on BuChE. Cholinesterase activity measurements were performed using the Ellman's method. Enzyme activity was measured at 37 °C by monitoring the formation of the thionitrobenzoate anion at 412 nm using 0.5 M HEPES (4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid) as buffer. The study looked at the effect of 10-4M bisphosphates on BuChE activity at different pH, i.e., 6.9, 7.2, 7.5, 7.8 and 8.1. Tetrabutyl pentyl bisphosphate was the most potent inhibitor. It was shown that relative to sodium phosphate buffer, HEPES activates enzyme activity as a function of pH.

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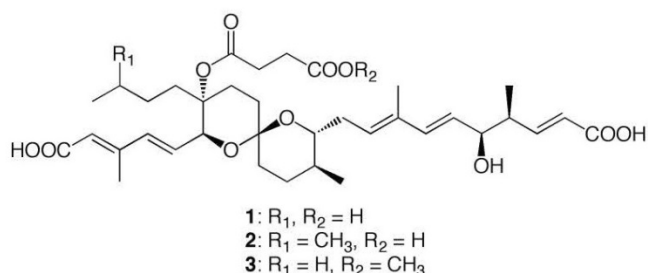
2015 Western Regional Meeting 60

A unique approach to identify solid tumor selective compounds using a combination of two *in vitro* cancer cell screenings

Lisa Liu, *lliu@mail.sfsu.edu. Department of Chemistry and Biochemistry, San Francisco State University, San Francisco, California, United States*

As part of our research program to discover novel cytotoxic compounds with excellent solid tumor selectivity, we have recently initiated a new anticancer screening campaign from marine-derived actinomycetes using the CP-DDA approach. This screening method uses two powerful *in vitro* cancer cell screening assays – cytological profiling (CP) in combination with the disk diffusion assay (DDA). We tested a mini-library containing 60 organic extracts created from the strains of marine sediment-derived actinomycetes against a series of cancer cell lines. In this library, four strains showed significant selective cytotoxicity against the cancer cell lines. One of the active strains, *Streptomyces* sp. CP53-67, showed potent and significant selective activity against the ovarian cancer cell line (OVC-5). The mini-library was also tested against HeLa cells to generate its cytological profile (CP) for identifying potential cellular targets. The CP data of the extract clustered with the known protein and RNA synthesis inhibitor anisomycin, indicating that the cytotoxic compounds in this extract were protein/RNA synthesis inhibitors. Dereplication

of the extract from a small-scale culture (200 mL) using HRLCMS indicated that the major compounds were known cytotoxic polyketide reveromycins. In fact, we isolated and identified reveromycins A (**1**) and C (**2**) from a medium-scale culture (1L) of the extract. Reveromycins were originally reported as protein synthesis inhibitors with selectivity against eukaryotic cells. More recent research determined isoleucyl tRNA synthetase as the molecular target of **1**. We have also detected reveromycin A 4'-methylene ester (**3**) in the extract. This compound was known to possess solid tumor selectivity against human cancer cell lines, which attributed the potent and selective cytotoxic effect of the extract to **3**.



2015 Western Regional Meeting 61

Progress toward the synthesis of gelsedilam

Carla M. Saunders², cmsaunders@ucdavis.edu, **Fabio D. Fernandes**², **Jared T. Shaw**¹. (1) Dept Chemistry, UC Davis, Davis, California, United States (2) University Of California At Davis, Davis, California, United States

Herein a concise approach to the complex alkaloid gelsedilam is described. Gelsedilam, an alkaloid isolated from the shrub *Gelsemium elegans*, has a challenging monoterpene oxindole structure making it an interesting natural product target. The γ -lactam core of gelsedilam can be easily accessed through the anhydride Mannich reaction (AMR). Using the AMR allows for the diastereoselective synthesis of gelsedilam from the chiral pool molecule D-Malic Acid.

2015 Western Regional Meeting 62

New α -helix mimetics targeting the E6 protein in the human papillomavirus

Ernest Armenta, ernest.armenta@csu.fullerton.edu. Department of Chemistry and Biochemistry, California State University - Fullerton, Fullerton, California, United States

Protein-protein interactions (PPIs) are involved in many cellular processes, making them potential drug targets. Many of these interactions involve amino acid residues projecting off of an α -helix. Small molecules have been designed to mimic short amino acid sequences important for binding to target proteins. Many of these small molecules mimic only the hydrophobic face of the α -helix, possibly excluding important interactions arising from polar residues. The Orchard Group has designed novel, amphiphilic, small-molecule α -helix mimics capable of mimicking consecutive amino acid residues on both faces of the helix for treatment of various diseases, such as Human Papillomavirus (HPV) infection. HPV is a small DNA virus that infects epithelial cells. The E6 oncogenic protein in HPV allows for survival of infected cells by

binding to the human protein E6AP. Binding allows for degradation of p53, a tumor suppressing protein. Inhibition of E6 should allow for apoptosis of infected cells, clearing the infection in a non-invasive way. Our proposed library of potential α -helix mimetics has been rationally designed with the aid of Molsoft ICM Pro software, and synthesis of these compounds is underway. Herein, we present promising docking results and our proposed synthetic route toward a small subset of compounds capable of mimicking 4 of the 5 residues known to be important for E6 binding. Once synthesis is complete, compounds will be tested for their ability to cause apoptosis in infected cells as well as their ability to specifically inhibit the E6-E6AP interaction.

2015 Western Regional Meeting 63

Investigation of LEF-1 flexibility vs. DNA binding activity

Ariana Pientka, *ariana.pientka@gmail.com*. Department of Chemistry and Biochemistry, San Diego State University, San Diego, California, United States

LEF-1 is a transcription factor that bends DNA 100 degrees into a mutually induced fit, via a mechanism not currently understood. LEF-1's flexibility when free in solution is hypothesized to be necessary. To investigate, protein design techniques are used to alter the flexibility of free LEF-1 and observe the binding affinity shift.

The suite of LEF-1 variants were designed using a combination of site directed mutagenesis, total gene synthesis, and ORBIT. Structural stability was determined via circular dichroism, NMR, and *in vitro* proteolysis. Binding affinities were measured via gel shift assay, and an area of ongoing effort is using microscale thermophoresis.

The LEF-1 variants demonstrated subtle differences in binding affinity. Since LEF-1's C-terminal tail is a major factor in the stability of the complex, truncating the tail of wild type and the variants should pronounce the difference in binding affinities, allowing easier identification of stabilized variants. This stage is ongoing.

2015 Western Regional Meeting 64

An efficient domino amination-oxidation reaction for the copper-catalyzed synthesis of anilines

Christopher Thomas, *iamchristhomas@gmail.com*. Department of Chemistry and Biochemistry, San Francisco State University, San Francisco, California, United States

Metal-catalyzed processes for carbon-nitrogen bond formation have become fundamental to the drug discovery industry. Over 90% of the current top-selling brand name pharmaceuticals contain at least one nitrogen atom in their molecular structure, and advancements in palladium- and copper-catalyzed carbon-nitrogen bond synthesis have substantially impacted the design and identification of these drug candidates. For example, aryl amines (anilines) are ubiquitous structural motifs in pharmaceutically-interesting compounds, but classical methods are generally not amenable for the synthesis of a wide range of anilines. Copper catalysis obviates these issues by providing an operationally simple method for reacting an aryl electrophile (e.g., aryl halide) with an alkyl or aryl amine to form the desired carbon-nitrogen bond. Despite these advancements, the synthesis of monoarylated anilines by catalytic methods remains challenging as often di- and triarylated anilines are observed as undesired byproducts. To address these

issues, we developed a domino copper-catalyzed process in which aryl iodides and bromides can be efficiently transformed into the corresponding monoarylated anilines. This method employed a non-traditional nitrogen source, valine, to promote carbon-nitrogen bond formation and importantly prevented the formation of di- and triarylated aniline byproducts. Based upon mechanistic experiments, we have proposed that the reaction proceeds in two distinct steps: (1) carbon-nitrogen bond formation and (2) oxidation of the amine to an imine. Hydrolysis of the imine post-reaction afforded the corresponding monoarylated aniline. This novel copper-catalyzed method allowed for the synthesis of arylamines in modest to excellent yields and represents a mechanistically innovative process for selective carbon-nitrogen bond formation with aryl halides.

2015 Western Regional Meeting 65

PLGA film formulations for sustained release of a water-soluble drug

Ayauzhan Tumabayeva^{1,2}, ayauzhan.tumabayeva@gmail.com. (1) *Biomedical Engineering, Purdue University, West Lafayette, Indiana, United States* (2) *Faculty of Chemistry and Chemical Technology, al-Farabi Kazakh National University, Almaty, Kazakhstan*

Poly(lactic-co-glycolic acid) (PLGA) has been used widely for development of sustained release drug delivery systems. Drugs delivered from the PLGA formulations ranges from small molecular weight drugs to proteins. In most formulations, the initial burst release is large to release a significant portion of the total loaded drug is released in a matter of a day. This is not desirable, especially for long-term delivery up to several months. The problem is magnified for water-soluble small molecular weight drugs. We examined different methods to find a way to minimize the initial burst release and sustained release for weeks and months. In our study, acetazolamide (ACT) was used as a model drug. To examine the factors involved in controlling the drug release rate, polymer films were prepared using different solvents and polymers. Our results indicate that it is difficult to control the drug release with the single layer of monolithic polymer. If the drug-containing polymer layer is covered by blank PLGA films followed by compression, the initial burst release is minimized. The results are consistent with our current understanding that drug molecules are cumulated on the surface of PLGA matrix and interconnected channels are formed during drying process. Compression of the films is a key step to minimize the initial burst release and sustained delivery of a loaded water-soluble drug.

2015 Western Regional Meeting 66

Identification, characterization, and modification of fatty acid alkyl esterases found in *Staphylococcus aureus*

Benjamin Saylor¹, hahsanumat@yahoo.com, John J. Love². (1) *Department of Chemistry, San Diego State University, San Diego, California, United States* (2) *Department of Chemistry, San Diego State University, La Mesa, California, United States*

Our work constitutes an attempt to explore enzymatic synthesis of biodiesel with lipids like those derived from emerging fuel crops. Previous literature describes fatty acid alkyl ester formation in *Staphylococcal* lesions, formed by esterase activity from an unidentified source. We have identified the enzymes responsible for this activity in MRSA *Staphylococcus aureus*. These two highly similar enzymes catalyze the synthesis of fatty acid alkyl esters.. We have expressed

these Staphylococcal esterases in *E. coli*, and shown that the expressed proteins catalyze the formation of fatty acid alkyl esters.

Based on sequence similarity to homologous proteins, we have predicted a structure for these enzymes and have engineered mutants with higher rates of catalysis. Based on the hypothesis that increased avidity for substrate molecules will yield a higher substrate concentration local to the enzyme, we have designed and expressed one of the enzymes as a chimeric fusion with the *Drosophila melanogaster* alcohol-binding protein LUSH.

Determination of biodiesel production rate shows that the chimeric fusion has a lower-order rate constant with respect to ethanol indicating that the rationally designed modification of binding avidity constitutes a potential avenue for improving the ability of enzymes to catalyze reactions with low-concentration or low-solubility substrates.

2015 Western Regional Meeting 67

Development of redox mediators for lithium-sulfur batteries

Angelique Scheuermann, *angeliquescherman@berkeley.edu*. Department of Chemistry, University of California-Berkeley, Berkeley, California, United States

We have developed redox mediators based on polycyclic aromatic hydrocarbons to facilitate charge transfer and increase sulfur utilization in lithium-sulfur (Li-S) batteries. The compounds were designed to target the reduction potential of polysulfides to insoluble Li₂S at 2.0 V vs. Li/Li⁺. We compare two redox mediators, one that assembles into a network by π -stacking (RM-1) and one that does not assemble (RM-2). RM-2 was developed in a four-step synthesis with a 52% yield. RM-2 is shown to have a reduction potentials of 1.95 V vs. Li/Li⁺ and functions as a redox mediator to polysulfides, shown by an increase in current at 2.0 V vs. Li/Li⁺. We found that RM-2 does not self-assemble by measurement extinction coefficients of the compound at different concentrations using UV-visible spectroscopy. Both RM-1 and RM-2 increase sulfur utilization by changing the morphology of deposition of Li₂S. Li-S battery capacity is shown to increase by a factor of 2.4 by using RM-2 in conjunction with carbon felt in Li-S batteries. In contrast, RM-1 assembles into supramolecular networks on carbon felt and increases Li-S capacity by a factor of 2.2. With the addition of RM-2, we have expanded our library of redox mediators with different properties such as solubility, assembly, and reduction potential.

2015 Western Regional Meeting 68

X-ray single crystal analysis of *n*-type organometallic dopants for organic semiconductors

Evgheni Jucov, *evgheny.jucov@gmail.com*. Department of Chemistry, New Mexico Highlands University, Las Vegas, New Mexico, United States

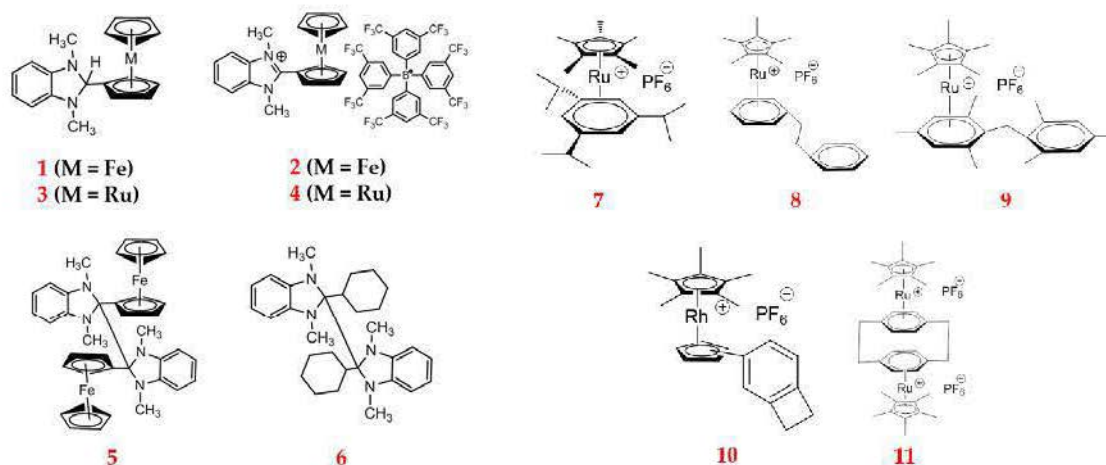
The promise of low-cost processing and flexible circuitry has driven intense research in carbon-based electronics. The performance of carbon-based materials can be effectively tuned by the application of redox dopants, through increasing the conductivity and decreasing the injection barrier. Effective *n*-dopants that are nevertheless relatively inert to ambient conditions, facilitating their handling, have been developed by coupling electron-

transfer reactions to chemical reactions: approaches include the use of dimers of highly reducing species and of hydride-reduction products of stable cations.

Examples of both classes have been designed and synthesized including of new benzoimidazole dopants (1, 3, 5 and 6). The dimers 5 and 6 are moderately air-stable in the solid state, but *n*-dope a variety of electron-transport materials, including fullerenes and TIPS-pentacene, as shown by solution vis-NIR spectroscopy, by conductivity measurements, and by UV photoelectron spectroscopy. The hydride-reduced species 1 and 3 are more stable, but have much more limited utility as dopants, reacting with fullerenes such as PCBM, but, due to the necessity of transferring both an electron and a hydrogen atom, not with other materials with similar reduction potentials, such as perylene diimide. A variety of hexafluorophosphate salts of organoruthenium cations, 7-11, have also been obtained as potential precursors to new organometallic dimers, or as side products in the synthesis of intended precursors.

X-ray single crystal analysis was used to compare geometrical parameters between hydride-reduced (1, 3), dimeric (5,6), and cationic (2, 4) (precursors to dimers and formed subsequent to doping) benzimidazole species. The central C-C single bonds of dimers 5-6 have unusually large values of ca. 1.6 Å that is necessary for accommodation of bulky substituents, and consistent with the breaking of this bond that occurs during the usage of these materials as dopants. The crystal packing for all hexafluorophosphate salts 7-11 is governed by the CH...F cation-anion hydrogen bonds. The octahedral PF₆⁻ anion acts as multiple acceptors joining several bulky cations. All molecular packings show short intermolecular contacts which stabilize cation and anion moieties present in these compounds.

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2015 Western Regional Meeting 69

Targeting bacterial antioxidant defense to improve antibiotic treatment efficacy of stationary phase *E. coli*

Jing-Hung Wang, wangjh26@stanford.edu. Department of Microbiology and Immunology, Stanford University School of Medicine, Stanford, California, United States

Stationary phase bacteria are important in disease and are hard to eradicate. We previously showed that the antioxidant defense of bacteria in this phase significantly contributes to their gentamicin resistance. We now show this also for ampicillin, norfloxacin and ciprofloxacin. A strain missing the stress-response regulator σS , which controls antioxidant defense, was more sensitive, as were mutants missing the reactive oxygen species (ROS) quencher proteins (e.g., SodA/SodB and KatE/SodA), or the pentose shunt pathway (e.g., Zwf, TalA), which provides NADPH for the ROS quencher activity. ROS generation during antibiotic treatment was directly demonstrated, using *sfiA::lacZ* induction and ROS detectors, HPF and amplex red. Different mutants varied in increasing antibiotic vulnerability, suggesting that loss of a vital antioxidant function can activate metabolic networks with differing compensating capacities.

2015 Western Regional Meeting 70

Sensitive nonlinear multi-photon laser wave-mixing detection methods for environmental and biomedical applications

Megan Murphy, *mmurp123@my.smccd.edu. Department of Chemistry and Biochemistry, San Diego State University, San Diego, California, United States*

Nonlinear multi-photon laser wave-mixing spectroscopy interfaced to capillary electrophoresis or microfluidics is presented as ultrasensitive methods for a wide range of environmental and biomedical applications including simultaneous analysis of malachite green, crystal violet, their metabolites leuco-malachite green and leuco-crystal violet. Nonlinear wave mixing offers inherent advantages over conventional laser methods including zepto-mole detection sensitivity, excellent chemical selectivity and specificity levels, and high spatial resolution suitable for single-cell analyses. The wave-mixing signal is a coherent laser-like beam, and hence it can be collected with excellent signal-to-noise ratios and high detection efficiency levels. Chromatic and leuco forms of crystal violet and malachite green absorb in the UV and visible wavelength ranges. We use a 266 nm UV laser to probe label-free analytes in their native form and a visible laser to probe labeled analytes. The wave-mixing signal has a quadratic dependence on analyte concentration, and hence, wave mixing is especially effective for monitoring small changes in analyte properties. In order to further enhance chemical selectivity levels, a capillary (75 μm inside diameter) is used to flow and separate analytes in our custom-built capillary electrophoresis system. The wave-mixing probe volume is small (nL, pL), and hence, it is inherently suitable for interfacing to lab-on-a-chip, microfluidics and microarray systems. Excellent detection sensitivity levels (atto-mole levels) have been demonstrated using capillary- and chip-based separation systems for different environmental samples and biomarkers. Wave-mixing methods allow application in the field for a wide range of environmental and biomedical applications (biomarkers, viruses and early detection of cancer, etc.).

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2015 Western Regional Meeting 71

Synthesis and *in vitro* evaluation of asymmetric 1,5-diheteroaryl-penta-1,4-dien-3-ones as anti-prostate cancer agents

Xiaojie Zhang, zhangxiaojie87@gmail.com. Department of Chemistry and Biochemistry, California State University-Fresno, Fresno, California, United States

The symmetric 1,5-diheteroaryl-1,4-pentadien-3-ones have been established by us as a promising class of curcumin-based anticancer agents, which has been recently published in the Journal of Medicinal Chemistry. Among this set of compounds, the most promising ones showed over 100 times more potent than curcumin against both androgen-dependent (LNCaP) and androgen-independent prostate cancer cell lines (PC-3 and DU145). Moreover, certain promising symmetric 1,5-diheteroaryl-1,4-pentadien-3-ones have been demonstrated to have capability in inducing cell apoptosis *in vitro* and in improving bioavailability in an *in vivo* animal model. To further explore the in-depth structure-activity relationships of this scaffold, we designed and synthesized 27 asymmetric 1,5-diheteroarylpenta-1,4-dien-3-ones for the evaluation of their *in vitro* anti-proliferative activity towards both androgen-sensitive and androgen-insensitive prostate cancer cell lines. They were synthesized with an Honor-Wadsworth-Emmons reaction as the key step reaction. The cell-based experimental data showed that asymmetric 1,5-diheteroarylpenta-1,4-dien-3-ones also possess promising anti-proliferative activities towards three prostate cancer cell lines. The most promising one has been selected for the exploration of cell death pathway (apoptosis or necrosis) using F2N12S/SYTOX AADvanced doubling staining assay and cell cycle regulation using PI staining assay through flow cytometry.

2015 Western Regional Meeting 72

Assessment of UCH-L3 substrate selectivity using engineered ubiquitin fusions with varying linker lengths

Peter Suon¹, pssuon@gmail.com, John J. Love². (1) Department of Chemistry and Biochemistry, San Diego State University, San Diego, California, United States (2) Department of Chemistry and Biochemistry, San Diego State University, La Mesa, California, United States

The Ubiquitin Proteasome System (UPS) is a complex system composed of multiple structural and functional elements that play key roles in cellular processes such as signal transduction, cell cycle regulation, apoptosis, and protein degradation. Proteins destined for degradation are first tagged with the protein, ubiquitin, which is covalently attached to internal lysine residues. Once the target has been degraded by the proteasome; the enzyme Ubiquitin Carboxy Hydrolase L3 (UCH-L3) is believed to prepare ubiquitin for additional rounds of ubiquitination by cleaving small peptides and chemical adducts from the ubiquitin C-terminus. Previously in our laboratory, protein substrates of UCH-L3 were engineered and used to characterize UCH-L3 substrate selectivity. The engineered substrates consisted of N-terminal monoubiquitinated test variants derived from *Streptococcal* protein G (protein G β 1) and *Staphylococcal* protein A (SpA_B). The thermal denaturation temperatures (T_m) of the fusion proteins were measured using circular dichroism and span a range of over 60 °C. More importantly, the rate of hydrolysis for the fusion proteins is demonstrated to be directly correlated to the T_m of the test variant fused to the C-terminus of ubiquitin. Previously, the engineered substrates were designed to emulate natural ubiquitin fusions and thus did not contain any 'linker' residues between the C-terminus of ubiquitin and the N-terminus of the test protein. To explore the effects of linker length on UCH-L3 hydrolysis we are engineering new UCH-L3 substrates that contain an unstructured 12 amino acid linker between ubiquitin and the test protein. To further explore the catalytic efficiency of UCH-L3 we will revisit diubiquitin (Ub-Ub), which is not hydrolyzed by UCH-L3, and will make mutations in the hopes of generating a hydrolysable substrate. Using rational design, the new

variants will be engineered to destabilize the C-terminal ubiquitin to determine if this results in hydrolysis of the new Ub-Ub construct. The thermal stability of these new fusion protein substrates will be measured using circular dichroism spectroscopy (CD) and UCH-L3 hydrolysis rates will be characterized using existing assays. Our goal is to continue the use of engineered substrates to further explore the catalytic properties of UCH-L3 activity and the potential role in protein trafficking and degradation within living cells.

2015 Western Regional Meeting 73

Anti-mycobacterial drug discovery using extract UA 774 from the surface of *Ulva californica*

Javier Guzman², guzma044@cougars.csusm.edu, **Jacqueline A. Trischman**¹. (1) Chemistry & Biochemistry, California State Univ San Marcos, San Diego, California, United States (2) Department of Chemistry and Biochemistry, California State University - San Marcos, San Marcos, California, United States

The growing need to find new alternatives to treat tuberculosis is higher than ever due to the fact that much of *Mycobacterium tuberculosis* (TB) strains are drug resistant. *Mycobacterium marinum*, the closest genetic relative to TB, is used in the assay and the extract is from the culture broth of a bacterium (UA-774) collected from the surface of a marine alga called *Ulva californica*. Research is being performed to isolate and identify organic compounds from UA-774 that potentially inhibit growth of *M. marinum* and may also inhibit TB. Strain UA 774 was cultured on a 10L scale, challenged with *M. marinum* when stationary phase was reached, extracted using solid-phase techniques, and the extract underwent an assay that indicated positive signs of inhibition of *M. marinum*. A series of UA 774 fractions were analyzed using ¹H NMR technique, of which fraction 5 showed the greatest inhibitory activity. This same fraction was further analyzed using reverse phase HPLC in methanol, isopropyl alcohol, and water. Further analysis is underway to identify the chemical structure of this fraction.

2015 Western Regional Meeting 74

Analytical method for reliable H₂O-ice production for astrochemical experiments

Manesseh Park, park070@cougars.csusm.edu. Department of Chemistry and Biochemistry, California State University-San Marcos, San Marcos, California, United States

Understanding how astrophysical processes affect different isotopologues of water (H₂¹⁶O, H₂¹⁷O, H₂¹⁸O, HD¹⁶O) is important for astronomical observations of molecular clouds and solar system objects such as comets. We have constructed a ultrahigh vacuum (UHV) system consisting of a multi-port spherical stainless steel chamber, a closed-cycle He cryostat and a stainless steel vacuum line connected to cavity ring down spectrometer (Picarro, L2120-i). One of the main challenges of studying astrophysical ices at the isotopic level is delivering H₂O ices of known isotopic composition reproducibly. Here we show that aliquots of ambient atmospheric air may be sampled to reliably produce H₂O ices of known isotopic composition.

2015 Western Regional Meeting 75

Effect of hydrophobicity and charge in the oligomerization of amyloidogenic peptides and the design of a pH-switchable oligomer

Yilin Wang², yilinw4@uci.edu, **James S. Nowick**¹. (1) *University of California, Irvine, California, United States* (2) *Department of Chemistry, University of California, Irvine, Irvine, California, United States*

β -Sheet interactions are important in amyloid diseases such as type 2 diabetes (T2D). The aggregation of islet amyloid polypeptide (IAPP) in T2D to form toxic oligomers is central to the progression of the disease. Here we describe studies of the effects of charge and hydrophobicity on the oligomerization of peptides derived from residues 11-17 of IAPP (RLANFLV). By systematically varying the arginine residue at position 11 of the heptapeptide and observing the propensity of the resulting peptides to oligomerize, we find that hydrophobicity promotes assembly whereas positive charge disrupts assembly. We conclude these experiments by designing a pH-switchable oligomer with a histidine residue at position 11. These studies demonstrate that a good understanding of factors involved in oligomerization can lead to control of the assembly process.

2015 Western Regional Meeting 76

Using protein design to engineer the Cif epoxide hydrolase for neutralization of mycotoxins

Maileen Acevedo¹, maileen.is@gmail.com, **Peter Suon**², **John J. Love**³. (1) *Department of Chemistry and Biochemistry, San Diego State University, San Diego, California, United States* (3) *Department of Chemistry and Biochemistry, San Diego State University, La Mesa, California, United States*

Protein Design is a technique used to engineer proteins with new and potentially enhanced functional properties. Proteins are designed by making judicious changes to the amino acid sequence, which can lead to changes in the protein structure and thus function. The goal of our research is to re-engineer the active site of an epoxide hydrolase that will then be used to detoxify genotoxic compounds. A toxin that we are targeting for degradation with the engineered epoxide hydrolase is the compound Deoxynivalenol, also known as vomitoxin. Vomitoxin belongs to a family of mycotoxins called trichothecenes, many of which are produced by the fungal genus *fusarium*. Exposure to vomitoxin can constitute a serious economic and health concern (hence its name). Thus far we have employed standard laboratory techniques, such as recombinant DNA technology, to clone a Cif epoxidase gene from *Pseudomonas aeruginosa*. We are now sub-cloning this gene into standard bacterial expression vectors and also into a recently engineered bacterial display system. This system incorporates the red fluorescent protein mCherry, and a number of strong structural linkers, which enables the display of proteins on the surface of *E. coli*. We are using this tool to re-engineer and assess the effectiveness of the modified Cif epoxidase enzyme. The goal of this process is to ultimately generate a new enzyme that will be used to catalytically breakdown and thus neutralize the effects of vomitoxin. We hope that our findings will demonstrate the utility of protein design, in combination with the bacterial display system, to engineer novel enzymes that can be used to safely degrade toxic compounds such as Deoxynivalenol (vomitoxin).

2015 Western Regional Meeting 77

Isotopic fractionation as a result of sublimation of water-ice

Elizabeth Christensen, chris087@cougars.csusm.edu, Manesseh Park. Department of Chemistry and Biochemistry, California State University-San Marcos, San Marcos, California, United States

Understanding the multi-isotopic fractionation of water-ice that results from its sublimation may be important for understanding the isotopic composition of molecular clouds and cometary ices. Here we describe a laboratory experiment whose purpose is to understand the effects of various astrophysical processes on the dD , $d^{18}O$ and $d^{17}O$ composition of water-ice. Our setup consists of an ultrahigh vacuum (UHV) chamber, a closed cycle He cryostat (capable of reaching 6K), and a vacuum line connected to the chamber via a UHV feed-through. Water isotopologues $H_2^{16}O$, $H_2^{18}O$, $H_2^{17}O$, and $HD^{16}O$ samples can be measured after sublimation of water-ice with a cavity ring-down spectrometer (Picarro L2120-*i*) that is connected to the vacuum line. To perform these experiments, ambient water vapor was introduced into, frozen, and purified inside the UHV chamber ($T < 150$ K). Water-ice samples were sublimated for varying amounts of time and at various temperatures to collect fractions of the original reservoir.

We will present the first results on the oxygen and deuterium isotopic fractionation of water-ice sublimation and discuss their implications for interpreting the isotopic compositions of cometary ices.

2015 Western Regional Meeting 78

Identification of anti-mycobacterial compounds from the extract of a marine bacterial isolate (UA446) taken from the surface of *Ulva californica*

Tyler Fallert², falle006@cougars.csusm.edu, Jacqueline A. Trischman¹. (1) Chemistry & Biochemistry, California State Univ San Marcos, San Diego, California, United States (2) Department of Chemistry and Biochemistry, California State University - San Marcos, San Marcos, California, United States

Tuberculosis is one of many diseases that require continued research. As the bacterium, *Mycobacterium tuberculosis*, evolves and adapts to new antibiotics, research is needed to maintain viable treatment plans. This study has focused on the effectiveness of marine bacterial extracts in inhibiting the growth of *M. marinum*, a close relative of *M. tuberculosis*. A bacterial strain, UA446, was isolated from the surface of *Ulva californica* obtained off of the California coastline and its culture broth extract inhibited *M. marinum* when tested in a growth assay. In an attempt to isolate the compound responsible for the inhibition, the UA446 strain was cultured on a 10L scale, challenged with *M. marinum* at stationary phase, extracted, and then fractioned using both a C-18 flash column and HPLC. The separated fractions were then analyzed using proton NMR to determine which fractions had compounds of interest and subjected to the growth bioassay. Finally, each fraction containing the compound of interest was analyzed using a GCMS to help determine its composition if known and to help in elucidation of the structure if not in the MS database.

2015 Western Regional Meeting 79

Optimization of a designed protein-protein interface

Brian Maniaci¹, brianmaniaci@gmail.com, John J. Love². (1) Department of Chemistry and Biochemistry, San Diego State University, San Diego, California, United States (2) Department of Chemistry and Biochemistry, San Diego State University, La Mesa, California, United States

The structure and properties that control dimerization of Protein G B1 domain were studied using a metal templated design of the protein interface. Previously, mutations in the core of the protein were used to induce dimer formation along the antiparallel beta-sheet between the edge strands in two monomers. Using de novo protein design we docked Protein G B1 to itself in a helix-to-helix motif, where the de novo protein-protein interaction resulted in a dimer of modest binding affinity. A variety of convergent design elements were used to improve binding specificity and decrease off-target protein-protein interactions. The measured interactions were quantified using heteronuclear NMR methodologies, size-exclusion chromatography with multi-angle light scattering, and x-ray crystallography. The experimental results suggest the formation of a dimer with some protein variants existing as higher order oligomeric states. Further structural determination is required for some of the new Protein G B1 domain variants to determine the orientation and mechanism of protein dimerization.

2015 Western Regional Meeting 80

Synthesis of small molecules for potential hepatitis C virus translation inhibition

Walter Frauman, wfrauman@ucsd.edu. Department of Chemistry, University of California, San Diego, San Diego, California, United States

Hepatitis C contains a noncoding region known as an internal ribosome entry site (IRES) attached upstream of the coding region of the RNA. This site allows for the virus to undergo cap-independent translation of viral RNA, removing the need for many host initiation factors. A certain highly conserved loop segment of this IRES RNA has been found by our lab to play an essential role in the IRES-driven translation initiation. Previous studies in our lab have found that this IRES domain can be bound by guanine, and that this binding changes the conformation of the internal loop. I have synthesized multiple benzene-fused heterocycles, designed around the hydrogen bonding profile of guanine. Many of these heterocycles contain scaffolds already found in approved drugs. Through a FRET based screening method used by the Hermann lab we can determine the binding affinities of these compounds to the target RNA loop. The compounds with strong enough affinities will then be tested through *in vivo* models.

2015 Western Regional Meeting 81

New small molecule α -helix mimetics targeting protein-protein interactions of the human papillomavirus

Elizabeth Kroneberger, ekroneberger@csu.fullerton.edu. Department of Chemistry and Biochemistry, California State University-Fullerton, Fullerton, California, United States

Many cellular processes consist of protein-protein interactions (PPIs), which serve as potential drug targets for various diseases. Many of these PPIs consist of an interface between amino acid residues projecting off of an α -helix. Small molecules have been designed to mimic short amino acid sequences that are crucial for binding to target proteins. Several of these molecules have mimicked only the hydrophobic face of the α -helix, possibly excluding important

interactions arising from polar residues. The Orchard Group has designed novel, amphiphilic, small-molecule α -helix mimics capable of mimicking consecutive amino acid residues on both faces of the helix for treatment of various diseases, such as Human Papillomavirus (HPV) infection. High risk strains of HPV are DNA viruses that infect epithelial cells and can lead to numerous cancers, such as cervical cancer. The HPV E6 oncoprotein allows for survival of infected cells by binding to the human protein E6AP and causing degradation of p53. An inhibitor of the E6-E6AP binding event should allow infected cells to undergo apoptosis, clearing the infection in a non-invasive way. With the support of Molsoft ICM Pro software, we have designed and begun synthesis on a library of potential α -helix mimetics. Herein, we present promising docking results and our proposed synthetic route toward a small subset of compounds capable of mimicking 3 of the 5 residues known to be important for E6 binding while maintaining small drug-like properties. Once synthesis is complete, libraries of compounds will be tested for their ability to cause apoptosis in infected cells as well as their ability to specifically inhibit the E6-E6AP interaction.

2015 Western Regional Meeting 82

Synthesizing redox probes to increase the capabilities of biosensors

Henry Effarah, hheffarah@ucdavis.edu. Department of Chemistry, University of California, Davis, Davis, California, United States

Redox probes are important for transducing signals, such as in applications for biosensor design. This poster presents the design and synthesis of novel redox probes with distinct redox potentials with the goal to apply these probes to differentiate electrical signals and increase the number of different target molecules that can be simultaneously monitored based on redox response. The effects of various derivatives of redox probes are being evaluated with the hypothesis that altering the conjugated system and substituents will affect the redox potential. New redox active molecules have been synthesized and characterized by ^1H NMR spectroscopy and ESI-MS. The redox potential of new derivatives are measured using cyclic voltammetry and several have shown significant variation in redox potential compared to the original probe, providing insight about how altering the conjugated system affects redox potential. In further research, novel derivatives will be conjugated to biomolecules to examine the efficacy and robustness of new redox probes.

2015 Western Regional Meeting 83

Chapters in novel antibiotics: Isolating a natural product of marine bacteria challenged with *Mycobacterium marinum*

Anneke Bulthuis², annekebulthuis@gmail.com, Jacqueline A. Trischman¹. (1) Chemistry & Biochemistry, California State Univ San Marcos, San Diego, California, United States (2) Department of Chemistry and Biochemistry, California State University - San Marcos, San Marcos, California, United States

With the global increase of Multidrug Resistant-TB, increased focus on the purification and characterization of new antimicrobials is urgently needed. The marine environment is relatively unexplored in terms of potential pharmaceuticals. This study examines the metabolites of a marine bacterium, strain UA-461, which was shown to inhibit the growth of *Mycobacterium*

marinum, a close genetic relative of *M. tuberculosis*. The extract had peaks of interest in the NMR spectra that could potentially be the source of the biological activity. The bacterium was grown on a 10L scale, centrifuged, filtered, then placed on a C-18 column. Elution was performed with 1:1 methanol:water (F1), followed by methanol (F2) and then ethyl acetate (F3). NMR analysis showed the Fraction 2A components to contain the interesting material, therefore further purification of these components using HPLC is underway.

2015 Western Regional Meeting 84

3-O-alkyl-2,3-dehydrosilibinins: Synthesis and antiproliferative activity towards prostate cancer cells

Sheng Zhang, *shengzhang2014@mail.fresnostate.edu. Department of Chemistry and Biochemistry, California State University-Fresno, Fresno, California, United States*

Silibinin is a naturally occurring flavonolignan extracted from milk thistle seeds. The cell-based and animal studies have revealed the potential of silibinin in treating prostate cancer. Its good safety profiles as suggested by its long use as dietary supplements and as confirmed by a phase I clinical study make it a better candidate of an anti-prostate cancer chemotherapeutics. However, its drug candidacy is largely compromised by its moderate potency and poor bioavailability. The long term goal of our project is to engineer silibinin derivatives with enhanced potency and bioavailability. We started to explore the optimal functional groups in silibinin for our chemical modifications and to optimize the reaction conditions for our target compounds. As part of this ongoing project, eight 3-O-alkyl-2,3-dehydrosilibinins have been synthesized from commercially available silibinin. The optimized reaction conditions for the synthesis of this group of derivatives have been identified. The structures of the synthesized derivatives have been elucidated based on their 1D and 2D NMR data. Their antiproliferative activity has been evaluated towards both androgen-dependent (LNCaP) and androgen-independent prostate cancer cell lines (PC-3 and DU145) using WST-1 cell proliferation assay. Our findings clearly suggest that 3-OH and C2-C3 in silibinin serve as the optimal functional groups for further structure manipulations, and all synthesized silibinin derivatives possess markedly improved potency as compared with silibinin. The synthesis, structure characterization, and *in vitro* antiproliferative activity will be presented in this poster.

2015 Western Regional Meeting 85

Regulation of vascular mitochondrial plasticity: Role of cellular crosstalk

Consuelo Saucedo, *sauce008@cougars.csusm.edu. California State University San Marcos, San Marcos, California, United States*

Diabetes affects 29 million Americans and it is a leading cause of cardiovascular disease and premature mortality. Diabetes impairs mitochondrial function and turnover. Our lab previously reported that the diabetic blood vessel lacks mitochondrial adaption to stress. Specifically, that mitochondrial function (respiration), mitochondrial turnover and dynamics are less dynamic or plastic in diabetes. This project focuses on the cross talk between two cell types in the blood vessel in order to understand more about the contributors to failed mitochondrial adaptation, plasticity, in the vasculature. We hypothesized that factor(s) secreted by diabetic smooth muscle cells (SMC) would be toxic to endothelial cell (EC) mitochondria and conversely, that factor(s)

secreted by control EC would improve mitochondrial function in SMC isolated from a diabetic model. To test this human umbilical vein endothelial cells (HUVECs) and primary aortic SMC were isolated from control Wistar(W) and diabetic Goto-Kakizaki(GK) rat aorta. Both W and GK cells were treated in control media over a 48-hour period (starvation or fed state). We introduced EC conditioned media (CM) to SMCs and SMC conditioned media to ECs (1,4 and 24 Hr periods) in order to analyze their response, or lack-of, to the cytokines secreted by the cells within the CM and the possible differences in these responses to starvation or fed states. Western blotting and confocal microscopy were employed to define mitochondrial content and plasticity. Endpoints were: mitochondrial content, mitochondrial biogenesis, mitochondrial dynamics, and mitochondrial structure.

2015 Western Regional Meeting 86

Ball milling as an approach to molecular encapsulation

Sara Journey, *sara.journey@aol.com*, Byron W. Purse. Department of Chemistry and Biochemistry, San Diego State University, San Diego, California, United States

Supramolecular chemistry examines the unique capability of large molecules to orient themselves around smaller guest molecules by self-assembly through weak intermolecular forces (e.g. metal coordination and hydrogen bonding). Molecular encapsulation acts as a way to segregate guest molecules within supramolecular capsules for the purposes of sequestration or controlling guest properties such as reactivity. Most of the supramolecular capsules available today quickly entrap guest molecules at thermodynamic equilibrium, meaning that guest molecules can enter and exit the capsule rapidly, thus sampling other species in the surrounding environment. However, capsules that are kinetically stable have a diminished exchange of guest molecules, allowing for more useful sequestration with complete guest isolation.

Pyrogallol[4]arene has the ability to self-assemble through hydrogen bonding to form kinetically stable hexamers by cooling a molten mixture of host and guest. A downside to this approach is that thermal energy input through melting can degrade the guest molecules or the capsule components, limiting the scope of this method. Ball milling is a method that can be used to perform chemical reactions by mechanochemistry, which is the introduction of mechanical energy to induce solid-state reactions, a process that can activate otherwise inaccessible reaction pathways. The hypothesis for this project is that ball milling will generate sufficient mechanical energy to successfully form kinetically stable capsules without the presence of solvent. Stoichiometric amounts of the desired guest molecule and pyrogallol[4]arene were placed into metal chambers with a small ball as a grinding tool and oscillated at 30 Hz for a minimum of 10 minutes to obtain encapsulated complexes as confirmed by ^1H NMR. The percentage of guest encapsulation was tracked over time by removing a sample of ball milled pyrogallol[4]arene hexamers from the chambers periodically and subsequently analyzing them by ^1H NMR. This optimization technique concluded that the capsule components needed to mill for two hours to obtain the greatest percent encapsulation without any material degradation. The data shows unique encapsulation complexes, as compared to the melting method, proving mechanical energy as a successful alternative to other energy sources.

2015 Western Regional Meeting 87

Investigation and review of surrogate parameters to evaluate oxidation of trace organic contaminants during ozonation of wastewater effluents

Rodrigo Tackaert, Rodrigot@trusselltech.com. *Trussell Technologies, Inc., Solana Beach, California, United States*

The presence of trace organic compounds (TrOCs) in wastewater effluents has been of significant concern to the public and water utilities are seeking new approaches for monitoring the removal of such contaminants in advanced wastewater treatment processes. Ozone has been demonstrated as an effective treatment technology for the oxidative removal of many of these contaminants yet lacks an on-line and reliable method to assess and estimate treatment performance in wastewater applications. For this reason, surrogate monitoring has been investigated with encouraging results suitable for regulatory compliance purposes. The objective of this study was to investigate and review two of the most promising surrogate parameters for ozone-based wastewater treatment – differential UV254 (ΔUV254) and total fluorescence (ΔTF). Empirical correlations were developed for both surrogates on a number of TrOCs using three different wastewater effluents and a river-derived water (Isar). Results from in-house experiments were comparable to existing studies with only minor observed divergences. Findings of this study suggest that the use of these surrogates is applicable across different water matrices and may ultimately be used as feedback control parameters to optimize ozone dosages for TrOC oxidation in advanced wastewater treatment and gain instant insight about process stability and efficiency.

2015 Western Regional Meeting 88

Mixed quantum and classical simulation of the hydrated electron: Temperature dependence in resonance Raman spectra, excited states relaxation, and whether the electron resides in a cavity

Chen-Chen Zhou, cc_zhou1991@hotmail.com. *Department of Chemistry and Biochemistry, University of California, Los Angeles, Los Angeles, California, United States*

The structure of hydrated electron has been studied by mixed quantum/classical (MQC) simulations in the past decades, but there's still massive controversy in its structure. Previous pseudopotentials (Schnitker et al. 1987; Turi et al. 2001) are generally highly repulsive and give a cavity-like structure where the electron interrupts the hydrogen bonding of the water molecules, 'digs out' an empty space and resides in it. Our model (Larsen et al. 2010) however suggests a different picture where wave function of the hydrated electron overlaps with several solvent molecules. The cavity and non-cavity models, being the results of different pseudopotentials, behave differently in response to a change of temperature. This work gives some definitive experimental predictions that can help distinguish between the two. Resonant Raman Spectra has been calculated with a semi-classical method, where non-cavity model exhibits a strong temperature dependence while the cavity model does not have significant variation with change of temperature. Non-adiabatic dynamics has also been done to study the excited state relaxation of hydrated electron. The non-cavity model shows a fast relaxation from the excited state and slow ground state cooling, while the cavity model gives a slow relaxation and fast cooling. These two mechanisms result in different features in transient absorption spectra that can be experimentally observed.

2015 Western Regional Meeting 89

Formation and stability of silver nanoparticles formed by the reduction of silver ions by humic acid

Renee Leslie, *reneeleslie96@live.com. Department of Chemistry and Biochemistry, San Diego State University, San Diego, California, United States*

This study investigated the formation and stability of silver nanoparticles (AgNPs) formed from the reduction of silver ions by humic acid in the presence of UV light. The interest in AgNPs comes from an increased concentration of silver ions entering the environment and whether or not these ions can be reduced by humic acid to form stable nanoparticles. This study shows that silver nanoparticles can form in a solution of silver nitrate and humic acid in the presence of UV light. The rate of AgNP growth increased linearly as the concentration of humic acid or silver nitrate was increased. The rate of formation also increased linearly with the addition of ferric nitrate. AgNP growth was monitored by UV Vis and AgNP size was monitored by dynamic light scattering. This study demonstrates the potential for silver ions to reform nanoparticles which can disrupt sensitive ecosystems.

2015 Western Regional Meeting 90

Oxidative cyclization reactions of benzaldehyde oximes with built-in heteroaromatic nucleophiles

Abdullah A. Alshreimi, *aalshreimi@csu.fullerton.edu. Department of Chemistry and Biochemistry, California State University-Fullerton, Fullerton, California, United States*

The development of new and convenient methodologies for the efficient synthesis of heteroaromatic ring systems remains an area of high interest. Oxidative cyclizations with radical or radical ion intermediates are potentially useful strategies to achieve these types of cyclizations. Based on previous results from our group, would be susceptible to intramolecular nucleophilic attack whereas radicals would preferentially react with built-in radical traps. Our research has focused on evaluating different groups in terms of their nucleophilicity or radical trap ability when built into the oxime derivative at a strategic location. The oxime derivatives were subjected to photooxidation or thermal oxidation in different solvents and the product formation was followed by GC/MS and NMR. Oxime ethers with built-in aromatic groups were found to undergo a cyclization reaction yielding phenanthridines. Mechanistic studies are consistent with a pathway that involves the aromatic ring acting as a nucleophile, attacking the nitrogen of the oxime ether radical cation.² methodology is potentially useful for the synthesis of heterocyclic structures if it can be expanded to involve aromatic nucleophiles that can contain additional heteroatoms such as nitrogen, oxygen, or sulfur. We have prepared a series of pyridinyl, furanyl, and thiophenyl-substituted benzaldehyde oximes to determine whether it is possible to use these heteroaromatic ring systems as nucleophiles. Preliminary results suggest that under the PET conditions used for our previous studies, cyclization does not occur. We hypothesize that the heteroaromatic rings are activated as a result of the presence of the heteroatom and therefore less reactive similar to aromatic rings with strong electron-donating groups. Other methodologies to achieve the desired cyclization reactions such as direct photolysis and metal-catalyzed cyclization reactions of the oximes, oxime ethers and oxime esters will be considered next. The results from these reactions will be presented and discussed.

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2015 Western Regional Meeting 91

Antimycobacterial ceramides produced by a marine surface bacterium

Jacqueline A. Trischman, **Gbegninon Allognon**, allog001@cougars.csusm.edu, Anneke Bulthuis. Chemistry & Biochemistry, California State Univ San Marcos, San Diego, California, United States

A strain of marine bacterium (strain UA 088) was isolated from the surface of a marine alga. When cultured, UA088 was challenged by introducing another marine bacterium, *Mycobacterium marinum*, that coexists naturally in the same habitat. This challenge technique induced the production of secondary metabolites by UA088 that inhibited mycobacterial growth. Differences could be observed on the ^1H NMR of the challenged strain (UA 088C) versus the non-challenged strain (UA 088). The secondary metabolites were isolated for further analysis through solid phase extraction on a C-18 column and the HPLC was used for further purification. After performing the ^1H NMR on the fractions with the most growth-inhibition activity, it was discovered that the secondary metabolites have a ceramide like components.

2015 Western Regional Meeting 92

Catalytic anhydride-Mannich reactions of *N*-sulfonyl imines

Stephen W. Laws³, swlaws@ucdavis.edu, Michael J. Di Maso², Jared T. Shaw¹. (1) Dept Chemistry, UC Davis, Davis, California, United States (2) University Of California At Davis, Davis, California, United States (3) Chemistry, University of California, Davis, Davis, California, United States

Herein we describe our progress toward the development of a catalytic, diastereo- and enantio-selective anhydride-Mannich reaction (AMR) for converting cyclic, enolizable anhydrides and *N*-sulfonyl imines to substituted γ - and δ -lactams. Reducing imine basicity by *N*-sulfonyl protection eliminates uncatalyzed background AMR rate and creates the opportunity for restored activity in the presence of an added base. Achiral bases have been demonstrated as capable AMR mediators and catalysts, producing a wide variety of γ - and δ -lactams in high yield and diastereoselectivity. An extensive screen of basic asymmetric organocatalysts in a model AMR has led to good diastereo- and enantio-selectivities. This new catalytic methodology has also contributed to our progress towards the diastereo- and enantio-selective total synthesis of anti-tumor natural product 7-deoxypancratistatin.

2015 Western Regional Meeting 93

Structural study of isotopically modified antifreeze glycoproteins (AFGPs) using high-resolution nuclear magnetic resonance (NMR) spectroscopy

Cheenu Her³, cheenuher09@mail.fresnostate.edu, Sal Vazquez³, Santanu Maitra², Krish V. Krishnan¹. (1) California St Univ Dept Chem, Fresno, California, United States (2) Chemistry

Dept MS SB 70, California State University Fresno, Fresno, California, United States (3)
California State University, Fresno, Fresno, California, United States

Intrinsically disordered protein (IDP) resembles the denatured states of ordered proteins, best described as an ensemble of rapidly inter-converting alternative structures, which, nevertheless, is their native, functional state. Their function is realized via molecular recognition in which structural disorder confers specific advantages, such as increased speed of interaction and specificity without excessive binding strength. Antifreeze glycoproteins (AFGPs) are intrinsically disordered proteins. The ice-crystal growth inhibition property of AFGPs is crucial for the survival of certain Arctic and Antarctic fishes in subzero temperature. The primary structure of AFGPs consist of a number of repeating tri-peptide sequence of (Ala-Ala-Thr*)_n in which the Thr* is glycosylated with the disaccharide *beta-D-galactopyranosyl-(1-3)-2-acetamido-2-deoxy- α -D-galactopyranose*. We hypothesize that the inherent flexibility of AFGP to be disordered is closely coupled to its function.

Nuclear magnetic resonance (NMR) spectroscopy provides a powerful option to investigate the dynamics of proteins in the solution state. As the AFGPs behave as IDPs in the solution state, there is a significant overlap of resonance peaks in the proton (¹H) NMR spectrum even at high magnetic fields. To overcome this problem, we isotopically modified the N-terminus of AFGPs with two NMR active carbon-13 (¹³C) labeled methyl groups to increase the sensitivity of the carbon spectrum (natural abundance of ¹³C is ~1%). NMR based dynamic of the chemically modified AFGPs in pure DMSO-d₆, pure D₂O, and a mixture of the two solvents will be measured with respect to the ¹³C-labeled methyl groups using modern NMR methods. The NMR measurements are expected to provide a comprehensive view of the role of AFGPs as they function to keep the water 'cool' even at ice forming temperatures.

2015 Western Regional Meeting 94

Development of molecular photoswitches as MRI contrast agents

Andrea Faulkner², alfaulkner@ucdavis.edu, Edward I. Balmond¹, Brandon K. Tautges¹, Blanka M. Hodur¹, Jared T. Shaw¹, Angelique Louie³. (1) Dept Chemistry, UC Davis, Davis, California, United States (2) University of California - Davis, Davis, California, United States (3) 2303 Genome and Biomedical Sci Facilities, University of California - Davis, Davis, California, United States

Monitoring gene expression in deep tissues is a critical issue that must be addressed to further develop new therapeutic techniques, such as stem cell transplantation. While current imaging modalities may possess shortcomings such as limited depth of visualization and inhibition of normal cell function, MRI is relatively non-invasive and can penetrate deep tissues. We aim to develop a light activated gadolinium contrast agent that responds to a bioluminescent gene reporter that is expressed concurrently with a gene of interest. Light emitted from luciferase will cause a structural change in the probe, enabling it to be monitored using MRI. To determine an optimal probe, various photoswitch architectures will be incorporated into a contrast agent. The photoswitching capabilities of spiropyran and spirooxazine are known and have been well studied. However, there have been no systematic study and comparison on how the electronic properties of substituents effect the photoswitching of these compounds. A matrix of spiropyran and spirooxazines was synthesized in which electron donating and withdrawing groups were varied and incorporated on either side of the photoswitches. This would enable us to elucidate

the electronic effects of photoswitching and directly compare spiropyrans to spirooxazines. Herein, synthetic efforts to access spiropyran and spirooxazine photoswitches are described.

2015 Western Regional Meeting 95

First semester general chemistry undergraduates' ability to distinguish variables in the experimental design of a stoichiometry activity in structured and guided inquiry modes

Eric Hoong, *ehoong719@csu.fullerton.edu*. Biochemistry, California State University Fullerton, Fullerton, California, United States

The ability to distinguish between experimental variables is crucial to understanding experimental design in college chemistry laboratory experiments. General chemistry laboratory experiences vary from verification, structured, guided to open inquiry formats. This study seeks to determine whether structured or guided inquiry lab experience is more effective for learning the concepts of experimental design, specifically the distinction between independent, dependent, controlled and ancillary variables. Responses from three different components of a stoichiometry laboratory, a pre-lab assessment, interim assessment, and post lab report from a total of 498 college students in general chemistry over three semesters were analyzed. The structured inquiry (SI) mode took place all three semesters (n=452). The guided inquiry (GI) format took place only in the third semester (n=46). The research questions probed in this study were: 1) Is there a statistically significant difference between students who experienced SI and GI laboratory formats in their ability to correctly identify: a) independent variables; b) dependent variables; c) control variables; d) ancillary variables? 2) Is there a statistically significant difference between the SI and GI groups in: a) mean lab report score; and b) total weighted lab points earned? The results show that there was no statistically significant difference in the ability to correctly identify independent, dependent, controlled and ancillary variables by the inquiry format. At least 60% of the students in both SI and GI formats were able to identify a dependent variable correctly. Students in both SI and GI groups had difficulty identifying independent (57%, 57%) controlled (58%, 51%), and ancillary (44%, 50%) variables. There was no statistically significant difference in mean lab scores or total weighted lab scores by inquiry format. Further analyses of qualitative data from student entries in laboratory notebooks and focus group interviews may assist in enriching our understanding of why experimental design is difficult and how inquiry approaches may play a role.

2015 Western Regional Meeting 96

Fabrication of wafer-scale, low resistance, single carbon nanotube devices

Arith Rajapakse¹, *arajapak@uci.edu*, **Philip G. Collins**². (1) Department of Physics and Astronomy, California State University - Long Beach, Long Beach, California, United States (2) University of California, Irvine, California, United States

The remarkable physical properties of carbon nanotubes (CNTs) have captivated nanoscience researchers since their discovery. In particular, their high current density and thermal conductivity make CNTs ideal conductors and semiconductors for nanoelectronics. In the Collins Research Group at UC Irvine, single CNT devices are utilized as field effect transistors to measure the activity of proteins such as lysozymes or DNA polymerase I on a single molecule scale. Despite the abundance of single CNT research, a primary challenge facing CNT-based

electronics remains the fabrication of clean, single CNT devices on a wafer-scale. This project explores new CNT synthesis and device fabrication methods that aim to produce high quality CNT devices with wafer-scale reproducibility in order to enable arrays of single molecule measurements. Specifically, the project combines a number of best practices developed by CNT experts worldwide, novel growth recipes developed at UC Irvine, and a sophisticated synthesis apparatus critical for achieving reproducible results. Acceptable device resistance, CNT noise, gate leakage and hysteresis can each be achieved with appropriate fabrication methods, and in this project these methods are being combined to efficiently produce clean, low-resistance CNT devices across 4" wafers.

2015 Western Regional Meeting 97

Conformational equilibrium dynamics of β -methyl-amino-L-alanine (BMAA) and its carbamate adducts using NMR spectroscopy

Aaron Alonzo, apalonzo@mail.fresnostate.edu. Department of Chemistry and Biochemistry, California State University - Fresno, Fresno, California, United States

The modified amino acid, β -methyl-amino-L-alanine (BMAA), is associated with the elevated incidence of the amyotrophic lateral sclerosis/Parkinsonism dementia complex (ALS/PDC). BMAA exhibited activity only in the presence of bicarbonate ions (HCO_3^-) at physiological concentrations and therefore the interaction is to play a critical role in the modality of BMAA's role in excitotoxicity. The interaction of BMAA and HCO_3^- leads to the formation of BMAA in its carbamylated forms (primary and secondary carbamate adducts). Furthermore, our recent research discovered that at physiological conditions, the BMAA and its primary and secondary adducts coexist in solution and undergo conformational exchange, which could be essential in order to address questions related their neuroactive potency.

Following the hypothesis that altering the nature of the cation in the solution may alter the equilibrium process, a comprehensive structure-mechanism study using high-resolution nuclear magnetic resonance (NMR) spectroscopy at equilibrium conditions is presented. The equilibrium dynamics of BMAA with different bicarbonate solutions are investigated: sodium bicarbonate, potassium bicarbonate, cesium hydrogen carbonate, and ammonium bicarbonate. In addition to following the chemical equilibrium process as a function of time, NMR chemical shifts and intensities are used to determine the structure and population of each species. Conformational exchange process is measured using NMR based two-dimensional exchange spectroscopy (EXSY) and exchange constants were measured for all the experimental conditions. Our results suggest the ionic contributions to the adduct formation may follow Hoff Meister series of ions that based on the 'salting' interaction occurs between the water molecules and the BMAA.

As our results suggest, BMAA may exert multiple modes of neurotoxic activity via formation of multiple adducts that coexist at physiological conditions, which we will be able to more accurately evaluate and assess the human health risks posed by exposure to this cyanotoxin.

2015 Western Regional Meeting 98

Analysis of mercury concentration in three common cigarette brands sold in the United States as a viable source of human exposure

Samantha Freitag², samantha.freitag375@myci.csuci.edu, **Simone Aloisio**¹. (1) California State University, Camarillo, California, United States (2) Department of Chemistry and Biochemistry, California State University-Channel Islands, Channel Islands, California, United States

Cigarette smoke inhalation exposes individuals to thousands of different substances including carcinogens and toxic metals such as mercury. Previous studies have been performed on mercury concentrations in cigarettes, but very few recent ones in the United States. According to the CDC, nearly 17.8% of adults in the United States smoke cigarettes today making tobacco a possible source of human exposure to mercury. The top two brands sold in the US, Marlboro and Newport, were studied both regular and menthol varieties. The organic American Spirit brand was also studied. This data was gathered through the techniques of Thermal Decomposition, Amalgamation, and Atomic Absorption Spectroscopy. This study of 24 cigarettes found an average value of 15 (± 1.3) ppb (ng/g) of mercury concentration in each cigarette. The average concentrations in ppb found in the Marlboro, Newport, and Newport Menthols were 16 (± 1.0), 14 (± 1.4), and 14 (± 1.1) respectively. This is a 15% increase from a 2008 study of mercury concentration in cigarettes that found an average of 13 (± 1.3) ppb Hg in a whole cigarette out of 30 samples on three different non-specified brands. Implications of these findings will be discussed. Further studies on human Hg level changes after smoking cigarettes would indicate if cigarette smoking is a reasonable pathway for mercury accumulation. The addition of electronic cigarettes to the market in recent years provides another area to investigate possible mercury exposure risks to humans.

2015 Western Regional Meeting 99

A lanthanum(III)-catalyzed multi-component reaction for the synthesis of substituted malonamides with interesting photophysical properties

Julia Jennings, jjjennings@ucdavis.edu, **Chinmay P. Bhatt**, **Annaliese K. Franz**. UC Davis, Davis, California, United States

We have discovered a new class of fluorescent molecules that can be prepared using an efficient lanthanum(III)-catalyzed multi-component reaction (MCR) of coumarin-3-carboxylates with amines and indoles, resulting in densely-functionalized malonamides. The mechanistic details of the multi-component reaction have been explored. The mechanism proceeds first through addition of the nucleophile to the coumarin-3-carboxylate, followed by amidation of both the methyl ester and the cyclic ester to afford an indolyl-malonamide with a phenol revealed upon opening of the cyclic ester. The range of catalysts has been investigated and different metals have been identified as effective catalysts for the MCR compared to the individual reactions when performed in a step-wise manner. In addition to indoles, we have demonstrated the Lewis acid-catalyzed addition of methallylsilane and *N,N*-dimethyl-*m*-anisidine to coumarin-3-carboxylates. The addition reactions proceed under mild conditions and the resulting 4-substituted chromanones are observed in high yields and excellent diastereoselectivities. The photophysical properties of the new malonamide products will be discussed.

2015 Western Regional Meeting 100

Effect of the overlap between the vertical ionization energies and the adiabatic ionization energies of DNA nucleobases

Hwoi . Kwon, hwckwon@puc.edu, Kieffer G. Bacani, Vola Andrianarijaona. CSMP, Pacific Union College, Angwin, California, United States

The ionization energies (IE) of the four nucleotides of DNA were intensively investigated during the last two decades because DNA ionization is considered as the number one cause of DNA damage. Both theoretical and experimental results systematically show that guanine has the least IE. Nevertheless, there was no true consensus on the measured and calculated values. Special attentions were given to the calculations and measurements of vertical IE and adiabatic IE. It is generally accepted that the difference between the vertical IE and the adiabatic IE of each nucleotide is significant. Vertical ionization and adiabatic ionization have a certain overlap, which is often relatively narrow for bigger molecules. But, even so, the ionization process that can take place in the overlap will affect the theoretical calculations which therefore will disagree with the experimental results. To calculate the IEs, we computed the potential curves of the cations while it still has the geometry of the neutral nucleotide even though the final geometry of cation is usually very different from the neutral one. Indeed, the simplest ionization scenario consists of a relaxed neutral nucleotide which lost one of its electron giving birth to a cation, which, thereafter, will evolve to its relaxed configuration. Considering each atom of the basis as a possible site of the departing electron, we were doing a systematic DFT-based computational calculations of potential curves in the three directions around the active site. These potential curves give a pretty good insight on the potential surface, which is not accessible yet due to the size of the molecule and the memory required. For each potential calculation, we assume that all atoms are frozen during the ionization, but the position of the atom at the hole site is virtually changed in the considered direction. The results are reported in this poster.

2015 Western Regional Meeting 101

Development of separation and detection method for chemotherapeutic drugs

Karno Ng, kng@csusm.edu. Department of Chemistry & Biochemistry, California State University San Marcos, San Marcos, California, United States

Phenytoin is a drug commonly used to treat seizure disorder. It has a narrow therapeutic window. Some patients receiving chemotherapy experienced side effect that resulted in seizures. Thus, phenytoin is commonly prescribed along with chemotherapy drugs such as methotrexate and dexamethasone. The side effect of seizure as a result of chemotherapy is particularly pronounced among brain tumor patients. Previous studies have shown that dexamethasone caused a decrease in phenytoin concentration in patients who took both drugs simultaneously. Methotrexate exhibits the same effect on phenytoin as well. Previous studies have also shown that dexamethasone decreases the efficacy of methotrexate *in vitro*. Due to the various interactions among these 3 drugs, it is essential to be able to separate and detect them simultaneously. The purpose of this study is to develop an efficient separation and detection method to separate these 3 drugs.

2015 Western Regional Meeting 102

Sensitive detection of nicotine and its metabolites by laser wave-mixing spectroscopy for second- and third-hand smoke studies

Zarina Munshi², *zarina.munshi@gmail.com*, Jean S. Pradel³, William G. Tong¹. (1) San Diego State University, San Diego, California, United States (2) Department of Chemistry and Biochemistry, San Diego State University, San Diego, California, United States

Ultrasensitive detection methods for nicotine and its major metabolites are needed in order to reliably study first-, second- and third-hand smoke effects on children. We demonstrate laser wave-mixing spectroscopic methods as sensitive, inexpensive, portable, compact detectors suitable for field use for a wide range of applications in environmental and biomedical fields. Reliable sensitive detection of nicotine is essential to track and understand numerous health and psychological effects caused by first-, second- and possible third-hand smoking. Our results indicate that nicotine and cotinine can be detected and separated in their native forms label-free using a 266 nm UV laser or a visible laser if a label is used. In a typical laser wave-mixing setup, the input laser beam is split into two input beams and then focused and mixed inside the sample cell. Since the signal is a coherent laser-like beam, it can be collected by a simple photodetector with excellent signal-to-noise ratio (S/N). wave mixing only requires a small amount of sample (nanogram), and hence, it can be conveniently interfaced to microarrays, microfluidics, chip-based capillary electrophoresis and other flow systems to yield excellent chemical specificity and detection sensitivity levels (picomolar or femtomole). Potential applications include separation of trace nicotine metabolites, and detection of biomarkers, monitoring of environmental samples and early detection of diseases.

Acknowledgment: We acknowledge partial support of this work by the NIH (R01), NIH NIHGMS IMSD (2R25GM058906), NSF, DoD, Army, DHS, Lockheed Martin and Johnson and Johnson.

2015 Western Regional Meeting 103

Development of an analytical method for quantifying chemical tracers associated with livestock activities

David Ricci, *dricci531@gmail.com*, Justin Miller-Schulze. Chemistry, California State University, Sacramento, Antelope, California, United States

An analytical method has been developed to quantify a suite of potential chemical tracers for agricultural runoff in surface and ground water. Environmental concentrations of these tracers range from about 1-100 ng/L. The concentrations of ceftiofur (non-human antibiotic), clindamycin (human and animal antibiotic), erythromycin (human and animal antibiotic), fenbendazole (animal deworming antibiotic), lincomycin (cattle and poultry antibiotic), trimethoprim (human and animal antibiotic), and tylosin (non-human antibiotic) can currently be extracted from deionized water and spiked river water samples with corrected recoveries between 70-120%. The application of this method will be as a potential source tracking tool for bacterial pollution, allowing the investigation of bacterial pollution by agricultural practices. Samples were spiked with a known amount of each tracer and a known amount of isotopically labeled recovery standard (d3-fenbendazole, d6-erythromycin, d3-lincomycin, and d3-trimethoprim), acidified with sulfuric acid, and EDTA was added in order to prevent any metals in the sample from complexing with tetracycline compounds. Samples were then filtered and extracted by solid phase extraction. The antibiotics were eluted from the cartridges with methanol, evaporated, reconstituted in methanol and water, and finally analyzed by HPLC-MS/MS (triple quadrupole). Because the final extract volume was 200 μ L, concentrations in the collected samples were increased by a factor of 5,000 from collected water to sample extract.

The limit of detection ranged from 1 ng/L for trimethoprim to 25 ng/L for erythromycin, allowing for quantification of these antibiotics at environmentally relevant levels.

2015 Western Regional Meeting 104

Development of paper- and thread-based microfluidic assays for point-of-care (POC) diagnostic devices

Frank A. Gomez, *fgomez2@calstatela.edu*, Lissette Estala, Mary Arrastia, Ani Avoundjian, Ariana Gonzalez, Coreen Gallibu, Chrisha Gallibu. Chemistry and Biochemistry, California State University, Los Angeles, Los Angeles, California, United States

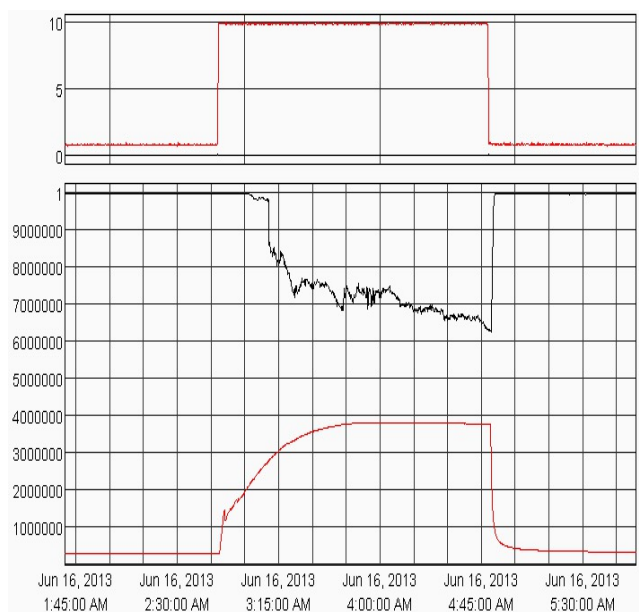
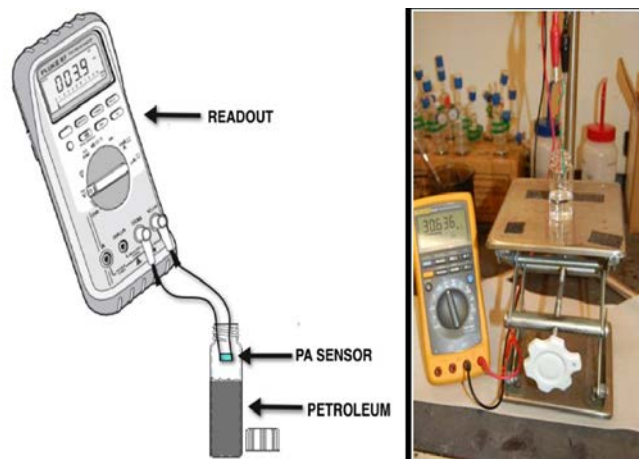
Microfluidic technologies have made great strides in the areas of bioanalysis, healthcare, medicine, and point-of-care (POC) diagnostics. Paper and thread-based microfluidics are a burgeoning area whose potential has only recently been tapped. Both paper and thread are natural platforms for microfluidic-based applications mainly due to their availability, low cost, and ability to wick aqueous fluidics allowing for facile transport of fluidics without the use of active pumping. Furthermore, they are available in a variety of thicknesses, lightweight, easy to stack, store, and transport, are compatible with biological samples given their composition, available in white thereby amenable for colorimetric tests, and available in many forms with a diverse range of properties. Herein, we describe several enzyme assays and other colorimetric tests using paper and thread as platforms demonstrating the efficacy of the technology. For example, a glucose assay employing glucose oxidase (GOX), horseradish peroxidase (HRP), and KI is demonstrated on microfluidic paper analytical devices (mPADs) fabricated from a wax printer and Sharpie permanent markers as well as a thread-based microfluidic device. The use of these technologies in the POC diagnostic sector holds great promise for home healthcare.

2015 Western Regional Meeting 105

Sensor for the detection of petroleum analytes in air and aqueous environments

Stephen T. Hobson, *sthobson@seacoastscience.com*. Seacoast Science Inc, Carlsbad, California, United States

Detection and quantification of petroleum products is crucial for environmental, safety, and security applications. A sensor platform for the detection of oil & gas analytes displayed impressive performance in the vapor phase and/or as dispersions/solutions in water. Changing either sensor geometry or polymer/conductive particle selection resulted in dramatic effects on the sensor performance (sensitivity, response speed, sensor recovery/hysteresis). Sensors were prepared by coating suspensions of conductive particles/polymers or by vapor-phase polymerization of pyrrole onto a FeCl₃/perfluoroalkyl silsesquioxane matrix. In the presence of saturated toluene vapor, one sensor structure displayed a 1000x signal increase in less than 30 seconds. Change in the polymer structure resulted in a sensor with a 250 fold signal decrease upon exposure to saturated THF vapor. With material modifications, the sensor also responded to the presence of polar and non-polar compounds in aqueous solution/suspension. The sensor displayed impressive resiliency after exposure to extreme temperatures and relative humidities. Upon optimization, the sensors have multiple applications in disparate industries.



2015 Western Regional Meeting 106

Applications of nuclear magnetic resonance spectroscopy in nanomaterials characterization

Chengchen Guo², daniel_guo1226@hotmail.com, Jeffery L. Yarger¹. (1) Dept Chemistry Biochemistry, Arizona State University, Tempe, Arizona, United States (2) Dept of Chemistry and Biochemistry, Arizona State University, Tempe, Arizona, United States

Nanostructures have attracted considerable attention in recent research due to their wide applications in various fields such as material science, physical science, electrical engineering, and biomedical engineering. Researchers have developed many methods for synthesizing different kinds of nanostructures, where the sizes and surface chemistry of the nanostructures are considered to be the two key factors. Traditionally, the sizes of nanostructures are determined by electron microscopy while the surface chemistry is characterized by optical spectroscopies such as IR spectroscopy and Raman spectroscopy. Compared with that,

Nuclear Magnetic Resonance (NMR) spectroscopy provides a more advanced and convenient way for size determination and surface chemistry characterizations by combining one and multiple dimensional NMR spectroscopy and diffusion-order NMR spectroscopy. NMR spectroscopy is a powerful tool for obtaining structural information of materials at molecular/atomic level and it has been frequently used in synthetic chemistry and molecular biology. Here, we showed a proof-of-concept that NMR spectroscopy can be applied to determine the sizes of several common nanoparticles such as thiol-protected gold nanostructures and protein protected nanostructures that have already been demonstrated to have wide applications in different areas. We also established a solid protocol for people to use NMR spectroscopy to characterize sizes and surface chemistry of nanostructures.

2015 Western Regional Meeting 107

Purification and characterization of the *Drosophila melanogaster* (Dm) IκKβ/IκKy complex

W Eric Rogers^{1,2}, rogers85748@gmail.com, Tom McDowell¹, Tom Huxford¹. (1) Chemistry, San Diego State University, San Diego, California, United States (2) Chemistry, University of California-San Diego, La Jolla, California, United States

Inhibitor of KappaB Kinase (IKK) is a major regulation point in the activation of innate immunity. The kinase subunit of the complex has undergone extensive study including biophysical and structural characterization. The IKK complex that includes the regulatory subunit has been extremely difficult to study due to its inherent instability, and propensity to aggregate. Here we present initial purification and characterization of an IKK complex from *Drosophila melanogaster*. This two component system is the *in vivo* functional unit and composed of a kinase (IKKβ) and a regulatory subunit (IKKy).

2015 Western Regional Meeting 108

Structural study of prolonged NF-κB responses regulated by IκBβ

Thuy Dung T. Nguyen, ellie.d.nguyen@gmail.com, Tom Huxford. Chemistry and Biochemistry, San Diego State University, San Diego, California, United States

NF-κB (Nuclear Factor kappa B) is homo- or heterodimer protein complex. It was characterized as a transcription factor because when bound to DNA, it activates the transcription of genes. NF-κB controls the activation of genes that is responsible for cell growth, cell death, and the immune system. NF-κB is also a first responder to harmful cellular stimuli. However, persistent activation of NF-κB has been linked to many diseases like cancer, autoimmune diseases, and etcetera.

IκB (Inhibitors of kappa B) is a group of proteins that is responsible for regulating NF-κB activity. IκB binds to NF-κB, keeping it inactive in the cytoplasm. Under stimuli effect, IκB is destroyed, NF-κB is freed from the control of IκB and will enter the nucleus, turning on transcription to respond to the stimuli.

The IκB family of proteins consist of 3 members: alpha, beta and epsilon. These proteins are characterized by the presence of alkryn (ANK) repeats, which mediate binding of IκBs to the NF-κB family of proteins. Structure and mechanism of IκB alpha are well characterized why IκB beta mechanism still remain unclear. My research goal is elucidating the mechanism of IκB beta. It's significant because drugs against NF-κB are reputed to be anti-cancer drugs, thus the

more we know about the inhibitor of NF- κ B, the better chance we have to develop anti-cancer drugs.

It's hypothesized that the difference in the abilities of I κ B alpha and I κ B beta to disrupt NF- κ B:DNA complex are phosphorylation-dependent. According to unpublished data of Dr. Sankar Ghosh, Serine346 of I κ B beta is a potential site that responsible for this difference. Serine346 of I κ B beta was mutated to either Alanine or Glutamic Acid. *In vitro* kinase assays, MALDI-MS, LC-MS were used to study three versions of I κ B beta protein: WT, S346A, S346E.

2015 Western Regional Meeting 109

Biophysical characterization of reflectin isoforms from squid and cuttlefish

Long Phan², longp1@uci.edu, Ward G. Walkup², David D. Ordinario², Yegor van Dyke², Alon A. Gorodetsky¹. (1) Chem Eng Mtrl Sci, University of California, Irvine, Irvine, California, United States (2) Chemical Engineering and Materials Science, University of California, Irvine, Irvine, California, United States

Cephalopods are well known for their remarkable camouflage abilities; they can modify their coloration, texture, pattern, and reflectivity to blend into the surrounding environment. Such dazzling camouflage abilities are partially enabled by specialized intracellular nanostructures that are composed of a unique structural protein known as reflectin. We have developed high throughput protein expression and purification strategies for the isolation of reflectin isoforms from the cephalopod species *L. pealei* and *E. scolopes*.¹ We have performed extensive biophysical characterization of these proteins, discovering that they possess common yet unique optical and electrical properties, including protonic conductivities that are on par with state-of-the-art artificial materials.² Our findings may hold implications for not only better understanding the mechanisms that cephalopods employ to dynamically control their coloration but also for the development of bioinspired proton conducting materials.

1. Phan, L.; Walkup IV, W. G.; Ordinario, D. O.; Karshalev, E.; Jocson, J.-M.; Burke, A. M.; Gorodetsky, A. A. *Adv. Mater.* **2013**, 25, 5621-5625.

2. Ordinario, D. D.; Phan, L.; Walkup IV, W. G.; Jocson, J.-M.; Karshalev, E.; Hüsken, N.; Gorodetsky, A. A. *Nat. Chem.* **2014**, 6, 596-602.

2015 Western Regional Meeting 110

An *in-vitro* sample generation strategy for single-molecule spectroscopy

Kambiz M. Hamadani¹, khamadani@csusm.edu, Susan Marqusee³, Peng Wu⁴, Jamie Cate². (1) Chemistry and Biochemistry, California State University San Marcos, San Marcos, California, United States (2) Chemistry, University of California, Berkeley, California, United States (3) Molecular and Cellular Biology, University of California, Berkeley, Berkeley, California, United States (4) Dept of Biochemistry, Albert Einstein College of Medicine, Bronx, New York, United States

Single-molecule methods access information-rich yet transient biomolecular species which are challenging to detect using ensemble techniques. The ability to screen large biomolecular libraries with single-molecule sensitivity for such transient species and phenotypes can uniquely enable the *in-vitro* engineering of dynamic bioconformational properties like robust folding,

allostery, biocatalysis, or conformational heterogeneity. While fluorescence-based single-molecule detection platforms are well-suited to such applications, methods for the *generation* and *screening* of large libraries of dye-labelled proteins are currently lacking. Here, we combine purified and reconstituted in-vitro translation, robustly-quantitative unnatural amino acid incorporation via sense codon reassignment, and highly-efficient strain-promoted or copper-catalyzed azide-alkyne cycloaddition to begin addressing both of these bottlenecks. We present an off-the-shelf, purification-free, and parallelizable in-vitro approach to generating dual-labeled proteins and ribosome-nascent-chain (RNC) libraries suitable for single-molecule FRET (smFRET)-based structural phenotyping. Using this approach we achieve sample generation throughputs which exceed the screening throughputs of non-parallelized single molecule detection platforms. Importantly, dual-labelled RNC libraries enable single molecule colocalization of genotypes with phenotypes. This enables highly-multiplexed as well as parallelized single molecule screening within zero-mode-waveguides. Such an approach to high-throughput single molecule screening will enable the in-vitro directed evolution of proteins with designer single molecule phenotypes.

2015 Western Regional Meeting 111

Using QM/MM to guide the engineering of an artificial haloperoxidase

Gregory Anderson¹, ganderson@bvinst.edu, Ravi Gomatam^{1,2}, Raghu N. Behera³. (1) Bhaktivedanta Institute, Berkeley, California, United States (2) Institute of Semantic Information Sciences and Technology, Berkeley, California, United States (3) Department of Chemistry, Birla Institute of Technology and Science, Pilani, K. K. Birla Goa Campus, Zuarinagar, Goa, India

Vanadium chloroperoxidase (VCPO) catalyzes the electrophilic chlorination of substrate in the presence of hydrogen peroxide. The X-ray crystal structure of VCPO reveals an active site with possible protonation states, **1-3** (Figure 1).¹ Vanadium can be removed by dialysis using phosphate and then reincorporated.² Using a combination of quantum mechanics (ie., DFT/B3LYP) applied to the active site and molecular mechanics (OPLS) as implemented in QSite³, we wish to predict whether replacing the vanadium of VCPO with niobium will result in an active enzyme.

The resting state of VCPO as well as of the niobium substituted VCPO was determined by geometry optimizations on each of the possible structures (**1-3**), and we found that the resting state of natural VCPO is **2-V** while the resting state of niobium substituted VCPO is **3-Nb**. The first step in the catalytic cycle involves protonation of **2-V** to yield **4-V**, and we find that protonation of **3-Nb** still yields a structure **4-Nb** which is lower in energy than **3-Nb**. Hence, we conclude that the first step in the catalytic cycle of a niobium substituted VCPO is favorable.

¹Macedo-Ribeiro, S.; Hemrika, W.; Renirie, R.; Wever, R.; Messerschmidt, A. *J. Biol. Inorg. Chem.* **1999**, *4*: 209-219; Protein Data Bank ID# 1VNI.

²Tracey, A.S.; Willsky, G.R.; Takeuchi, G.R. *Vanadium: Chemistry, Biochemistry, Pharmacology and Practical Applications*; CRC Press: New York, 2007, p. 162.

³QSite, version 6.7, Schrödinger, LLC, New York, NY, 2015.

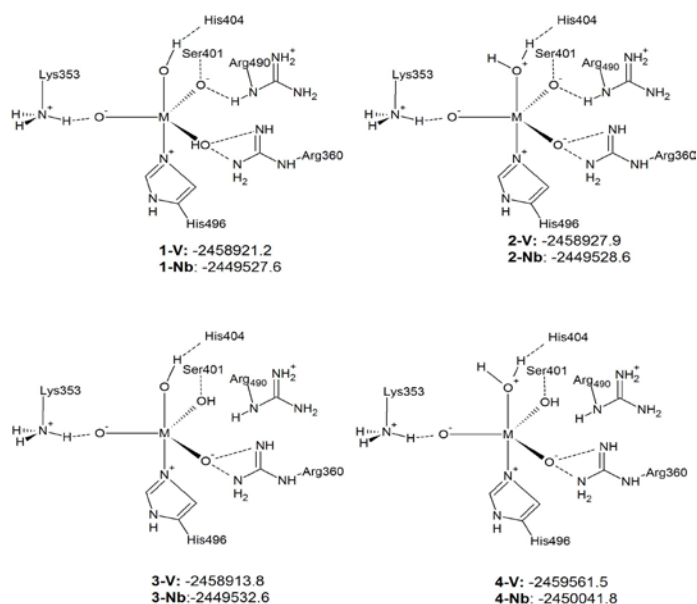


Figure 1. Structure **1-3** are various possibilities for the resting state of VCPO or niobium substituted VCPO. Structure **4-V** or **4-Nb** results from protonation of **2-V** or **3-Nb**, respectively.

2015 Western Regional Meeting 112

Design of self-assembling RNA nanotriangles from crystal structures

Mark A. Boerneke, markb2u@hotmail.com, Sergey Dibrov, Thomas Hermann. Chemistry & Biochemistry, University of California, San Diego, La Jolla, California, United States

Nucleic acid can be used to build nano-sized objects designed to assemble by specific base pair interactions. RNA structural motifs observed in crystal structures have been incorporated into complex nano-objects. Ligand-responsive RNA switches have been shown to form stable bent conformations. Here we describe the crystal structure-guided design and construction of highly stable RNA nanotriangles that self-assemble from short oligonucleotides, including the high resolution x-ray crystal structure of an RNA nanotriangle containing 81 nucleotides which was determined at 2.6 Å and forms the smallest yet circularly closed double-stranded RNA nano-object. Incorporating ligand-responsive switches as the corner units in these nanotriangles makes them tunable and allows for their dissociation in response to binding ligands. The unique structural features of these nanotriangles promise applications in medicine, nanomaterials engineering, and as tools to test nanoscale phenomena.

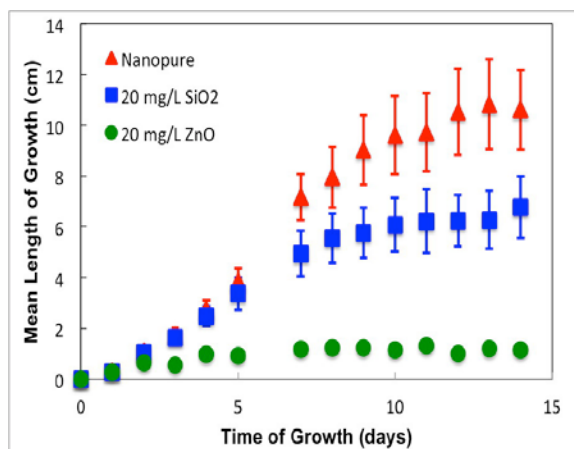
2015 Western Regional Meeting 113

A simple experiment to introduce nanophytotoxicity to first-year undergraduate students

Shailise Ross¹, Matthew Owen², Brian Pedersen¹, Gang-Yu Liu¹, **William J. Miller²**, millerb@scc.losrios.edu. (1) Dept Chemistry, Univ of California, Davis, California, United States (2) Dept Chemistry, Sacramento City College, Sacramento, California, United States

This experiment focuses on introducing the evaluation of the phytotoxicity of nanomaterials to first-year undergraduates using a simple system, mung beans or *Vigna radiata*, and industrially

relevant nanomaterials, SiO₂ and ZnO nanoparticles. In comparison to solutions of Nanopure water, the growth of mung beans in solutions of zinc oxide nanoparticles with a concentration of 20 mg/L is severely stunted, showing clear evidence of nanophytotoxicity. Similarly, the growth of mung beans is significantly stunted in solutions of silicon oxide nanoparticles with the same concentration. An evaluation of student learning showed significant advances in the understanding of topics such as nanophytotoxicity by the students completing the experiment.



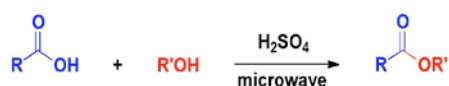
Mean and standard error values for the length of mung bean growth versus time grown in Nanopure water (triangles), solutions of 20 mg/L SiO₂ NPs (squares), and solutions of 20 mg/L ZnO NPs (circles).

2015 Western Regional Meeting 114

Microwave-assisted esterification: A discovery-based microscale laboratory experiment

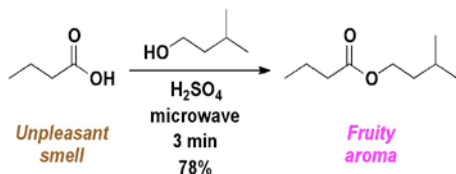
Maureen Reilly¹, Ryan P. King^{4,5}, Alexander J. Wagner³, **Susan M. King²**, s3king@uci.edu. (1) Department of Chemistry, University of California Irvine, Irvine, California, United States (3) Chemistry, University of California, Irvine, Laguna Beach, California, United States (4) Chemistry, University of California, Irvine, Huntington Beach, California, United States (5) Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts, United States

An undergraduate organic chemistry laboratory experiment has been developed that features a discovery-based microscale Fischer esterification utilizing a microwave reactor. Students individually synthesize a unique ester from known sets of alcohols and carboxylic acids. Each student identifies the best reaction conditions given their particular reagents (either excess alcohol or excess carboxylic acid) as well as the ideal work-up procedure for their reaction. Products are analyzed using ¹H NMR spectroscopy, IR spectroscopy, and scent. This modern adaptation of the classic Fischer esterification provides the opportunity for discussion of important chemistry concepts, including acid catalysis, Le Châtelier's Principle, and green chemistry.



- no organic solvent in reaction
- organic/aqueous work-up
- no purification necessary

Typical reaction:



2015 Western Regional Meeting 115

Optimizing the learning experience in the general chemistry laboratory

Sam Abbas, dr.abbaschem@gmail.com. Chemistry, Palomar, MiraCosta, & Saddleback Colleges, San Marcos, California, United States

In order to maximize the learning experience for the students of the general chemistry laboratory, educators have resorted to utilization of various group sizes: from individual, to pairs, to larger groups. Therefore, the question becomes, what is the optimal group size? In order to answer this question, ten different experiments were chosen as they tested various concepts and skills associated with general chemistry topics. The ten experiments were conducted using all three modalities over the course of five semesters. Results indicate that most experiments are best conducted individually (70%), while others are most effectively conducted by a pair-team of students (20%), and very few are appropriate for larger group type settings (10%). A detailed discussion of the nature of the investigated experiments, the results, and their implications in designing curriculum and classroom dynamics in the chemistry laboratory will be presented.

2015 Western Regional Meeting 116

Trying to elucidate the spectroscopic and electrochemical properties of substituted anthraquinones using undergraduate research students using a joint experimental and computational chemistry approach

Marco M. Allard, savantfou@gmail.com. Chemistry, La Sierra University, Riverside, California, United States

Undergraduate research in chemistry can be a very complicated endeavor. Our approach to using Junior and Senior undergraduate students as part of their degree requirement involves quite a few challenges. One of the most pressing problems is the fact that students usually do not have enough background knowledge to perform cutting edge chemical research, and they usually do not have enough time in their busy schedule to perform adequate research. Our approach for the last two years has been multifold: assign small assignments and research tasks that are part of the overall project, assign students in pairs, and have weekly meetings to report progress. Our approach is also based on gathering limited experimental data, and

complementing all the data with computational chemistry analysis. Our focus has been on studying the spectroscopy of newly synthesized anthraquinones, and analyses their excited states, in both their native forms, and their reduced/radical states. This involves synthetic work, followed by experiments in electrochemistry, computational chemistry and spectroscopy.

2015 Western Regional Meeting 117

Qualitative analysis in the general chemistry II laboratory: How much is too much?

Sam Abbas, *dr.abbaschem@gmail.com. Chemistry, Palomar, MiraCosta, & Saddleback Colleges, San Marcos, California, United States*

The General Chemistry II Laboratory curriculum at various community colleges varies in the extent of coverage of qualitative analysis (QA) experiments whereby some programs barely touch on the topic while others include a sizable chunk of experiments on QA. A survey of twelve general chemistry lab educators in 5 community colleges was conducted in order to test the authors assertions that an optimal QA component in the general chemistry II lab is one that consists of four experiments: The first explores groups I and II, the second explores group III, the third groups IV and V, and the fourth sums it all up by testing for a general unknown from all five analytical groups. A detailed discussion of the important role QA plays in the General Chemistry II Laboratory curriculum, as well as, the rationale behind the choice of experiments will be presented.

2015 Western Regional Meeting 118

Electronic lab notebooks in the organic chemistry laboratory: Optimization of hardware and software parameters

Kim Albizati, *kalbizati@yahoo.com. Chemistry and Biochemistry, Univ. of Calif San Diego, La Jolla, California, United States*

In the past 10 years, electronic lab notebooks (ELN's) for scientific record-keeping have become standard in many industries, especially the chemical and pharmaceutical industries. Academia has been much slower to adopt this technology, especially in the US, for a variety of reasons, both financial and infrastructural. Prior to our work, in the University of California system, there was no organized effort in this area, and only sporadic efforts of any kind to bring this technology to either the research or teaching realms. As part of a broader initiative, we have conducted a series of studies on the use of ELN's in the undergraduate teaching labs at the University of California, San Diego. In the past three years, six studies have been completed which have uncovered various hardware, software and infrastructure aspects that are important to an optimized student learning experience. Further, as we have zeroed in on the optimal configurations, the acceptance of ELN's as measured by student satisfaction surveys has hit the 90% level. This talk will discuss the evolution of our program, which has resulted in consistently high levels of satisfaction and achievement in undergraduate organic chemistry laboratories, relative to the identical lab courses using a traditional paper lab notebook format. The hardware, software and related lab infrastructure as well as the associated monetary costs and support structure will be discussed.

2015 Western Regional Meeting 119

Proton conduction in a cephalopod structural protein

David D. Ordinario, dordinar@uci.edu, Long Phan, Emil Karshalev, Jonah Jocson, Alon A. Gorodetsky. *Chemical Engineering and Materials Science, University of California, Irvine, Irvine, California, United States*

Proton conducting materials play a central role in a diverse array of renewable energy and bioelectronics technologies. Thus, a great deal of research effort has been expended to develop improved artificial proton conducting materials, including ceramic oxides, solid acids, porous solids, polymers, and metal-organic frameworks. Within this context, proton conductors from naturally occurring proteins have received relatively little scientific attention, despite advantages that include intrinsic biocompatibility, structural modularity, tunable physical properties, ease and specificity of functionalization, and generalized expression/purification protocols. We have recently discovered unexpected protonic conductivity in the cephalopod structural protein reflectin, and characterization of this material with a diverse array of electrical and electrochemical techniques has resulted in the finding that its electrical figures of merit compare favorably to those of artificial proton conductors. Moreover, reflectin's favorable electrical properties have enabled the fabrication of diverse protein-based protonic devices. Our findings may hold implications for the development of the next generation of biologically-inspired polymeric proton conductors

2015 Western Regional Meeting 120

Protein-based protonic transistors

David D. Ordinario, dordinar@uci.edu, Long Phan, Jonah Jocson, Tam N. Nguyen, Alon A. Gorodetsky. *Chemical Engineering and Materials Science, University of California, Irvine, Irvine, California, United States*

Ionic transistors from organic and biological materials represent an emerging class of devices for bioelectronics applications. Within this context, protonic transistors represent exciting targets for further research and development despite the fact that they have received relatively little attention. Given the ubiquity of proton transport and transfer phenomena, protonic devices represent a natural choice for interfacing rugged traditional electronics and biological systems, facilitating the sensitive transduction of biochemical events into electrical signals. We have recently fabricated and characterized protonic transistors from the cephalopod structural protein reflectin. We have investigated these devices with standard electrical and electrochemical techniques, and our findings indicate performance comparable to the state-of-the-art for protonic transistors. Moreover, we have developed simple strategies for improving the performance of our devices by altering their active layer geometry. Overall, our findings may hold significance for a broad range of biomedical and bioelectrochemical devices.

2015 Western Regional Meeting 121

Polymer hydrogel nanoparticles used as artificial heat shock proteins for immunoglobulin G

Beverly Chou², beverlc1@uci.edu, **Rishad Dalal**², **Kenneth J. Shea**¹. (1) Univ of California, Irvine, California, United States (2) Chemistry, University of California, Irvine, Irvine, California, United States

Monoclonal antibodies are currently one of the largest classes of drug products on the market because of their high specificity, therapeutic impact, and long *in vivo* half-life. Immunoglobulin G (IgG) is the most popular type of therapeutic antibody on the market now. Their popular usage has encouraged the discovery of new methods to protect IgG to expand its' usage in distant locations. *N*-isopropylacrylamide (NiPAm) nanoparticles (NPs) have been used in the past for a variety of different purposes. One of the most recent applications takes advantage of the lower critical solution temperature (LCST) of these NiPAm NPs, which causes the particle to undergo an entropically favored collapse when heated above LCST, and to become water swollen when cooled below LCST. Shea *et. al.* have taken advantage of this property and discovered that they can alter the affinities of these NiPAm NPs to biomacromolecules by changing temperature, therefore creating a situation where they can catch and release their biomacromolecular targets. Based on our knowledge of IgG, we are using lightly crosslinked NiPAm NPs with various amounts of *t*-butylacrylamide (tBAm), *N*-octylacrylamide (OAm), *N*-hexylacrylamide (HAm), and acrylic acid (AAc) co-monomers to find NPs with the highest affinity for IgG.

2015 Western Regional Meeting 122

Box effects in nonliving and living polymerization of slow or nondiffusing monomers confined to a 2D surface

Alto Benedicto, alto.benedicto@imperial.edu. Chemistry, Imperial Valley College, Imperial, California, United States

The molecular weight distribution for living polymerization confined to a surface with little or no monomer diffusion is very different from that in solution. At low [initiator]/[monomer] (*I/M*), the average number of monomers consumed per initiator (X_n) reaches a limiting value of 72 with polydispersity index = 1.50, because the active chain end is *boxed-in intramolecularly* by its own growing chain. Large amounts of monomers remain unreacted. At higher *I/M*, X_n decreases further because the active chain end is *boxed-out intermolecularly* (from pools of monomers) by other propagating chains. In particular, $1/X_n = 0.0133 + 0.9 I/M$, and monomer conversion is $X_n = 75 - 2/3 \times$ percent conversion. For nonliving polymerization, X_n is limited to $8 < X_n < 72$, for the entire *I/M* range, regardless of the kinetic parameters.

2015 Western Regional Meeting 123

Possible factors in seagrass decline

Ellen L. Johnson¹, ellenj87@gmail.com, **Sandy Wyllie-Echeverria**², **Rebecca A. Lyons**¹. (1) Chemistry, University of Redlands, Escondido, California, United States (2) College of the Environment, Friday Harbor Laboratories, University of Washington, Friday Harbor, Washington, United States

Seagrass populations, including eelgrass, are in decline worldwide, and rates of loss are accelerating. Westcott Bay and Garrison Bay in San Juan County, Washington, have experienced losses of over 35 acres as of 2003 and have not recovered since. It is not clear

what has caused the decline, but it is clear that the problem and possible explanations for it should be examined. Considering the importance of eelgrass beds as habitat for many species, loss of this significance has the potential to threaten the health of entire regional ecosystems and economies. Nutrient loading is a significant threat to eelgrass directly, due to toxic effects of excess nitrates and ammonium, or indirectly, from resulting eutrophication and phytoplankton blooms. Herbicides can also pose a threat to eelgrass health. Nutrients, organic toxicants such as herbicides and pesticides, and other pollutants may be introduced to nearshore eelgrass habitat via submarine groundwater discharge, which has been observed and quantified in some parts of San Juan County. This project was an effort to investigate the potential link between nutrient, herbicide and pesticide pollution and eelgrass decline in San Juan National Historical Parks.

2015 Western Regional Meeting 124

Co-digestion of high strength wastes: Need for a holistic approach

Ganesh Rajagopalan, *RGanesh@kennedyjenks.com. Kennedy/Jenks Consultants, Irvine, California, United States*

Wastewater treatment plants have increasingly been investigating co-digestion of organic materials as an approach to improving their energy portfolio. Addition of external organic matter to anaerobic digesters has been shown to increase gas production, while reducing the amount of organic matter sent to landfills. Co-digestion is a sustainable approach for the use of organic matter as it produces energy, and coupled with beneficial reuse of the biosolids, this practice recycles vital nutrients and organic matter back to soils. Another driver for co-digestion is the increasing regulations associated with disposal of organic matter in landfills. Most of the past co-digestion studies have focused primarily on increased gas production. However, addition of “non-sludge” organic matter can alter several digester operating parameters and has the potential to affect digester performance of downstream processes. For example, organic waste addition has the potential to affect digester stability, gas quantity and quality, sludge dewaterability, biosolids characteristics as well as centrate quality. The project team has performed a several bench scale and field studies for a number of agencies to evaluate unintended consequences and optimization of co-digestion using processed food waste, poultry, creamery and winery wastes. The studies investigated the effects of organic waste addition to not only gas production, but also on digester stability, gas quality, dewatering, biosolids odor and side-stream quality. The presentation will share data from these studies to help utilities planning co-digestion to maximize the benefits and minimize undesirable consequences.

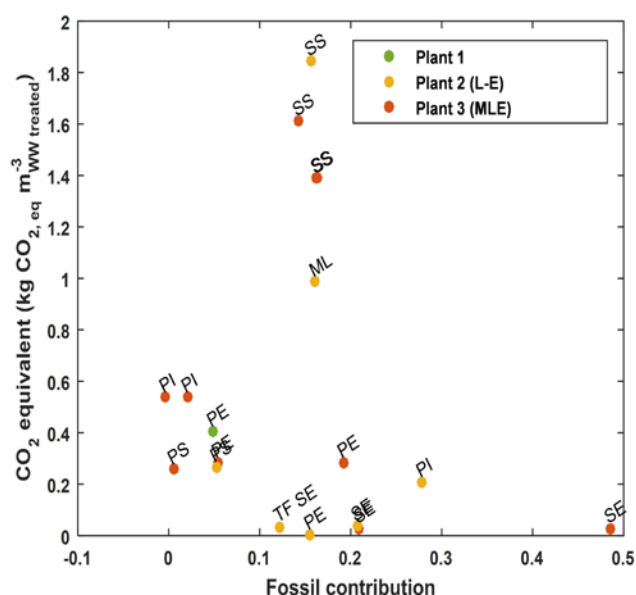
2015 Western Regional Meeting 125

Radiocarbon dating of wastewater: Effect on fossil carbon emission quantification

Linda Y. Tseng¹, *ytseng@uci.edu*, **Alice K. Robinson**¹, **Xiaomei Xu**², **John Southon**², **Diego Rosso**¹. (1) *Civil and Environmental Engineering, University of California, Irvine, Irvine, California, United States* (2) *Earth System Science, University of California, Irvine, Irvine, California, United States*

The procedures on estimating wastewater treatment published by the Intergovernmental Panel on Climate Change (IPCC) assume all carbon dioxide (CO₂) emissions are modern and are not

included in the greenhouse gas (GHG) emission estimation. However, municipal wastewater contains various petroleum-derived chemicals with an older radiocarbon signature, thus the municipal wastewater CO₂ emission would not be completely modern and the GHG may be underestimated. Moreover the carbon at different wastewater processes could carry distinct ¹⁴C signature due to different biological processes employed. We used radiocarbon dating to determine the fate of fossil and modern carbon throughout the treatment at three different municipal wastewater treatment plants in Southern California, and we compared the radiocarbon results to the carbonaceous CO₂-equivalent emission per volume wastewater treated. The results showed that primary influent, sludge, and effluent generally had similar radiocarbon signature and had 0 to 28% fossil carbon contribution, while secondary effluent had 12 to 49% fossil contribution. A comparison of CO₂-equivalent emission and the radiocarbon results at different points of the treatment revealed that secondary sludge and mixed liquor had similar radiocarbon signature with 14 to 16% fossil carbon contribution, but the secondary sludge had the highest CO₂-equivalent emission potential of 1.6 to 1.9 kg CO₂-equiv m⁻³_{wastewater} treated. These results demonstrated that there are fossil carbon CO₂ emissions from the wastewater treatment, and the practice of digesting secondary sludge and converting secondary sludge to agricultural biosolids may help mitigate the fossil GHG emissions.



Fossil carbon contribution and CO₂-equiv per volume wastewater (WW) in Plants 1, 2 (operated in Ludzack-Ettinger, L-E), and 3 (modified Ludzack-Ettinger, MLE). PI, primary influent; PE, primary effluent; PS, primary sludge; SS, secondary sludge; ML, mixed liquor; SE, secondary effluent; TF, trickling filter.

2015 Western Regional Meeting 126

A novel isolation and separation scheme for the characterization of dissolved organic matter in landfill leachate

Barbara Cottrell², bcottrel@uci.edu, **Maria Pinto**⁵, **Stephanie Bolyard**⁴, **David P. Soulsby**³, **William J. Cooper**¹, **Debra Reinhart**⁴. (1) Univ of California Irvine, Irvine, California, United

States (2) Civil and Environmental Engineering, University of California Irvine, Irvine, California, United States (3) Chemistry, University of Redlands, Redlands, California, United States (4) Civil, Environmental and Construction Engineering, University of Central Florida, Orlando, Florida, United States (5) Departamento de Quimica, Universidade NOVA de Lisboa, Lisboa, Portugal

Landfills are used for the disposal of approximately 50% of municipal solid waste worldwide. The solid waste undergoes anaerobic digestion in moist conditions generating a highly concentrated mixture of soluble organic and inorganic compounds and particulate matter that is termed landfill leachate. The development of new methods for treating landfill leachate is essential because the disposal of this highly concentrated, colored material in wastewater treatment facilities is problematic. Understanding the chemical composition of this highly variable mixture is important for the development of improved methods for its disposal. Landfill leachate organic matter (LOM) is characterized by its bulk properties, by UV- visible and fluorescent spectroscopy, molecular size, NMR, and FT-IR however fractionation of this complex mixture would enhance our ability to understand its chemical composition. In this study, the bulk LOM was first profiled by size exclusion chromatography (SEC). A combination of solid phase extraction (SPE)/step-gradient elution with reversed phase chromatography was developed to fractionate and separate the LOM. Analysis of the fractions by ^1H NMR, EEMs, and UV-visible spectroscopy was used to study the temporal variation in LOM composition from landfill sites in Florida and Southern California. This combination of techniques has improved our understanding of some of the variation in LOM composition.

2015 Western Regional Meeting 127

Detecting neonicotinoid pesticides with QCM detectors in a gas chromatograph

William K. Tolley, *b_tolley@juno.com. Seacoast Science, Inc., San Diego, California, United States*

Neonicotinoid pesticides have been suggested as causing colony collapse among honeybees. Portable instrumentation to detect these pesticides in the field are highly sought. Thus, the interest in improving robust, compact, low-power chemical sensors.

Polymer sorbents have been coated onto a number of electronic transducers to create chemical sensors. For example, polymer coatings on quartz crystal microbalance (QCM) detectors creates chemical sensors that respond to changes in mass as the polymers absorb target analytes. An attractive feature of these sorbent-based sensors is the small foot-print and low power requirements.

A novel application of QCM detectors is as the detector in gas chromatography to detect potential contamination of honeybees by pesticides. The QCM is spray-coated with multi-wall carbon nanotubes and polymer with intrinsic microporosity. Model neonicotinoid pesticides thiametoxam and clothianidin, which have potential implication in honeybee colony collapse, were desorbed from standard wipes into the gas chromatograph. Results of analytical method development are discussed.

2015 Western Regional Meeting 128

Enzymatic treatment of dye wastewater using fungal laccases and peroxidases: An overview

Keisuke Ikehata, kikehata@pacewater.com. Pacific Advanced Civil Engineering, Fountain Valley, California, United States

Synthetic organic dyes such as azo dyes in wastewater discharged by dye manufacturing and textile industries constitute a major environmental concern due to their poor biodegradability and toxicity, as well as aesthetics and inhibition of photosynthesis and other biological activities in receiving water. Most synthetic dyes contain characteristic multiple aromatic rings that are fused and/or linked by various C-C, C-O, and C-N linkages and substituted by multiple functional groups such as amino, nitro, hydroxyl, sulfonate, carbonyl, and carboxylate groups. Because of the similarity of dye molecules and lignin, a natural polymer of aromatic alcohols, many of the synthetic dyes can be degraded and decolorized by lignin-degrading white rot fungi such as *Phanerochaete chrysosporium* and *Trametes versicolor* and their oxidoreductase systems including peroxidases and laccases. This paper discusses the sources and application of these ligninolytic enzymes for the treatment of synthetic dyes, reaction mechanisms, and other development and challenges associated with this enzymatic process.

2015 Western Regional Meeting 129

Discovery of potent and kinase-selective p21-activated kinase 1 (PAK1) inhibitors

Wendy Lee, sauhanle@comcast.net. Discovery Chemistry, Genentech, Inc., South San Francisco, California, United States

The p21-activated kinases (PAKs) play important roles in cytoskeletal organization, cellular morphogenesis and survival and have generated significant attention as potential therapeutic targets for cancer. Following a high-throughput screen, we identified an aminopyrazole scaffold-based series that was optimized to yield group I selective PAK inhibitors. A structure-based design effort aimed at targeting the ribose pocket for both potency and selectivity led to much-improved group I vs. II selectivity. Early lead compounds contained a basic primary amine, which was found to be a major metabolic soft spot with *in vivo* clearance proceeding predominantly *via* N-acetylation. We succeeded in identifying replacements with improved metabolic stability, leading to compounds with lower *in vivo* rodent clearance and excellent group I PAK selectivity.

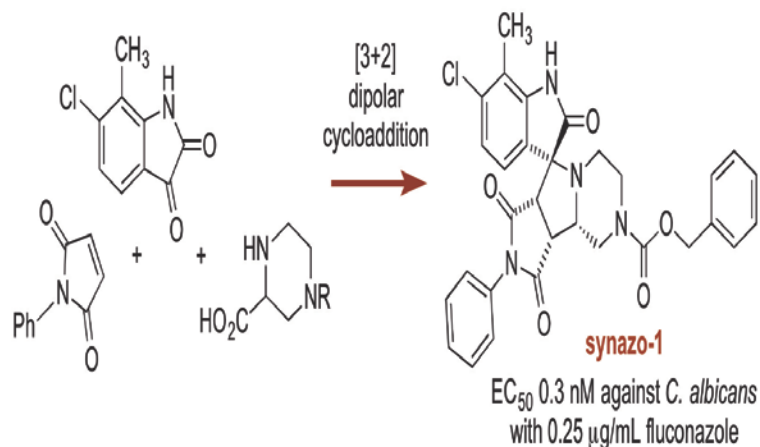
2015 Western Regional Meeting 130

Potent synergy between small molecules and fluconazole against *Candida albicans*

David Van Vranken², david.vv@uci.edu, Haoping Liu¹, Udara Ilandari Dewage², Fuqiang Wang¹, Kevin A. Scott², Chengtian Shen², Shelley Lane¹. (1) Department of Biological Chemistry, University of California at Irvine, Irvine, California, United States (2) Department of Chemistry, University of California at Irvine, Irvine, California, United States

Candida albicans accounts for 80% of major systemic fungal infections and fluconazole is the first-line treatment for candidiasis. Azole resistance is a growing problem that is typically met with higher doses sometimes without success. There is growing interest in drugs that can potentiate the effect of fluconazole against *C. albicans*. We explored the use of stereoselective [3+2] dipolar cycloadditions of azomethine ylides and other strategies to access small molecules

that act synergistically with fluconazole. The most potent compound was active with an EC_{50} below 1 nM against a susceptible strain and was potent against some of clinical isolates.



2015 Western Regional Meeting 131

Wnt mimetics as anti-cancer drugs: Design and synthesis of drugs that reduce β -catenin and attenuate cell proliferation

Aneta Jelowicki, anetka.jelo@csu.fullerton.edu. Department of Chemistry and Biochemistry, California State University-Fullerton, Fullerton, California, United States

A survey of data obtained from a variety of biological assays on a drug library consisting of more than 200 synthesized small organic molecules has revealed significant potential anticancer activity for molecules containing a specific structural motif. Previously, several of the compounds in a library of drugs, which were designed to activate the Wnt pathway (to promote stem cell pluripotency), were found to decrease β -catenin levels in cancer cells. The dysregulation of β -catenin has also been linked to various types of cancer and we therefore decided to investigate the potential influence of these drugs on cell proliferation. Cell proliferation was determined by the CyQuant assay, which uses DNA content of the cells to quantify the number of plated cells. HeLa cells were treated with the drug (10 μ M) for 24 hours and the DNA content was quantified. Preliminary results show that several drugs inhibit cell proliferation significantly, in some cases even better than known anticancer drugs such as mitomycin C and cisplatin. Certain trends regarding the structure of the drug and the activity have been observed. For instance, longer alkyl chains on one part of the molecule in combination with a polar group on the opposite part of the molecule show to reduce HeLa cell growth more efficiently than shorter alkyl chains. Further experiments have shown that the presence of two polar substituents on opposite sides of the drug does not reduce HeLa cell growth effectively. Further studies are currently underway to optimize the drug library with more efficient anti-cancer drugs and to determine the mechanism of action underlying the anti-proliferative effect of these drugs.

2015 Western Regional Meeting 132

X-ray crystallographic structure of oligomers formed by a toxic β -hairpin derived from α -synuclein: Trimers and higher-order oligomers

Patrick Salveson, psalveso@uci.edu. Chemistry, University of California, Irvine, Irvine, California, United States

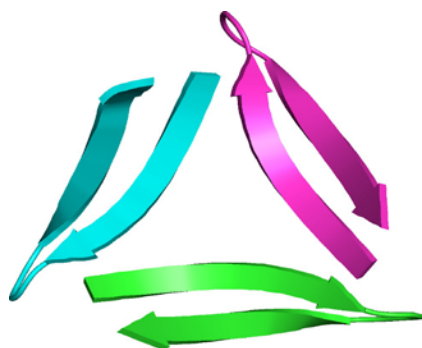
Oligomeric assemblies of the protein α -synuclein are believed to be responsible for the neurodegeneration of Parkinson's disease and related synucleinopathies. Little is known about the structures of the α -synuclein oligomers due to their transience and heterogeneity. The absence of high-resolution structures of oligomers formed by α -synuclein impedes understanding the synucleinopathies at the molecular level. Here we report the first X-ray crystallographic structure of oligomers of peptides derived from α -synuclein. This structure reveals a hierarchical assembly of β -hairpins. Three β -hairpins assemble to form a triangular trimer. Three copies of the triangular trimer further assemble into basket-shaped nonamers and related octadecamers. These oligomers are cytotoxic against human neuroblastoma cells; further, their cytotoxicity appears to result from aberrant interactions with the cell membrane, thus mimicking the mechanism of action of oligomers formed by the full-length protein. The X-ray crystallographic structure presented here may represent the general motif of oligomers formed by full-length α -synuclein and may allow the rational development of diagnostics and therapeutics for Parkinson's disease.

2015 Western Regional Meeting 133

X-ray crystallographic structures of amyloid oligomers: A toxic crosslinked trimer of β -hairpins derived from $A\beta_{17-36}$

Adam Kreutzer³, akreutze@uci.edu, Ryan K. Spencer³, Stan Yoo², James S. Nowick¹. (1) University of California, Irvine, California, United States (2) Chemistry, University of California - Irvine, Irvine, California, United States (3) Chemistry, University of California Irvine, Irvine, California, United States

The neurotoxic oligomers formed by the β -amyloid ($A\beta$) peptide are thought to be central to neurodegeneration in Alzheimer's disease. The structures of these oligomers are not known. Understanding their structures offers the promise of determining the molecular basis for neurodegeneration and ultimately developing effective prevention and treatment of Alzheimer's disease. Our research group recently elucidated the X-ray crystallographic structure of a triangular trimer formed by a β -hairpin derived from $A\beta_{17-36}$ [*JACS* **2014**, 136, 5595]. We have now developed a strategy to stabilize the trimer through disulfide cross-links among the three component β -hairpins. The cross-linked trimer is toxic toward the human neuroblastoma cell line SH-SY5Y and is reactive with the conformation dependent amyloid oligomer antibody A11. Here we report the X-ray crystallographic structure of the crosslinked trimer and describe biological and biophysical studies.



X-ray crystallographic structure of a trimer
derived from A β ₁₇₋₃₆
(PDB 4NTR, JACS 2014, 136, 5595)

2015 Western Regional Meeting 134

Mechanistic insights into photo-induced, copper-catalyzed alkylations of amines

Jun Myun Ahn, jahn@caltech.edu, Kareem Hannoun, Tanvi Ratani, Sidney Creutz, Jonas C. Peters, Gregory C. Fu. California Institute of Technology, Pasadena, California, United States

Photoinduced, copper-catalyzed cross-couplings have emerged as an attractive class of light-driven transformations to construct carbon-nitrogen bonds in recent years. Despite the broadening scope with respect to coupling partners, the understanding of the operating mechanisms has been limited to date. Herein, a mechanistic investigation of a photoinduced, copper-catalyzed cross-coupling of amines and alkyl halides, including spectroscopic evidence for a copper intermediate, is presented.

2015 Western Regional Meeting 135

Methodology and mechanistic studies of catalytic asymmetric annulations to form silyl-spirooxindoles

Brittany Armstrong, barmstrong@ucdavis.edu, Benjamin Shupe, Annaliese K. Franz. Chemistry, University of California, Davis, Davis, California, United States

We have developed a Cu(II)-catalyzed addition of allylsilanes to iminoxindoles to yield spirocarbamate oxindoles. This reaction proceeds in high yield with good diastereoselectivity. An enantioselective variant, which proceeds with excellent selectivity, has been developed in tandem with mechanistic studies to obtain information about the catalyst complex. Electron paramagnetic resonance (EPR) is used to study the geometry and electronic environment surrounding the Cu(II) complex. This information is utilized to assess the role of both chiral ligand and essential additive, sodium tetrakis[(3,5-trifluoromethyl)phenyl]borate (NaBARF), in the enantioselective reaction. Catalytically active species are identified by EPR and correlated with experimental data.

2015 Western Regional Meeting 136

Counterion effects in the catalytic stereoselective synthesis of 2,3'-pyrrolidinyl spirooxindoles

Jacob P. MacDonald, jakemacd@msn.com, **Benjamin H. Shupe**, **John Schreiber**, **Annaliese K. Franz**, Chemistry, University of California-Davis, Davis, California, United States

Oxindoles and spirooxindoles are recognized as privileged scaffolds in natural products and biologically-active compounds. This presentation describes a Lewis acid (e.g. Cu(II) and Sc(III) salts) catalyzed [3+2] annulation of enantioenriched crotylsilanes with imino-oxindoles to access 2,3'-pyrrolidinyl spirooxindoles. The presence of a sodium tetrakis[3,5-bis(trifluoromethyl)phenyl]borate (NaBARF) counterion source was necessary for reactivity. In addition to Lewis acid catalysis, the acidic clay montmorillonite has also been shown to promote the annulation reaction in the presence of NaBARF. The methodology also provides mechanistic insight into details of the product differentiation that is observed between unsubstituted and substituted allylic silanes.



2015 Western Regional Meeting 137

Condensation versus hydroamination for the one-step synthesis of α -tetrasubstituted amines

Catharine H. Larsen, catharine.larsen@ucr.edu, **Conor Pierce**, **Mary Nguyen**, **Zachary L. Palchak**, **Hoseong Yoo**, **Daniel Lussier**, University of California, Riverside, Riverside, California, United States

Reactions designed to incorporate aldehydes in the synthesis of α -trisubstituted amines fail when attempted with hindered ketones. The high barrier to condensation of a ketone and an amine and to nucleophilic attack on the resultant ketimine electrophile is surmounted by a dual Cu(II)/Ti(IV) catalyst system for the first direct conversion of unactivated ketones, amines, and alkynes to tetrasubstituted propargylamines. Markovnikov alkyne hydroamination provides an alternate catalytic route to ketimine intermediates, and tandem alkynylation rapidly forms the desired α -tetrasubstituted products. Both reactions are environmentally friendly as they operate without adding solvent, ligand, base, or other promoters.

2015 Western Regional Meeting 138

Nickel-catalyzed cross-electrophile coupling reactions of primary and secondary benzylic esters with aryl halides

Mikhail Konev, mkonev@uci.edu. Department of Chemistry, University of California, Irvine, Irvine, California, United States

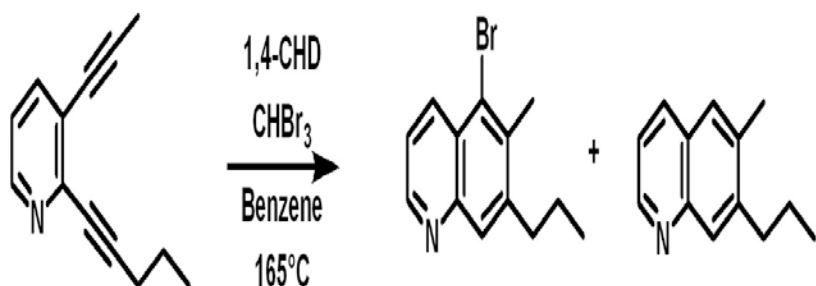
Nickel-catalyzed cross-electrophile coupling reactions of benzylic esters and aryl halides has been developed. Both inter- and intramolecular variants proceed under mild conditions. A variety of heterocycles and functional groups are tolerated under the reaction conditions. Additionally, the first example of a stereospecific cross-electrophile coupling of a secondary benzylic ester is described.

2015 Western Regional Meeting 139

Thermal- and metal-mediated cycloaromatization reactions of conjugated tri- π systems

Kate M. Veccharelli², kvecchar@ucsd.edu, **Joseph M. O Connor**¹. (1) Univ of California, La Jolla, California, United States (2) Chemistry, University California San Diego, San Diego, California, United States

Cycloaromatization reactions allow for the construction of substituted arenes via thermal transformations of enediyne substrates. While thermal cycloaromatizations are intriguing, the high temperatures and low yields limit their utility in organic synthesis. Previous work in our lab demonstrated the room temperature conversion of enediynes to arene products by the use of stoichiometric quantities of $\text{CpRu}(\text{MeCN})_3^+$ or $\text{Cp}^*\text{Ru}(\text{MeCN})_3^+$. Thus, the focus of this current work is on fundamental studies, via an examination of nitrogen containing enediyne substrates; which will establish the scope and limitations of thermal and ruthenium-mediated cycloaromatizations. 2-(pent-1-yn-1-yl)-3-(prop-1-yn-1-yl)pyridine was synthesized and upon heating in the presence of bromoform and 1,4-CHD, led to the formation of a mono-brominated quinoline derivative along with a quinoline derivative. It is hypothesized that the formation of the mono-brominated quinoline derivative results from an in-situ generation of HBr, which adds across an alkyne to form a dienyne intermediate. The dienyne can then form the mono-brominated quinoline via a Höpf-type cycloaromatization mechanism. The quinoline product was hypothesized to form via protonation of the pyridine by HBr, thus generating a more electron-deficient enediyne which undergoes the Bergman cycloaromatization.



2015 Western Regional Meeting 140

Isolation of bis(copper) key intermediates in Cu-catalyzed azide-alkyne "click reaction".

Daniel Tolentino, *dtolenti@ucsd.edu*, **Liqun Jin**, **Mohand-Ameziane Melaimi**, **Guy Bertrand**. *UC San Diego, La Jolla, California, United States*

The development of click chemistry has been one of the most important discoveries in synthesis, and its broad scope of applications ranges from materials to biology. Its most popular reaction, the copper-catalyzed azide-alkyne cycloaddition (CuAAC) is easily accessible, and much work has been done to elucidate its mechanism. However, key catalytic species have never been directly observed. Mononuclear copper species were initially thought to be the active species, with dinuclear complexes being proposed only recently. By using cyclic(alkyl)(amino)carbenes, which have been shown to stabilize reactive transition metal and main group species, we have isolated a previously postulated π,σ -bis(copper) acetylide as well as an unprecedented bis(metallated) triazole. Their involvement in the catalytic cycle and the kinetically favored pathway of the CuAAC reaction will be presented.

2015 Western Regional Meeting 141

Highly encumbered group VI transition metal catalysts capable of exploiting minor polarization of alkynes to give high regioselectivity in hydrostannation

Kyle Mandla, *kmandla@ucsd.edu*. *Department of Chemistry, University of California, San Diego, La Jolla, California, United States*

The development of fast, efficient, selective organic transformations catalyzed by earth abundant transition metals is of increasing importance as demand for 'greener' and more cost effective alternatives to noble metal-catalyzed processes continues to grow. The strategy of this work has been to interrogate a known process, molybdenum catalyzed hydrostannation of alkynes, and elucidate mechanistic features which might be tuned toward enhanced catalyst performance as well as altogether new reactivities. In these studies, a sterically encumbered molybdenum pre-catalyst, $\text{MoI}_2(\text{CO})_2(\text{CNArDipp}_2)_2$ (Dipp = 2,6-diisopropylphenyl), has provided a well-defined system to probe the mechanism of hydrostannation while also providing exceptional activity and regioselectivity in hydrostannation. Stability imparted by encumbering m-terphenyl isocyanide ligands has enabled isolation and structural characterization of several species relevant to the mechanism of hydrostannation, including an exceedingly rare example of a MoI -alkyne thought to be an intermediate in pre-catalyst activation. Activity of $\text{MoI}_2(\text{CO})_2(\text{CNArDipp}_2)_2$ in hydrostannation is unprecedented—at 1 mol% loading, complete conversion of an alkyne substrate to the corresponding vinylstannane can be achieved in 15 minutes. Most notably, this system extends regioselectivity beyond previous examples which have shown good α -selectivity in alkynes featuring a propargyl-substituted electron withdrawing (EW) group. In this work, $\text{MoI}_2(\text{CO})_2(\text{CNArDipp}_2)_2$ maintains α -selectivity when a propargyl-substituted EW group is present, but when an electron donating group is present (i.e. aryl, alkyl groups) selectivity is reversed giving β -substituted products in high yields. NMR evidence suggests the well-defined coordination sphere modulates regiocontrol by exploiting minor differences in electron-density of two alkynyl C-atoms.

2015 Western Regional Meeting 142

Synthesis of a functionalized metal-ligand supramolecular complex for incorporation into polymers

Sadie G. Martin¹, sadie.g.martin@gmail.com, **Kristine Claudine Teppang**¹, **Sara Journey**¹, **Stephen Moss**^{2,1}, **Byron W. Purse**¹. (1) Department of Chemistry and Biochemistry, San Diego State University, San Diego, California, United States (2) University of Colorado, Denver, Colorado, United States

One of the aims of supramolecular chemistry is to study molecular units that self-assemble in a distinct arrangement due to intermolecular forces (e.g. hydrophobic effects, hydrogen bonding, metal-ligand coordination) between specific functional groups in the constituents that comprise the larger supramolecular structure. Supramolecular complexes have been widely studied for applications in controlling chemical reactions since such capsules have been demonstrated to compartmentalize guest molecules and release substrates (e.g. catalysts) in response to applied stimuli^{1,2,3}. The primary objective of our research is to functionalize a metal-ligand coordinated supramolecular unit by appending it to a polymer network for further applications in materials and polymer chemistry. The capsule is modeled after the M₄L₆ capsule developed by the Raymond group⁴ but functionalized using a novel synthetic route optimized for incorporation into a polymer network. The beginning stages of the synthesis uses 2,3-dimethoxybenzoic acid and 1,5-diaminonaphthalene as commercially-available starting materials and includes a series of protection/deprotection and amide bond coupling reactions. The final step involves a copper-catalyzed azide-alkyne cycloaddition (CuAAC) reaction that will click the terminal alkyne on the metal-ligand capsule to the azide on a polymer of choice. Results from our work will be useful for a range of applications, including the development of novel stimuli-responsive polymeric materials.

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2015 Western Regional Meeting 143

Organoferrous compounds as antitumor agents

Christina Hoong, christina.hoong.09@gmail.com. Chemistry and Biochemistry, University of California-San Diego, San Diego, California, United States

Organometallic antitumor complexes are an increasingly important class of medicinal agents. Organoferrous prodrugs in particular are promising due to their low cost and relative ease of synthesis. We have focused our efforts on designing and synthesizing new, innovative molecules for cancer therapy that generate free iron(II) on demand via stable organometallic precursors in order to disrupt iron homeostasis. This new class of organoferrous prodrugs are designed to circumvent iron transport and storage mechanisms in tumor cells, generating iron(II) and causing rapid conversion of endogenous hydrogen peroxide (H₂O₂) to hydroxyl radicals (•OH) with a high degree of spatiotemporal control. It is proposed that the resultant rapid disruption of hydrogen peroxide and iron homeostasis will shut down beneficial hydrogen peroxide cell signaling processes and increase the fatal concentration of hydroxyl radical in cells, ultimately leading to cell death.

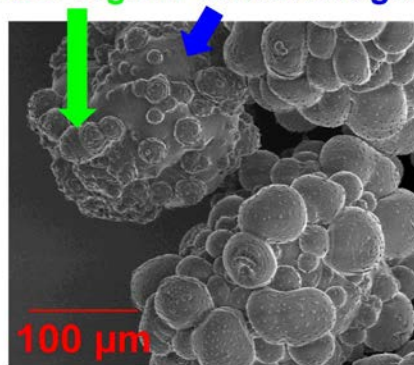
2015 Western Regional Meeting 144

Insight into the mechanism and reactivity of ruthenium ROMP catalysts at the single-molecule and single-particle level

Quinn Easter, qeaster@uci.edu. University of California, Irvine, Irvine, California, United States

The phase containing the active catalyst responsible for ring-opening metathesis polymerization (ROMP) in two ruthenium catalysts has been characterized at the sub-ensemble level. The reaction conditions and properties of ruthenium ROMP catalysts are critical areas of interest for optimization, because designing a catalyst with the highest efficiency is necessary for cost and materials reduction and in catalyst recyclability. We herein study the reactivity distribution among individual catalyst particles to provide additional mechanistic insight. At present, the ensemble rate of reaction is well-understood, but comparatively little is known about the reactivity on a single-particle level. In this vein, we describe single-molecule and single-particle ring opening metathesis polymerization studies using both the 2nd generation Grubbs catalyst and a commercially available, resin-supported Hoveyda-Grubbs catalyst; further, we present single-particle studies on the resin-supported catalyst. In both systems, we show a surprising reactivity distribution and describe heterogeneous catalysis which would traditionally be obscured by ensemble measurements.

active region inactive region



Nonuniform distribution of heterogeneous catalysis at the surface of one Ru catalyst bead. The adjacent neighboring catalyst bead is more catalytically active than the indicated bead.

2015 Western Regional Meeting 145

Characterization of metal-ligand interactions in artificial metalloproteins using electron paramagnetic resonance spectroscopy

Marco Flores, mafloresr@asu.edu, Tien L. Olson, Dong Wang, Selvakumar Edwardraja, Sandip Shinde, JoAnn C. Williams, Giovanna Ghirlanda, James Allen. Chemistry and Biochemistry, Arizona State University, Tempe, Arizona, United States

The design of binding sites for divalent metals in artificial proteins is a productive platform for examining the characteristics of metal–ligand interactions. In this report, we investigate the spectroscopic properties of small peptides and four-helix bundles that bind Cu(II). Three small peptides, consisting of 15 amino acid residues, were designed to have two arms, each containing a metal-binding site comprised of different combinations of imidazole and carboxylate side chains. Two four-helix bundles each had a binding site for a central dinuclear metal

cofactor, with one design incorporating additional potential metal ligands at two identical sites. The small peptides displayed pH-dependent, metal-induced changes in the circular dichroism spectra, consistent with large changes in the secondary structure upon metal binding, while the spectra of the four-helix bundles showed a predominant α -helix content but only small structural changes upon metal binding. Electron paramagnetic resonance spectra were measured at X-band revealing classic Cu(II) axial patterns with hyperfine coupling peaks for the small peptides and four-helix bundles exhibiting a range of values that were related to the specific chemical natures of the ligands. The variety of electronic structures allow us to define the distinctive environment of each metal-binding site in these artificial systems, including the designed additional binding sites in one of the four-helix bundles.¹

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2015 Western Regional Meeting 146

Quantum-mechanical definition of atoms and bonds in molecules

Peter W. Langhoff¹, *plangho1@san.rr.com*, Jeffrey D. Mills², Jerry Boatz². (1) *Chemistry and Biochemistry, University of California San Diego, San Diego, California, United States* (2) *RQRP, Air Force Research Laboratory, Edwards AFB, California, United States*

Assignments of indistinguishable electrons to particular atomic nuclei in a molecule are generally regarded as meaningless, preventing definitions of atomic and atomic-interaction operators in a molecular Hamiltonian. A generally agreed upon quantitative quantum-mechanical definition of a *chemical bond* between atoms in a molecule is consequently absent, in spite of considerable discussion of this issue through the years. This circumstance has not prevented many highly accurate *ab initio* quantum-mechanical calculations of the structure and properties of increasingly complex molecules, with physical and chemical interpretations of such calculations often based on subjectively defined spatial partitionings of one- and two-electron charge density matrices. Here, a computationally-viable quantum-mechanical definition of chemical bonds between atoms in molecules is presented in the Born-Oppenheimer approximation for Coulomb Hamiltonian operators employing a conditional context afforded by representation theory. An orthonormal (Eisenschitz-London) outer product of atomic spectral eigenstates in the absence of over-all aggregate electron antisymmetry is seen to provide meaningful assignments of electrons to particular atomic nuclei in a molecule, as well as support of corresponding well-defined self-adjoint atomic and atomic-interaction operators. The molecular Hamiltonian matrix in the atomic-product representation takes the form of a sum of atomic Hamiltonian matrices and a pairwise-atomic sum of universal interaction-energy matrices, whereas the total aggregate energy eigenvalues obtained are correspondingly partitioned into sums of atomic promotion energies and pairwise-atomic interaction-energies which describe the chemical bonds among the constituent atoms. The latter terms can be calculated employing the standard methods of computational quantum chemistry, modified to accommodate the requirements of the present approach. Illustrative applications to the ground and electronically excited doublet and quartet potential energy surfaces of the H₃ molecule provide atomic promotion and bond energies which are seen to sum to total energies in accord with the results of conventional variational calculations employing explicitly antisymmetric aggregate basis functions. The natures of the calculated atomic promotion and chemical bond energies are discussed, with some emphasis placed on atomic entanglements obtained in molecular dissociation limits.

2015 Western Regional Meeting 147

Range-separated hybrids with correct scaling to the high-density limit

Brandon Krull, *btkrull@gmail.com*, **Filipp Furche**, **Jason Yu**. *Chemistry, University of California, Irvine, Irvine, California, United States*

Using density functional theory to compute thermochemical properties such as atomization energies are strongly dependent on an approximate functional's ability to minimize self-interaction error and correctly describe static correlation. Hybrid density functional theory is widely used because it mitigates self-interaction error but often comes at the cost of a good description of static correlation achieved by cancellation of errors in semi-local density functional approximations. Range-separated hybrids (RSH) improve upon global hybrids by providing a controlled way to use approximate exchange in the short range where semi-local functionals are known to be accurate, and exact exchange in the long-range to describe the correct large-separation limit. However, RSHs often use a system-independent range-separation parameter that is chosen empirically, e.g., by fitting to data or enforcing Koopmans' theorem. In this work, a range-separated hybrid is constructed that satisfies proper coordinate scaling to the high-density limit. This is achieved through the use of a model range-separation function that is a functional of the density and its gradients at the center-of-mass coordinate. The resulting integrals are computed using a new semi-analytical integration technique that extends the Obara-Saika integration scheme to non-local integrals. The exchange-correlation functional is analyzed in terms of the well-known adiabatic decomposition demonstrating that the necessary curvature at or around zero coupling can be achieved only by a non-local functional of the density. The ramifications of proper scaling to the high-density limit on thermochemistry are discussed.

2015 Western Regional Meeting 148

Cubic scaling random phase approximation for molecular systems

Guo Chen, *guoc4@uci.edu*. *Department of Chemistry, University of California, Irvine, Irvine, California, United States*

The random phase approximation (RPA) in a density functional context is a promising method for computing ground-state correlation energies of small-gap systems such as transition metal compounds, reactive intermediates, and nanomaterials. The computational cost of RPA with resolution-of-the-identity (RI) approximation and numerical imaginary frequency integration scales as $O(N^4 \ln N)$ with the system size N . This work reduces the scaling of RPA by further exploiting the sparsity of the electron repulsion integrals in local basis representation. With a general tensor decomposition format and integral pre-screening, a new algorithm with $O(N^3 \ln N)$ operation count and $O(N^2 \ln N)$ memory usage is implemented. The new algorithm enables RPA correlation energy calculations for large-size small-gap molecular systems. The performance of the new algorithm is demonstrated by applications to polypeptides, actinide complexes, and metal clusters.

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2015 Western Regional Meeting 149

Reexamining the hydrated electron's first excited state lifetime through temperature-dependent femtosecond transient absorption

Erik Farr, *erik.peter.farr@gmail.com*. Department of Chemistry and Biochemistry, University of California, Los Angeles, Los Angeles, California, United States

The hydrated electron has been extensively characterized since its discovery in the 1960s. Despite these efforts there remain outstanding questions about its most fundamental interactions with water. There are two competing QM/MM models for the hydrated electron: one depicts the electron residing in a cavity created by excluding water molecules, while the other model predicts the electron to locally increase the density of water while the wave function resides in the interstitial spaces.¹ Despite this drastic change in geometry many of the observables are predicted to be similar. However, the first excited state lifetime is predicted to be short (<200 fs) for the non-adiabatic/non-cavity model and long for the adiabatic/cavity model (>300 fs). The results of transient absorption experiments have been mixed due to multiple local minima in global fits and high correlation between parameters—though transient photoelectron experiments suggest an excited state lifetime on the order of 75 fs.^{2,3} Additionally, recent simulations in our group show the non-cavity model can “switch” to cavity behavior at low temperatures. To differentiate these models and understand the effects of temperature on dynamics we present a new set of temperature dependent transient absorption experiments with a 65 fs cross-correlation time over the range of 0 to 45 C. The dynamics exhibit temperature dependence at both the ~200 fs and ~1 ps timescales. Kerr effect lifetimes for water change by roughly a factor of two over this temperature range and our lifetime parameters are qualitatively in agreement, though the relationship between dielectric relaxation times and hydrated electron dynamics is not clear. Consistent with previous attempts we find that unconstrained global fits cannot differentiate between a cavity and non-cavity picture. Comparison of the global fits with simulation is internally consistent with both cavity and non-cavity behavior depending on the choice of excited state lifetime. Lastly we present evidence of the hydrated electron's p-to-s stimulated emission which exhibits a Gaussian profile red-shifted by 10 nm from the equilibrated hydrated electron's peak absorption and decays in less than 200 fs—a strong indication of a short lifetime.

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2015 Western Regional Meeting 150

Visualization of electron-photon-plasmon coupling in single azulene molecules with the STM

Arthur Yu², *ayu1@uci.edu*, Shaowei Li², Wilson Ho^{2,1}. (1) Chemistry, University of California, Irvine, Irvine, California, United States (2) Physics and Astronomy, University of California, Irvine, Irvine, California, United States

Azulene has been the subject of many studies in photochemistry due to its interesting optical properties. While studied in detail in the gas phase, its electronic and optical properties when adsorbed on surfaces have not been widely reported. In this study, we investigate the interaction between the molecular orbital of an adsorbed azulene molecule on the Ag (110) surface and the surface plasmon of the silver. After adsorbing on the Ag (110) surface, STM

topography of azulene with bias less than 0.5 V resembles the structure of the lowest unoccupied molecule orbital (LUMO). This indicates that the interaction between molecule and substrate is weak enough that it preserves the independence of the molecular orbital. Scanning tunneling spectroscopy (STS) and imaging confirms the presence of the LUMO at 0.6 – 0.8 V. Furthermore, tunneling electron induced plasmon light emission intensity is enhanced when tip is placed over the molecule, with the same spatial extent as the LUMO. Enhancement occurs when the energy difference between the tunneling electron and LUMO matches the energy of a plasmon mode in the tunnel junction. The mechanism can be confirmed by light emission intensity imaging at a bias that leads to an energy mismatch and shows little to no spatial features, therefore no enhancement.

2015 Western Regional Meeting 151

Probing intermolecular coupled vibration by STM inelastic electron tunneling spectroscopy

Zhumin Han¹, zhan@uci.edu, **Chen Xu**¹, **Chi-lun Chiang**¹, **Gregory Czap**¹, **D. W. Yuan**¹, **Ruqian Wu**¹, **Wilson Ho**^{1,2}. (1) Department of Physics and Astronomy, University of California, Irvine, California, United States (2) Department of Chemistry, University of California, Irvine, California, United States

Intermolecular interaction between an adsorbed CO molecule on surface and CO-terminated tip is studied by probing the coupled vibrational mode of the CO dimer with sub-Kelvin scanning tunneling microscope (STM). STM inelastic electron tunneling spectroscopy (IETS) indicates an extra vibrational excitation besides CO hindered translation and hindered rotation near zero bias when the CO-terminated tip approaches the adsorbed CO on surface. With DFT calculation, we identified this mode is the out-of-phase hindered translation mode of the CO dimer. The energy and intensity of this coupled vibrational mode vary with the relative separation between the two CO molecules due to the interplay between CO tilting and orbital overlapping.

2015 Western Regional Meeting 152

Synthesis of polybenzoquinolines as graphene nanoribbon precursors

David J. Dibble¹, djoshdibble@gmail.com, **Young Park**¹, **Mehran Umerani**¹, **Amir Mazaheripour**¹, **Alon A. Gorodetsky**^{1,2}. (1) Department of Chemical Engineering and Material Science, University of California, Irvine, Santa Ana, California, United States (2) Department of Chemistry, University of California, Irvine, Irvine, California, United States

The bottom-up synthesis of all-carbon graphene nanoribbons (narrow strips of sp² hybridized carbon) has attracted much attention in recent years, with a number of contemporary demonstrations of the preparation of all-carbon systems. However, fewer studies have focused on the solution-phase synthesis of heteroatom-doped graphene nanoribbons, the preparation of which remains a significant synthetic challenge. We have developed an iterative route to oligobenzoquinolines based on the aza-Diels–Alder (Povarov) reaction and methodologies for controlling the length and sequence of our oligobenzoquinoline precursors. Our straightforward approach also provides access to crowded macromolecular polybenzoquinoline scaffolds with a unique architecture and connectivity, which are key intermediates for the preparation of nitrogen-doped nanoribbons. Our findings hold implications for the bottom-up synthesis of

graphene nanoribbons whose edge character, terminal functionalities, doping, and length are precisely controllable.

2015 Western Regional Meeting 153

Assembly of graphene oxide

Shanju Zhang, *szhang05@calpoly.edu. Dept of Chemistry and Biochemistry, California Polytechnic State University, San Luis Obispo, California, United States*

Graphene holds great promise for various emerging applications such as structural materials, solar cells, supercapacitors, transistors, etc. The precise control of alignment of graphene is needed for the full exploitation of the excellent properties of 2D crystals. However, it is challenging to fabricate macroscopically ordered assemblies of graphene. Graphene oxide is an excellent intermediate in the graphene synthesis. Reduction of graphene oxide to graphene is a cost-effective route for the large-scale production of graphene. Graphene oxide is highly soluble in water and common organic solvents. Great attention has been paid for assembly of graphene oxide. Here we report a series of experiments on precise control of alignment of graphene oxide in aqueous solutions. Graphene oxide exhibits a nematic liquid crystalline phase in concentrated solutions. The nematic order plays an important role in directing macroscopic assemblies of graphene oxide.

2015 Western Regional Meeting 154

Aza-Diels–Alder route to polyquinolines

David J. Dibble¹, *djoshdibble@gmail.com*, **Mehran Umerani**¹, **Amir Mazaheripour**¹, **Young Park**¹, **Alon A. Gorodetsky**^{1,2}. (1) *Department of Chemical Engineering and Material Science, University of California, Irvine, Santa Ana, California, United States* (2) *Department of Chemistry, University of California, Irvine, Irvine, California, United States*

Polyquinolines have been studied since the early 1970s due to their favorable chemical, optical, electrical, and mechanical properties. These materials have shown particular promise for applications in organic electronic devices, such as light emitting diodes. However, there are few synthetic strategies available for the preparation of polyquinolines, including transition metal catalyzed Suzuki and Sonogashira couplings, oxidative polymerizations, and the Friedlander synthesis. We have developed a new synthetic route to polyquinolines based on the aza-Diels–Alder (Povarov) reaction. Our approach furnishes polyquinolines with a unique architecture and connectivity in only two synthetic steps from inexpensive, commercially available reagents. The resulting products have been extensively characterized with chromatographic and spectroscopic techniques. Our strategy may represent a welcome addition to the polymer chemist's toolkit by providing ready access to a diverse library of polyquinoline-type materials.

2015 Western Regional Meeting 155

Molecular mechanisms of biomolecule binding at nanostructured interfaces

Haley Swanson¹, **Chengchen Guo**², **Stephen K. Davidowski**², **Gregory P. Holland**¹, *gholland@mail.sdsu.edu. (1) Department of Chemistry and Biochemistry, San Diego State*

University, San Diego, California, United States (2) Dept of Chemistry and Biochemistry, Arizona State University, Tempe, Arizona, United States

To achieve the overall goal of constructing sensors and devices that incorporate and exploit the physical properties of biomolecules relies on developing a fundamental understanding of how biomolecules interact and organize at abiotic interfaces, specifically the surfaces of nanomaterials. Recently, researchers have been making considerable headway identifying and studying peptides that bind various nanomaterials with combinatorial libraries and modeling techniques. However, experimental molecular level detail regarding how peptides and proteins are structured at nanoparticle (NP) surfaces is still lacking. A first step is the understanding of how specific amino acids in a given protein sequence bind to nanoparticle surfaces. Our research group is using a combination of solution and solid-state nuclear magnetic resonance (NMR) techniques to probe these interactions and ultimately, determine the structure of biomolecules at the surface of nanostructured materials. We believe a better understanding of the molecular structure and dynamics of peptides and proteins on NP surfaces will help advance the field and bring us closer to building devices that couple the unique properties of biomolecules with NPs. We have been developing and applying NMR methods to probe the conformational structure (peptide folding) and molecular interactions (hydrogen-bonding) responsible for the assembly of amino acids, peptides, and proteins at the interface of various nanostructured materials. Recent results from our research group on this topic will be discussed.

2015 Western Regional Meeting 156

Molecular dynamics simulations of stacked DNA base surrogates

Cade B. Markegard, Amir Mazaheripour, amazaher@uci.edu, Jonah Jocson, Austin G. Wardrip, Anthony M. Burke, Mary Nora Dickson, Alon A. Gorodetsky, Hung Nguyen. University of California, Irvine, Irvine, California, United States

Organic nanowires represent idealized model systems for understanding the interactions between organic semiconductor building blocks. We have synthesized nanowires consisting of pi-conjugated DNA-base surrogates covalently attached to a DNA-like backbone and studied the properties of these constructs with molecular dynamics simulations. The DNA base surrogates were first parametrized through quantum mechanics calculations to create an atomistic model. Constant-temperature molecular dynamics simulations then provided an improved understanding of the kinetics of stacking between adjacent DNA base surrogates. Replica-exchange simulations in turn yielded the atomic structures of our nanowires at equilibrium. By examining the lowest energy structures obtained from our simulations, we have gained insight into the structure and integrity of our nanowires, which would not be readily available through experimental techniques.

2015 Western Regional Meeting 157

Infrared invisibility stickers inspired by cephalopods

Long Phan¹, longp1@uci.edu, David D. Ordinario¹, Emil Karshalev¹, Ward G. Walkup¹, Michael A. Shenk¹, Alon A. Gorodetsky^{2,1}. (1) Chemical Engineering and Materials Science, University of

California, Irvine, Irvine, California, United States (2) Chem Eng Mtrl Sci, University of California, Irvine, Irvine, California, United States

The skin structure of cephalopods endows them with remarkable dynamic camouflage capabilities. Consequently, much research effort has focused on understanding and emulating these animals' color changing abilities in the visible region of the electromagnetic spectrum. In contrast, despite the importance of infrared signaling and detection for many industrial and military applications, few studies have attempted to translate the principles underlying cephalopod adaptive coloration to infrared camouflage. We have drawn inspiration from nanostructures implicated in cephalopods' camouflage abilities and developed strategies for the self-assembly of unique cephalopod structural proteins into dynamically tunable biomimetic camouflage coatings on both transparent and flexible substrates.^{1,2} Our substrates can adhere to arbitrary surfaces, and their reflectance can be reversibly modulated from the visible to the near-infrared regions of the electromagnetic spectrum with both chemical and mechanical stimuli.^{1,2} Thus, we can endow common objects with any shape or form factor with tunable camouflage capabilities.^{1,2} Our work represents a key step toward the development of wearable biomimetic color and shapeshifting technologies for stealth applications.

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2015 Western Regional Meeting 158

Intellectual property considerations for small and mid-size chemical businesses

Sandra P. Thompson, *thompsoniplaw@cox.net. Slater Hersey & Lieberman LLP, Irvine, California, United States*

There are many pressing issues when starting your own business, but in many instances, intellectual property considerations are not discussed early in the process. This presentation will focus on several key areas: a) setting up an IP review committee, b) patent information for small businesses and c) how to maximize your company's IP budget.

2015 Western Regional Meeting 159

Pay for delay settlements in pharmaceutical cases

Genevieve M. Halpenny, *ghalpenny@fishiplaw.com. Fish & Tsang LLP, Irvine, California, United States*

Pharmaceutical companies risk violating antitrust laws when the companies enter "reverse payment" settlement agreements. One aim of the Hatch Waxman Act is to decrease drug prices by providing 180 days of market exclusivity to the first generic pharmaceutical companies that challenge the validity of drug patents. The number of such challenges has increased. However, pharmaceutical companies have increasingly settled such litigation under terms in which the patentee pays the accused infringer, the reverse of how settlement payments are usually structured in patent litigation. Thus, these payments have been dubbed "reverse payments." In

many cases, reverse payment settlement agreements led to increased drug prices. The question in *FTC v. Actavis, Inc.* was “whether such an agreement can sometimes unreasonably diminish competition in violation of the antitrust laws.” The short answer is yes. In *Actavis*, the Supreme Court narrowed the applicability of the presumption that reverse payment settlements are anticompetitive to limited circumstances, such as when the size of the reverse payment was large compared to the amount saved by ending litigation. After the Supreme Court decided *Actavis*, there was uncertainty regarding what forms of compensation would be included in the putative reverse payment. In the First Circuit, a district court dismissed an antitrust suit, because the reverse payment was not in cash, interpreting *Actavis* narrowly. The First Circuit is reviewing that dismissal. Recently, the Third Circuit revived a case involving a non-cash reverse payment. Therefore, it appears likely that courts will include non-cash exchanges in the value of reverse payments.

2015 Western Regional Meeting 160

Processing invention disclosures at a university technology transfer office

Ryan C. Smith, RCSmith@duanemorris.com. *Duane Morris LLP, San Diego, California, United States*

The university is an important source of innovation in our economy. From the Bayh-Dole Act, universities are granted ownership of their inventions. Accordingly, universities apply for patents and seek to license said patents on their researchers' inventions. This presentation will present university patent and licensing practices from both private and public institutions.

2015 Western Regional Meeting 161

Review of recent federal circuit decisions relevant to what scientists need to know about patent filing and prosecution

Sandra P. Thompson, thompsoniplaw@cox.net. *Slater Hersey & Lieberman LLP, Irvine, California, United States*

Chemical and pharmaceutical companies invest enormous amounts of money and inventor hours to discover and develop new materials such as drugs and processes for making them, as well as other inventions. Such companies also attempt to protect their inventions by securing patents. The success of these inventions in the marketplace depends on a number of factors, the foremost of which being the strength of the patents obtained to protect them. These patents are expected to protect the vast investment of money and time in creating these inventions, and the product market share, for the next nearly twenty years. However, competitors will try to undermine the value of the inventions by challenging the strength of the patents, including their validity and coverage by the patent claims of their own products, in a court of law. Recently, many seemingly strong and valuable patents have been invalidated or narrowly viewed and found not infringed. Recent court decisions reinforce the axiom that every word that goes into describing the invention in a patent application must be chosen with extreme care. This session will provide insights into how to reduce the chances of losing in a patent battle against an infringer, including practical pointers on how to write winning patent applications. This session will also analyze recent Federal Circuit court decisions that have invalidated such patents or

found them not infringed, as real world examples of what can go right or wrong years after a patent is granted.

2015 Western Regional Meeting 162

Hidden in plain site: Discovery of a widespread, yet highly sought-after enzyme function

Justin B. Siegel, jbsiegel@ucdavis.edu. UC Davis Genome Center, Davis, California, United States

In 2005 a landmark paper describing the first recombinant enzyme capable of enabling the biological production of alkanes was reported. Since then huge efforts have gone into understanding what makes this enzyme "special". Here I will present that this function is actually widely spread and a common function found amongst the entire superfamily of one the largest protein families known. I will present a series of rules developed through molecular modeling and machine learning that enable prediction of function, as well as the utilization of these rules to engineer this function into proteins that previously had no known enzyme activity.

2015 Western Regional Meeting 163

Catalytic enantioselective dihalogenation for the synthesis of polyhalogenated natural products

Noah Z. Burns, nburns@stanford.edu. Chemistry, Stanford University, Stanford, California, United States

Nearly 2,000 halogenated natural products containing either a chlorine- or bromine-bearing stereocenter have been structurally characterized, many of which exhibit promising bioactivity and/or unknown biophysics. Further investigations into the therapeutic potential, mode of action, or bulk properties of such molecules has been hindered by an unreliable supply from natural sources and by a lack of fully selective synthetic methods for the synthesis of chiral polyhalogenated small molecules. A major focus of our research program has been the development of enabling catalytic chemo-, regio-, and enantioselective halogenation chemistry specifically for the construction of relevant natural product motifs. The applications of such efforts to the total syntheses of complex polyhalogenated natural products will be presented.

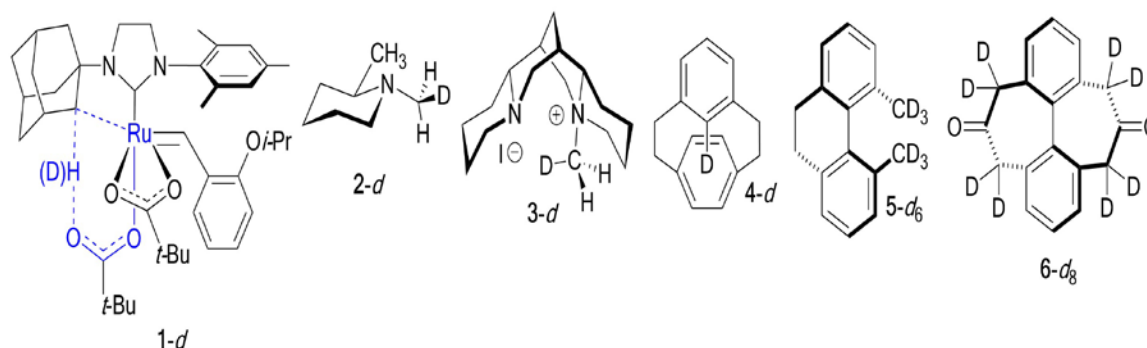
2015 Western Regional Meeting 164

Diverse origins of isotope effects revealed by experiment and theory

Daniel J. O'Leary, doleary@pomona.edu. Dept of Chemistry, Pomona College, Claremont, California, United States

This talk will highlight examples of isotope effects studied with combined experimental and theoretical approaches. Examples will include a kinetic isotope effect (KIE) in the C-H insertion reaction in ruthenium complex **1-d**, as well as equilibrium isotope effects (EIEs) that give rise to diastereotopic CH₂D protons with predictably different ¹H chemical shifts in 1,2-dimethylpiperidine **2-d** and *N*-(CH₂D)-isosparteinium iodide **2-d**. The conformational KIE in [2.2]-metaparacyclophane-**d** (**4-d**) can be accurately predicted and is found to be purely enthalpic in

origin. The situation is not so clear cut in in two other systems, namely, Mislow's 9,10-dihydro-4,5-dimethylphenanthrene **5-d₆** and the doubly bridged biphenyl diketone **6-d₈**. Interestingly, the effect of deuteration in these systems is opposite, accelerating the process in **5-d₆** ($k_H/k_D = 0.89$, 315 K) and slowing the rate of racemization of **6-d₈** ($k_H/k_D = 1.06$, 368 K). The computational predictions for these systems are in good agreement with experiment, and suggest that conformational KIEs in heavily deuterated molecules can have significant vibrational entropy contributions, which need to be considered in addition to zero-point vibrational energy differences.

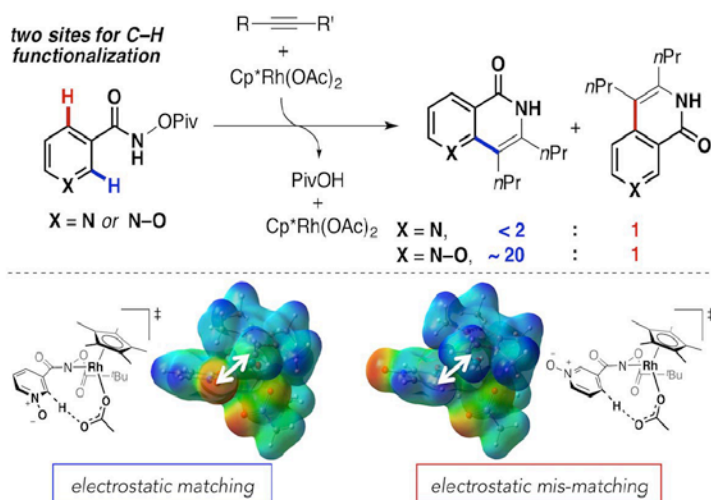


2015 Western Regional Meeting 165

Origin of the selectivity difference between pyridine *N*-oxide and pyridine substrates for Rh(III)-catalyzed C-H functionalization

Sharon R. Neufeldt², sharon.neufeldt@gmail.com, Gonzalo Jimenez-Oses², John R. Huckins¹, Oliver R. Thiel¹, Kendall N. Houk². (1) AMGEN Inc., Thousand Oaks, California, United States (2) UCLA, Los Angeles, California, United States

In a Rh(III)-catalyzed annulation reaction with an alkyne coupling partner, pyridine *N*-oxide substrates undergo site-selective C–H functionalization, whereas the analogous pyridine substrates are relatively unselective. The origin of this selectivity difference was investigated computationally, and was found to be influenced by two steps of the catalytic cycle: C–H cleavage and alkyne insertion. The pyridine and *N*-oxide substrates favor opposite sites for C–H activation, but they favor alkyne insertion at the same carbon. Electrostatic interactions play a role in the selectivity of both of these steps. Additionally, the selectivity of C–H cleavage correlates with C–H acidity and C–Rh bond strength. Our calculations allowed us to make a number of predictions that we tested in the lab, and the results of these experiments corroborate those of our computations.



2015 Western Regional Meeting 166

Phosphines and phosphinocatalysis

Ohyun Kwon, ohyun@chem.ucla.edu. Chemistry and Biochemistry, UCLA, Los Angeles, California, United States

Soft nucleophilic phosphinocatalysis has been known since the 1960s as a result of the pioneering work of Horner, Price, Rauhut–Currier, and Morita. In the 1990s, Trost and Lu made important discoveries, reporting isomerization, umpolung addition, and [3+2] cycloaddition. Nonetheless, it was not until the 2000s that the area of phosphinocatalysis began to flourish. My group, through careful analysis of the mechanism of the phosphinocatalysis reactions, has demonstrated over two dozen new reactions facilitated by phosphine catalysts. The results are a one-step conversion of simple acyclic starting materials into various carbo- and heterocycles. The practical values of these one-step phosphine-catalyzed annulation processes are significant since (1) they are atom-economic and environmentally friendly, and (2) the heterocycles are an immense class of organic compounds with numerous practical applications. One recent, particularly significant advancement is the creation of chiral phosphines that are derived from a natural amino acid, hydroxyproline. Their synthetic utility in the phosphine-catalyzed annulations, application in total syntheses of (+)-ibophyllidine and (–)-actinophyllic acid, and commercialization will also be discussed.

2015 Western Regional Meeting 167

Automated reaction analysis and the power of data-rich reaction progress measurements

Jason Hein, jhein@chem.ubc.ca. Chemistry, University of British Columbia, Vancouver, British Columbia, Canada

Designing a highly efficient and robust chemical reaction system requires detailed information regarding the interplay between key species on and off the productive mechanistic pathway. In general, optimization of a chemical transformation requires a detailed understanding of all ancillary processes in a reaction network that either directly or indirectly influence the chemistry

of interest. This is especially true in catalytic reactions where the generation and subsequent liberation of the catalyst from off-cycle reservoirs over the course of the reaction may result in unexpected behaviours, including anomalous reactivity, chemoselectivity and rate. Ultimately, a fundamental understanding of the ensemble of associated equilibria present within a synthetic transformation is critical in order to develop the reaction for practical application.

In order to efficiently study complex reaction networks we have developed an approach that leverages a combination of in-situ reaction monitoring techniques, including ReactIR, reaction calorimetry and automated reaction sampling. The tandem application of this suite of process analytical technology allows us to rapidly deconvolute complex pathways and competing reactions. This technology allows complex kinetic analysis of a reaction system to be reduced to simple pattern recognition. Our approach has been applied to the development of novel mesoionic carbene organocatalysts, the investigation of a Dy(III)-catalyzed aza-Piatelli rearrangement and the discovery of a new highly efficient Cu(I)-catalyzed cycloisomerization. Application of these techniques and current progress on other related systems will be discussed.

2015 Western Regional Meeting 168

Interplay of theory and experiment in (I) the design of GK-GKRP inhibitors and (II) the origins of rate acceleration in heteroaryl-substituted S_NAr substrates

Michael D. Bartberger, *michael.d.bartberger@gmail.com*. Molecular Engineering, Amgen, Inc., Thousand Oaks, California, United States

From synthetic chemistry to drug design, indeed-- this presentation will touch upon two of the numerous applications of computational chemistry in the therapeutic discovery setting. First, the role of electronic structure theory in the prediction (and subsequent experimental application) of an unconventional, conformational-stabilizing interaction in the design a novel, potent scaffold for the disruption of the glucokinase-glucokinase regulatory protein (GK-GKRP) interaction will be reported. Next, dissection of electron-withdrawing versus nucleophile-substrate hydrogen bonding characteristics at the TS involving a "click-and-activate" S_NAr scaffold will be discussed.

2015 Western Regional Meeting 169

The interplay of experiment and computation in rearrangement reactions relevant to alkaloid synthesis

Christopher D. Vanderwal, *cdv@uci.edu*. University of California, Irvine, California, United States

In the course of our studies on indole alkaloid synthesis and on the unusual intramolecular arene/allene Diels–Alder cycloadditions of Himbert, we have benefited tremendously from the expertise of the Houk group. Our collaboration has shed mechanistic insight on some pericyclic cascades, formal cycloadditions, dearomatizing cycloadditions, stepwise formal dyotropic rearrangements, and alkene metathesis cascades. In this lecture, I will discuss selected aspects of these investigations that nicely synergized computation and experiment.

2015 Western Regional Meeting 170

Mediated electron transfer: An electrochemical approach

Raymond D. Little, little@chem.ucsb.edu. Chemistry & Biochemistry, University of California Santa Barbara, Santa Barbara, California, United States

The presentation will highlight some of the advantages/disadvantages of using redox mediators to achieve electron transfer. An attempt will be made to integrate the role that quantum calculations have played in facilitating our understanding of the ion radicals generated in this manner. Finally, progress toward the development of a reusable surrogate for traditional supporting electrolytes will be described.

2015 Western Regional Meeting 171

Do aza-*ortho*-quinone-methide mediated transformations involve aza-*ortho*-quinone-methides?

Daniel M. Walden⁴, Ryne C. Johnston⁴, Ashley Jaworski¹, Michael T. Hovey², Matthew P. Meyer⁵, Karl Scheidt¹, **Paul Cheong**³, paulhcheong@gmail.com. (1) Northwestern University, Evanston, Illinois, United States (2) Chemistry, Northwestern University, Chicago, Illinois, United States (3) Chem Dept, Oregon State Univ, Corvallis, Oregon, United States (4) Chemistry, Oregon State University, Corvallis, Oregon, United States (5) UC Merced, Atwater, California, United States

Like the *ortho*-quinone methide (oQM), the aza analogue (aoQM) stands out as an exceptionally reactive intermediate owing to the sizeable rearomatization driving force. aoQMs have been postulated as short-lived intermediates in a number of pericyclic reactions and nucleophilic additions, though none have yet to be isolated. The use of Cs carbonate as base in two reactions provides a thermodynamically favorable means to form aoQMs at room temperature through the release of byproduct salt exotherms, independent of the salt solubility. By integrating experimental & computational approaches, we have discovered that aoQM intermediates are remarkably unstable ($\Delta G \sim 50$ kcal/mol), precluding their formation under ambient conditions. The exergonicity of the cesium salt formation provides a dramatic driving force (average $\Delta G \sim -40$ kcal/mol) compensating for the majority of this inherent unfavorable thermodynamics. This discovery reevaluates the mechanisms of room temperature aza-*ortho*-quinone-methide mediated reactions.

2015 Western Regional Meeting 172

Adventures in aldehyde C-H bond activation

Vy M. Dong, dongv@uci.edu. Chemistry, University of California at Irvine, Irvine, California, United States

Lactones and lactams make up a range of structurally complex and functional compounds, from antibiotics to nanomaterials. Inspired by Nature's cyclic architectures, we are developing catalytic methods that feature stereoselective hydroacylation. Hydroacylation, the formal addition of an aldehyde C-H bond across an unsaturated functional group, is an ideal approach to carbonyl functionalities commonly found in bioactive molecules. We aim to advance hydroacylation as a unified strategy for transforming aldehydes into chiral esters, ketones, and

amides. In this context, my lecture will discuss the design, scope, and mechanism for hydroacylation methods using rhodium, cobalt, and ruthenium catalysis. Our long-term goal is to develop more green, versatile, and efficient strategies for constructing heterocycles, polyketides, and other biologically relevant motifs.

2015 Western Regional Meeting 173

Computational studies of cation- π interactions and applications to neuroscience

Dennis A. Dougherty, dadougherty@caltech.edu. Caltech, Pasadena, California, United States

The cation- π interaction is important in many contexts throughout chemistry and biology. We have been particularly focused on its role in ligand recognition in neuroscience. We will show how a combination of computation and experiment has allowed us to identify key cation- π interactions in a range of neuroreceptors. We have also shown the crucial role the cation- π interaction plays in the addictive properties of nicotine.

2015 Western Regional Meeting 174

My career in chemistry with Woodward, cycloadditions, and the interplay of computation and experiment

Kendall N. Houk, hok@chem.ucla.edu. UCLA, Los Angeles, California, United States

After a brief account of my start in the research group of R. B. Woodward in 1965, I will describe my adventures in the explorations of cycloadditions and recount how the rise in computational methods and computer power has driven my career. We continue to combine experiment and computation to understand reactivity and selectivity in chemistry and to design catalysts, enzymes, and materials.

2015 Western Regional Meeting 175

Mechanical analysis of three coaxial electrospun synthetic biopolymers

Roy Anderson, randers2@umbc.edu. Mechanical Engineering, University of Colorado, Boulder, Colorado, United States

Cardiovascular disease is one of the leading causes of death in North America. Management techniques such as vascular grafting are essential to preventing death from cardiovascular disease. Synthetic vascular grafts are ideal, but currently the leading material is approximately 43% successful. There is a need for creating mechanically stable synthetic biopolymers for vascular grafting. Vascular grafting is a very important and effective treatment technique for treating heart disease. Improving synthetic vascular graft performance will lead to more patients having the ability to have this treatment. Mixtures of polymer solutions with a fixed ratio of 1:5 between a hydrophobic, synthetic, biodegradable polymer (PU, PCL or PLA) and hydrophilic, natural-derived gelatin. The hybrid composite nanofibers demonstrate highly-interactive layered structure between the hydrophobic core and the gelatin sheath. Varied interactions between the core materials and the sheath lead to the difference in the sheath thickness, core-sheath structure. Rheological analysis was conducted to characterize the mechanical properties of this

material. The linear viscoelastic region (LVR) was found for all three biopolymers, meaning further information can be found from this material which could lead to more material testing. Following the success of finding the LVR of all three polymers, frequency sweeps were conducted on two out of the three polymers to test the mechanical stability. Frequency sweeps illustrate that while the polymer has the potential to withstand the frequency of a heartbeat and other complex frequencies of the body. Preliminary data illustrates that PU:Gel displayed a higher complex modulus each biopolymer could withstand the average pressure of blood flow, and the frequency of a heart beat. Future tests regarding the effect of crosslink chain lengths on the mechanical property of biopolymers will be conducted.

2015 Western Regional Meeting 176

College students' understandings of phase transitions: Semantic, experiential, and energy-related difficulties

Paul G. Jasien, jasien@csusm.edu. *Chemistry & Biochemistry, California State University, San Marcos, Temecula, California, United States*

Scientific concepts related to phase transitions of matter are taught at various levels of instruction, ranging from elementary school to upper-division physical chemistry. Despite this coverage, students at all levels may still exhibit difficulties with these concepts. The reasons for this are many and varied, but this presentation will illustrate some common college student misconceptions that originate from semantics and experience. Building on this data, results from a more detailed follow-up study on college students' understandings of phase transitions will be presented. In this latter work, a series of multiple-choice questions was developed that investigated students' interpretations of energy changes in matter as they relate to a generic graph of *Temperature vs. Energy Added*. These questions specifically probed students' ideas about how the kinetic, potential, and total energy changed during a phase transition. Data was collected from second semester general chemistry and upper-division physical chemistry students. These data were analyzed both in terms of basic content knowledge and with respect to the internal consistency of answers from one question to another.

2015 Western Regional Meeting 177

Three questions: What have students absorbed from lecture?

Jessica A. Parr, parr@usc.edu. *Chemistry, University of Southern California, Culver City, California, United States*

Students often have difficulty identifying the key ideas that they are expected to take away from a lecture or unit. This fall I will be introducing a self-test for students to attempt directly after the lecture. The self-test will consist of three questions that students should be able to answer if they have absorbed what I expect them to. The questions will cover conceptual topics and quantitative problems. The questions will be posted on the course webpage directly after the lecture. The answers will be posted twenty-four hours later. To truly assess their own understanding and knowledge, students should attempt the questions without a solution available right away. A secondary function of these self-tests will be for students to seek help and intervention early, not just before a high-stakes exam. This will offer students an opportunity

to try and fail with no consequences to their grade. This talk will look at the evolution of these self-tests throughout the first half of the semester.

2015 Western Regional Meeting 178

Interdisciplinary and collaborative methods in chemical education

Lucy HG Solomon³, *Isolomon@csusm.edu*, David L. Garin¹, Matt McBane². (1) Chemistry Biochem, University of Missouri, Saint Louis, Missouri, United States (2) Music, Princeton University, Princeton, New Jersey, United States (3) Media Design School of Art, CSUSM, San Marcos, California, United States

We present a case study in interdisciplinary educational models for broadening interest in chemistry among school children and the public at large, utilizing an unconventional and engaging method that incorporates strategies and practices from the arts. The co-presenters, joined with choreographers and an architect, performed chemistry in a laboratory, in a dance studio, and on a public water barge. Their explorations and sharing of knowledge galvanized the interest of all participants in laboratory methods. Workshops with schoolchildren that layered chemistry with narrative connected the students with the subject material on multiple levels. In preparation for working together, the collaborators – from chemistry and from the arts – shared their methodologies. This included the demonstration of an oscillation reaction in the laboratory. The group then took the same experiment and “performed” it in different contexts, with movement and musical composition, altering how all participants conceptualized the original experiment.

Another example of applied and amplified chemistry involved a field trip with schoolchildren on a water barge in Brooklyn where they could learn about chemistry and the environment in a tactile, experiential way. This project involved the creation of miniature glaciers, expanding the children’s understanding of physical and chemical changes and their environmental consequences.

When educators, researchers, and students alike grapple with scientific problems with a larger set of tools, including music, movement, and the visual arts, new ways of looking at problems emerge, as do different solutions. This cross-pollination of ideas and approaches offers a more layered route to understanding chemistry and generates both an interest in exploring chemical solutions in particular and in creative problem solving in general.

2015 Western Regional Meeting 179

Nine years and counting: S-STEM scholarships as a tool for success at CSUSB

Kimberley R. Cousins, *kcousins@csusb.edu*. Chemistry Biochemistry, California State University, San Bernardino, California, United States

The S-STEM Scholarship program at CSUSB has been providing co-curricular and financial support for over 120 STEM majors, since 2007. A strong mentoring system and a culture of high expectations for participation in academic and professional opportunities, including undergraduate research, have lead to very high retention numbers and impressive graduation rates, in addition to moderately short times to degree. Partnerships across campus with other grant-funded and student success initiatives have provided additional opportunities for scholars. Exit interviews being conducted during the second phase of the program highlight some of the

less quantifiable reasons for scholar success. Recent revisions in the S-STEM program guidelines have provided new possibilities for future S-STEM projects at this Hispanic-Serving Minority University.

2015 Western Regional Meeting 180

Contextualized chemistry: Bringing career relevance to your classroom

Jewyl Clarke, *jewylalderson@gmail.com. Grossmont Community College and Sweetwater Union High School District, La Mesa, California, United States*

Bring chemistry to the classroom through career focused readings, labs and activities and free NGSS aligned resources. Look at new ways to integrate exciting career focused curriculum into your chemistry classroom from medical chemistry and green chemistry, to chemistry involved in global trade.

2015 Western Regional Meeting 181

Using technology to reach out to new generation for a fully online chemistry course

Karno Ng, *kng@csusm.edu. Department of Chemistry & Biochemistry, California State University San Marcos, San Marcos, California, United States*

On-line courses have become more and more popular over the past several years due to technological advances and the desire of many students to seek greater flexibility in their course schedules. In a study of 2,500 universities and colleges conducted by the Sloan Foundation, online enrollments in the year of 2009 experienced a 21% rate of growth. This increase far exceeds the 2% growth in the overall higher education student population.¹

On-line courses provide new opportunities to attract students, but they also lead to new challenges. One of the challenges involves the lack of face-to-face interaction between students and instructors. The purpose of this study is to explore the effectiveness of new technology tools to enhance interaction between instructors and students.

2015 Western Regional Meeting 182

Protein crystallography facilities at the Stanford Synchrotron Radiation Laboratory

Silvia Russi, *srussi@slac.stanford.edu. SMB Group, Stanford Synchrotron Radiation Lightsource, Menlo Park, California, United States*

The Structural Molecular Biology (SMB) group at the Stanford Synchrotron Radiation Lightsource (SSRL) operates five state-of-the-art macromolecular crystallography beam lines: BL7-1, BL9-2, BL11-1, BL12-2 and BL14-1. A new micro-focus station, BL12-1 is under construction. Users' access to these beam lines is possible by submission of a regular or rapid access proposal [1] and when cryo-cooled crystals are used experiments may be conducted remotely, by accessing the Blu-Ice beam line control software [2] through an internet connection. Remote users benefit from the same resources as local users: the capability to mount, center, and screen crystal samples; and collect, analyze and backup the diffraction data. Automated sample handling is accomplished with the Stanford Automated Mounting (SAM)

system [3] that mounts cryo-cooled samples stored in SSRL cassettes or UniPucks compatible with other robotic systems. Recently upgraded, the sample exchange cycle of SAM has been significantly reduced increasing the screening capability to over a thousand sample pins of crystals per day. The Web-Ice toolset [4] automatically processes the diffraction images during screening and analyzes the number of spots, Bravais lattice, unit cell, estimated mosaicity, and maximum diffraction resolution. Web-Ice also calculates data collection strategies for mounted samples. In addition, all users have access to ancillary equipment including an online UV-visible absorption spectroscopy system [5] to monitor metal oxidation states within protein crystals or for radiation damage studies, and a Visex microscope [6] that uses visible light emission to identify protein crystals. The undulator microfocus station BL12-2 is optimized for diffraction experiments using very small crystals and is outfitted with a Dectris Pilatus PAD detector that enables rapid data collection in a shutterless mode. New developments at BL12-2 include the implementation of low-dose shutterless micro-beam raster searches to quickly locate very small crystals (or the best diffracting areas of larger crystals) and the introduction of automated routines and new high density sample holders to facilitate the collection and combination of data from multiple micro-meter sized crystals. The BL12-2 instrumentation has also served as a model for a new goniometer-based setup supported by SMB staff for femtosecond diffraction experiments at the XPP instrument of the Linac Coherent Light Source (LCLS) [7].

2015 Western Regional Meeting 183

X-ray crystallography and HIV-1 vaccine design

Robyn Stanfield, *robyn@scripps.edu*. *The Scripps Research Institute, La Jolla, California, United States*

With over 2 million people newly infected with HIV-1 last year, the need for an effective vaccine to protect from viral infection is critical. The HIV-1 viral envelope proteins, gp120 and gp41, are the targets for antibodies that can 'neutralize', or protect against viral infection. If a vaccine can elicit such an antibody response, it should protect against infection. To help understand the mechanisms of HIV-1 neutralization and to develop immunogens to elicit neutralizing antibodies, we are using x-ray crystallography to determine structures for potent, broadly neutralizing antibodies, purified from infected patients, in complex with their viral antigens. These structures have revealed many novel features never before seen in human antibodies, and reveal strategies used by our immune system to evade this rapidly evolving virus.

2015 Western Regional Meeting 184

Protein molecular modeling for chemical biology

Andrew Orry, *andy@molsoft.com*. *Molsoft LLC, San Diego, California, United States*

The Protein Data Bank (PDB) has rapidly grown to more than 100,000 atomic resolution structures and contains multiple depositions for even the most recalcitrant to crystallization such as G-protein coupled receptors (GPCRs), ion channels and other drug target membrane proteins. Molecular modeling when applied carefully can be used to extend the PDB data and define details not observed directly in the crystal structure. Models can guide the solution to challenging problems such as predicting drug-receptor interaction and ligand-induced structural changes, understanding protein flexibility and predicting the effect of a mutation on binding and

stability.

High quality protein models built based on homology to a PDB structure have an application for drug discovery. The model can be used to map out the cavities on the surface of a protein which can aid the identification of an allosteric pocket or potential protein-protein interaction sites. Chemical modulators to these sites can then be predicted by modeling the interaction of a small molecule in the binding pocket using *in silico* docking and screening methods. This can lead to the development of a new inhibitor series, drug selectivity prediction, target de-orphanization or drug re-purposing.

Here the most recent molecular modeling methods will be discussed highlighting their use on structures downloaded from the PDB. The emphasis will be on the application of the methods for drug lead design and optimization.

2015 Western Regional Meeting 185

Elucidating chemical structure at beamline 11.3.1 at the advanced light source

Kevin J. Gagnon, *kjgagnon@lbl.gov*, Gregory Y. Morrison, James R. Nasiatka, Simon J. Teat. Advanced Light Source, Lawrence Berkeley National Lab, Pleasant Hill, California, United States

One of the greatest challenges facing crystallographers has always been how to collect good data. This has become especially challenging as chemists are creating more complex compounds and looking to extract new exotic structural information from crystals which are getting smaller and smaller. Often, these crystals produce little or no diffraction on a laboratory diffractometer with long exposures. The past two decades have provided world-class synchrotron facilities to help solve these problems through a combination of high flux and a small focused beam spot size. Station 11.3.1 at the Advanced Light Source is a dedicated chemical crystallography beamline which has been developed and improved over the last decade to provide a global user base with a high flux, focused beam which is capable of doing more than just providing excellent data on weakly diffracting samples. Recent developments on station 11.3.1 include an environmental gas cell for studying of samples under evacuation, up to 1 atm of gasses and mixtures of gasses, and under gas flow; a diamond anvil cell for studying samples under applied pressures up to 10 GPa; a photodiode array for in-situ photocrystallography; a tunable monochromator allowing energies between 6 and 22 keV; and a CMOS Bruker PHOTON100 detector running shutterless for rapid high quality data collection.

2015 Western Regional Meeting 186

Targeted crystal growth of rare earth intermetallics with synergistic magnetic and electrical properties

Julia Chan, *Julia.Chan@utdallas.edu*. Chemistry, University of Texas at Dallas, Richardson, Texas, United States

The discovery and characterization of novel intermetallic compounds is important for broadening the understanding of structure-property relationships of functional materials. Our current research areas in superconductivity, unusual magnetism, thermoelectrics, and magnetocalorics,

rely heavily on the intimate relationship between structure and physical properties. Likewise, the determination of anisotropic physical properties from high quality single crystals is vital in probing the intrinsic electrical and the competing magnetic interactions to understand the chemistry and physics of these materials. In this talk, I will highlight the crystal growth, characterization, and properties of magnetically frustrated intermetallics.

2015 Western Regional Meeting 187

Advanced oxidation applied to water reuse and drought mitigation

David Hokanson, *david.hokanson@trusselltech.com. Trussell Technologies, Inc., Pasadena, California, United States*

The effect of drought on California is to bring into play challenging source waters that were too expensive to be viable drinking water sources in the past. In search of reliable drinking water sources that are available even in times of drought, potable reuse is gaining traction as a source water for meeting future demand in the face of drought and population growth. The California Division of Drinking Water (DDW) adopted regulations for groundwater recharge reuse applications (GWR regulations) in June 2014. The GWR regulations require full advanced treatment (FAT) for groundwater recharge projects. FAT includes MF/RO, the subject of other presentations in the advanced treatment session, as well as advanced oxidation. Advanced oxidation is required for the removal of constituents of emerging concern (CECs), as demonstrated through removal of an indicator compound 1,4-dioxane to a prescribed level (0.5-log, or 69% removal). This presentation will provide the regulatory context, the basics of advanced oxidation, details on specific technologies that may be applied to meet DDW FAT requirements, and case studies where advanced oxidation is under consideration. Advanced oxidation processes discussed in this presentation include ozone and UV AOPs.

2015 Western Regional Meeting 188

Chloramine reactivity in wastewater: Kinetics and mechanisms of chlorinated byproduct formation

*Jamie Gleason, Jennifer Castillo, **Stephen P. Mezyk**, smezyk@csulb.edu. Ca State Univ, Long Beach, California, United States*

In order to control membrane biofouling in some wastewater treatment and water reuse systems chloramines (NH_2Cl , NHCl_2 , NCl_3) are deliberately generated by addition of free chlorine that reacts with the ammonia naturally present. These chloramines will readily pass through these membranes and could thermally react and impact a downstream UV-based Advanced Oxidation Process system. In addition to the UV-initiated radical chemistry of these chloramine species their thermal chemistry is also of interest. Their reaction with simple organic species, such as amino acids, are of concern in generating unwanted chlorinated byproducts. In this study the kinetics of chloramine reaction with amino acids have been measured with second-order rate constants elucidated. In addition, ^{15}N NMR studies were performed to determine the final chlorinated products of this reaction.

2015 Western Regional Meeting 189

Sulfate radical remediation of pharmaceutical contaminated wastewaters: Impact of dissolved organic matter

Trevor Reutershan, *treutershan@gmail.com*, **Stephen Mezyk**, *California State University at Long Beach, Seal Beach, California, United States*

Quantitative removal of pharmaceutical compounds from wastewater is a current problem facing utilities management today. Insufficient remediation of these compounds may lead to antibiotic resistant bacteria, feminization of fish, and increased health concerns in the public. Radical-based advanced oxidation and reduction processes (AO/RPs) have been shown to be a promising method to effectively mineralize these compounds. This study investigates the applicability of sulfate radical based oxidation of antibiotics towards their quantitative removal from water. Specifically, the influence of dissolved organic matter (DOM) as a scavenger of oxidative species was investigated as pharmaceuticals may interact with the DOM macromolecule and retard the remediation abilities of radical-based AOPs. Kinetic competition studies were performed between the sulfate radical, small organic pharmaceuticals and DOM. Kinetic traces were obtained to find the pseudo first order rate constant of sulfate radical and the equilibrium constant of association between various pharmaceutical compounds and DOM. The average equilibrium constant between a library of samples of organic matter and antibiotics was found to be 128.1 ± 13.8 using a Langmuir adsorption model. Using a similar model, the association constants from estrogenic steroids was observed to be an order of magnitude larger than the antibiotics, and the association of carcinogenic nitrosamines to DOM was correlated to the hydrophobic nature of the functional groups. The association of these small organic compounds must be taken into consideration when designing remediation processes.

2015 Western Regional Meeting 190

Investigating the impact of solution chemistry on advanced oxidative processes in reverse osmosis permeate treatment

Wei Li¹, *lucylee88@hotmail.com*, **Samuel D. Patton**³, **Haizhou Liu**². (1) *Chemical and Environmental Engineering, University of California Riverside, Riverside, California, United States* (2) *Chemical and Environmental Engineering, University of California, Riverside, Riverside, California, United States* (3) *Chemical and Environmental Engineering, University of California Riverside, Riverside, California, United States*

Increasing water scarcity due to drought calls for water management strategies such as groundwater recharge, wastewater reuse, and a diversification of treatment techniques. Reverse Osmosis (RO) alongside advanced oxidation processes (AOPs) is one such technique used in treating secondary wastewater effluent to produce high quality recycled water. The process relies on a semipermeable membrane, which allows water through and rejects large molecules, organics and salts. One of the problems with RO is that small, uncharged species such as 1, 4-dioxane can pass through in concentrations above the notification level (1 µg/L). Advanced Oxidation Processes (AOPs) are used as the last step to remove these trace contaminants from RO Permeate (ROP). Hydrogen peroxide (H₂O₂) is the common oxidant species employed in AOPs. However, monochloramine (NH₂Cl) and peroxydisulfate (S₂O₈²⁻) are also powerful oxidants. In this study, we investigate how different water matrices including pH, bicarbonate (HCO₃⁻) and initial oxidant dose can affect the oxidation efficiency of UV/ H₂O₂, UV/ NH₂Cl and UV/ S₂O₈²⁻. Oxidants in DI water and ROP were activated by low-pressure UV lamp at λ=254nm in quartz reaction tubes with a variation of pH, HCO₃⁻ and initial dosage. Benzene and 1,4-

dioxane were used as model contaminants to evaluate the efficiency of the three UV/APOs. Nitrobenzene, benzoic acid and dimethyl aniline were employed as radical probes to elucidate the steady state radical concentrations of $\text{HO}\cdot$, $\text{SO}_4^{\cdot-}$, $\text{Cl}\cdot$, and $\text{CO}_3^{\cdot-}$. A computational model was developed to map the radical transformation mechanism. Results indicate UV/ $\text{S}_2\text{O}_8^{2-}$ is the best AOP for treating benzene, while UV/ H_2O_2 is more efficient for 1,4-dioxane. pH has negligible effect on UV/ H_2O_2 and UV/ NH_2Cl , whereas UV/ $\text{S}_2\text{O}_8^{2-}$ is very sensitive to the increase of pH. Furthermore, bicarbonate acts as scavenger and decreases the overall oxidation efficiency. To achieve the maxima efficiency, an optimal dosage is required for three AOPs.

2015 Western Regional Meeting 191

Treatment of groundwater contaminated with volatile and semi-volatile organics using ozone- and UV-based advanced oxidation processes

Leo Qu³, *lqu@pacewater.com*, **Yuan Li**², *ali@pacewater.com*, **Ling Wang**⁴, **Keisuke Ikehata**¹.
(1) Pacific Advanced Civil Engineering, Fountain Valley, California, United States (2) Environmental Water, Pacific Advanced Civil Engineering, Irvine, California, United States (3) Civil and Environmental Engineering, University of California, Irvine, Fountain Valley, California, United States (4) OTG EnviroEngineering Solutions, Inc., Oakland, California, United States

Several volatile and semi-volatile organic compounds were detected in contaminated groundwater at a Superfund site in Greenville, South Carolina. Ozone- and ultraviolet (UV)-based advanced oxidation processes (AOPs), including ozone/hydrogen peroxide ($\text{O}_3/\text{H}_2\text{O}_2$), ozone/UV (O_3/UV), ozone/hydrogen peroxide/UV ($\text{O}_3/\text{H}_2\text{O}_2/\text{UV}$), and UV/hydrogen peroxide ($\text{UV}/\text{H}_2\text{O}_2$) were selected for the degradation of the organic compounds. A series of bench-scale water treatment study was performed to investigate suitable treatment technologies for the *in situ* and *ex situ* chemical oxidation to enhance the site remediation process at the Superfund site. Water samples were collected at the site and transported to the lab facility and tested using a bench-scale solution ozone test apparatus for the ozone-based treatment, and a UV collimated beam apparatus for the UV-based treatment. 1,4-dioxane, THF, 1,1-dichloroethene, and trichloroethene were found in the groundwater samples and their degradation was also monitored. Among the treatment processes tested, the $\text{O}_3/\text{H}_2\text{O}_2$ and $\text{UV}/\text{H}_2\text{O}_2$ AOPs were selected for further evaluation for *in situ* and *ex situ* treatment, respectively. Based on our bench-scale study, the $\text{O}_3/\text{H}_2\text{O}_2$ AOP with O_3 and H_2O_2 doses of 6 and 1.5 mg/L, respectively, and the $\text{UV}/\text{H}_2\text{O}_2$ AOP with UV and H_2O_2 doses of 1,000 mJ/cm² and 20 mg/L, respectively, were sufficient to degrade 200 µg/L of 1,4-dioxane, 110 µg/L of 1,1-dichloroethene, and 10 µg/L of trichloroethene below their performance standards of 10, 7, and 4 µg/L, respectively. Both AOP treatments were able to degrade 100 µg/L of THF as well as trace amounts of other chlorinated ethenes. Due to a high bromide concentration (0.35 mg/L) in the groundwater sample, bromate formation was found to be significant in ozone-based treatment, including $\text{O}_3/\text{H}_2\text{O}_2$, at high ozone doses (15 mg/L).

Key words: ozone, advanced oxidation processes, chlorinated solvents, contaminated site remediation, 1,4-dioxane, groundwater, SVOC, tetrahydrofuran, VOC

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Chlorine radical and chloramine reactivity with wastewater constituent species in support of advanced oxidation processes

Kylie D. Couch², kyliedcouch@gmail.com, **Stephen P. Mezyk¹**. (1) Ca State Univ, Long Beach, California, United States (2) Chemistry and Biochemistry, California State University, Long Beach, Long Beach, California, United States

The UV photolysis of chlorinated compounds as a potential Advanced Oxidation Process (AOP) treatment is of interest to many U.S. water utilities that maintain a chloramine residual in their wastewater treatment systems. In some wastewater treatment and water reuse systems chloramines are deliberately added before the reverse osmosis (RO) process to control membrane biofouling. Chloramines can readily pass through the RO membranes and this could impact a downstream UV/H₂O₂ AOP. Both direct photolysis and indirect reaction of produced HO[•] radicals with mono- and dichloramine will produce Cl[•] radicals. In this project Cl[•] atom kinetics with a suite of wastewater chemical contaminants, such as nitrosamines and estrogenic steroids will be measured using the methodology established for 1,4-dioxane. In addition to Cl[•] kinetics with a variety of contaminants, Cl[•] kinetics with wastewater constituent species such as bicarbonate, nitrate, and nitrite will be measured. Furthermore, efficiencies of these radical reactions will be determined using steady-state radiolysis plus LCMS/NMR techniques. The measurement of these kinetic parameters will provide quantitative understanding of the feasibility of this alternative AOP radical treatment.

2015 Western Regional Meeting 193

A one-step ligand synthesis and the systematic study of gold(III) complexes of substituted 2-(2'-pyridyl)quinolines

Michael D. Sterling¹, mster002@ucr.edu, **Lisa E. Bishop¹**, **Arnold L. Rheingold²**, **Catharine H. Larsen¹**. (1) University of California, Riverside, Riverside, California, United States (2) University of California, San Diego, San Diego, California, United States

Solvent-, metal-, and chromatography-free catalysis provides 4-phenyl-2-(2'-pyridyl)quinoline (PyQuin) ligands bearing various substituents in a single step. PyQuins act as bidentate ligands for a variety of metals, and this modular synthesis from inexpensive commercial starting materials will allow for rapid tuning of structure and function. A series of PyQuin gold(III) complexes have now been synthesized and studied by NMR spectroscopy and x-ray crystallography.

2015 Western Regional Meeting 194

Isolable variants of an iron nitridocarbonyl cluster [Fe₄N(CO)₁₂]ⁿ in two states of charge (n = 0, -1)

Myles J. Drance², mdrance@colgate.edu, **Joshua S. Figueroa¹**. (1) Chemistry Biochemistry, Univ of California, La Jolla, California, United States (2) Chemistry & Biochemistry, University of California - San Diego, San Diego, California, United States

The iron cluster [Fe₄N(CO)₁₂]ⁿ has been shown to access a variety of charge states electrochemically (n = 0, -1, -2, -3); however, only the monoanionic species has been isolated and well-characterized. Recently, this cluster has proven to electrocatalytically effect hydrogen evolution in aqueous media. Presented here is the synthesis and isolation of cluster variants possessing novel degrees of isocyanide-for-carbonyl substitution (n = 1, 2, 3, 4) utilizing the

sterically encumbering *m*-terphenyl isocyanide, $\text{CNAr}^{\text{Mes}2}$ (Mes = 2,4,6-Me₃C₆H₂). These mixed carbonyl/isocyanide species are more readily protonated than the parent cluster, which may have implications in catalytic proton reduction. Additionally, the paramagnetic neutral species $[\text{Fe}_4\text{N}(\text{CO})_8(\text{CNAr}^{\text{Mes}2})_4]$ has been isolated. This represents a possible analog to an isolable intermediate in the electrocatalytic evolution of H₂.

2015 Western Regional Meeting 195

Co(CNAr^{Mes2})₄, an isolobal analogue of Co(CO)₄, and its reactivity

Ching-Lin Chan, *chc127@ucsd.edu*, Joshua S. Figueroa. Chemistry Biochemistry, Univ of California, La Jolla, California, United States

For a long time, Co(CO)₄ has been proposed to be a crucial active intermediate in industrial hydroformylation and carbonylation processes. However, the mechanisms have never been fully proved due to the extreme unstability and high reactivity of the intermediates. By using a sterically encumbering *m*-terphenyl isocyanide (CNAr^{Mes2}) (Mes = 2,4,6-Me₃C₆H₂) acting as an isolobal analogue of CO, a zerovalent radical Co(CNAr^{Mes2})₄ was isolated, which may provide hints to understand the key role of Co(CO)₄. Herein, we show that Co(CNAr^{Mes2})₄ can undergo ligand exchange reactions with phosphines, alkynes and alkenes to afford the corresponding CoL(CNAr^{Mes2})₃. More interestingly, It reacts with stable radical like TEMPO (2,2,6,6-Tetramethylpiperidin-1-yl)oxyl), forming a diamagnetic n²-TEMPOCo(CNAr^{Mes2})₂.

2015 Western Regional Meeting 196

A room temperature stable singlet phosphinidene

David A. Ruiz, *david_ruiz06@yahoo.com*, Liu Liu, Guy Bertrand. UC San Diego, La Jolla, California, United States

For a long time compounds containing a low coordinate main group element defying the octet rule were considered only as reactive intermediates, the quest for stable versions even being unreasonable targets. This paradigm changed at the end of the 20th century with the preparation of stable singlet carbenes, a discovery that has opened the way for their application in numerous fields, ranging from synthetic chemistry to biological sciences. We will present on the synthesis of a phosphorus analogue of carbenes, namely a phosphinidene, which has a half-life at 25 °C of one day in benzene solution, and is stable for months in the solid state. This compound was prepared by irradiation-induced elimination of carbon monoxide from the corresponding phosphaketene. Similarly to carbenes, it undergoes a [2+1]-cycloaddition with an electron poor alkene and a [1+1]-coupling reaction with isonitriles. We also show that without steric protection, singlet phosphinidenes dimerize to give the corresponding diphosphene.

2015 Western Regional Meeting 197

Novel α-helix mimetics for inhibition of protein-protein interactions associated with human papillomavirus

Alexandra Orchard, *aorchard@exchange.fullerton.edu*. Department of Chemistry and Biochemistry, California State University-Fullerton, Fullerton, California, United States

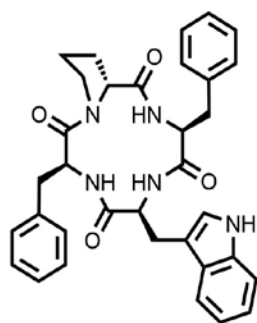
Protein-protein interactions (PPIs) are involved in many cellular processes, making them potential drug targets. As a method of inhibiting these PPIs, small molecule α -helix mimicry has had limited success, clinically, often due to insufficient affinities or poor pharmacokinetic properties. Many of these small molecules mimic only the hydrophobic face of the α -helix, possibly excluding important interactions arising from polar residues. We have designed novel scaffolds capable of mimicking consecutive amino acid residues on both faces of the helix for treatment of various diseases, such as Human Papillomavirus (HPV) infection. High-risk HPVs are DNA viruses that infect epithelial cells and can cause various cancers, such as cervical cancer. The HPV E6 oncoprotein allows for survival of infected cells by binding to the human protein E6-AP and causing degradation of p53. Inhibition of E6 should allow for apoptosis of infected cells, clearing the infection in a non-invasive way. Our proposed library of potential α -helix mimics has been rationally designed with the aid of computational software, and synthesis of these compounds is underway. Herein, we present promising docking results and our proposed synthetic routes, as well as progress toward target compounds. Once synthesis is complete, libraries of compounds will be tested for their ability to cause apoptosis in infected cells as well as their ability to specifically inhibit the E6-E6AP interaction.

2015 Western Regional Meeting 198

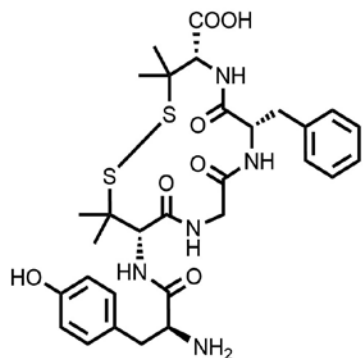
Docking studies illuminate a likely binding mode of noncanonical opioid peptides

Michael J. Ferracane, *michaelferracane@gmail.com*, Jane V. Aldrich. Department of Medicinal Chemistry, University of Florida, Gainesville, Florida, United States

The opioid receptors (μ , δ , and κ) are important targets for pain management and have shown promise as targets for treatment of addiction and mood disorders. X-ray crystal structures have been determined for the receptors in agonist- and antagonist-bound states, allowing for rational design of novel opioid receptor modulators that may possess greater therapeutic potential. Macrocyclic tetrapeptides such as CJ-15,208 have demonstrated unexpected opioid activity *in vivo* following oral administration. These compounds lack the canonical opioid pharmacophore, making docking studies and rational design of analogs particularly challenging. To circumvent this issue, docking studies were performed using a) the recently published crystal structure of the peptide-bound δ opioid receptor and b) model peptides DPDPE, [L-Ala³]DPDPE, and [D-Ala³]DPDPE to predict the likely binding modes of similar cyclic peptide opioid ligands. The observed poses are consistent with the peptides' known conformational features, the peptides' structure-activity relationship (SAR), and mutagenesis studies performed on the opioid receptors. This information was then used to guide docking studies of macrocyclic tetrapeptides to the κ opioid receptor to investigate their binding modes. Results from docking studies will be described and connected to prior structural data, peptide SAR, and mutagenesis studies.



CJ-15,208



DPDPE

2015 Western Regional Meeting 199

Exploiting atropisomerism to increase the target selectivity of promiscuous inhibitors

Jeffrey Gustafson, jgustafson@mail.sdsu.edu. Department of Chemistry and Biochemistry, San Diego State University, San Diego, California, United States

Many biologically active molecules exist as rapidly interconverting atropisomeric mixtures. Whereas one atropisomer inhibits the desired target, the other can lead to off-target effects. Herein, we study atropisomerism as a possibility to improve the selectivities of kinase inhibitors through the synthesis of conformationally stable pyrrolopyrimidines. Each atropisomer was isolated by HPLC on a chiral stationary phase and subjected to inhibitor profiling across a panel of 18 tyrosine kinases. Notably different selectivity patterns between atropisomers were observed, as well as improved selectivity compared to a rapidly interconverting parent molecule. Computational docking studies then provided insights into the structure-based origins of these effects. This study is one of the first examples of the intentional preorganization of a promiscuous scaffold along an atropisomeric axis to increase target selectivity, and provides fundamental insights that may be applied to other atropisomeric target scaffolds.

2015 Western Regional Meeting 200

Potential early diagnosis of multiple sclerosis based on sensitive analysis of biomarkers using nonlinear laser methods

Alexander Jackson², ajackson7158@gmail.com, **William G. Tong**¹. (1) San Diego State University, San Diego, California, United States (2) Department of Chemistry and Biochemistry, San Diego State University, San Diego, California, United States

Nonlinear multi-photon laser spectroscopic methods are presented as highly sensitive absorption-based detection methods for biomedical applications. Our laser methods offer inherent significant advantages including excellent sensitivity, small sample requirements, short optical path length, high spatial resolution and excellent standoff detection capability. The sensitivity levels are ideal for the detection of specific biomarkers, such as those associated with multiple sclerosis (MS). The symptoms of MS are caused mainly by destruction of myelin in the central nervous system. Due to its similarity with many other neurological disorders, MS is currently diagnosed based on symptoms and confirmed by MRI images of the brain showing

lesions. Sensitive chemical-based detection methods are needed in order to detect and diagnose MS before lesions grow to the size detected by MRI. There is still a wide range of proposed biomarkers for MS since the disease's pathology is not yet completely understood. This work will focus on early and reliable detection of myelin basic protein (MBP), a proposed biomarker for the disease. This biomarker is suitable for detection by our laser methods using both fluorophore and chromophore labels. In a typical wave-mixing setup, the signal is generated when the two input beams intersect in the sample containing labeled or native biomarkers. The signal is a coherent laser-like beam and can be collected with virtually 100% efficiency and minimal background noise. The signal has a quadratic dependence on analyte concentration, and hence, it is inherently suitable as a chemical sensor. Currently, biomarkers must be detected in cerebral spinal fluid as concentrations in the blood are extremely low. We plan to take advantage of our excellent detection sensitivity levels (zepto-mole or parts-per-trillion) to design and develop a reliable chemical-based detection system for early diagnosis of multiple sclerosis.

Acknowledgment: We acknowledge partial support of this work by the NIH (R01), NIH NIHGMS IMSD (2R25GM058906), NSF, DoD, Army, DHS, Lockheed Martin and Johnson and Johnson.

2015 Western Regional Meeting 201

Sensitive detection of colorectal cancer biomarker carcinoembryonic antigen by laser wave-mixing spectroscopy and capillary electrophoresis

Jean S. Pradel², jspradel@gmail.com, **William G. Tong¹**. (1) San Diego State University, San Diego, California, United States (2) Department of Chemistry and Biochemistry, San Diego State University, San Diego, California, United States

Nonlinear multi-photon laser wave mixing is presented as a sensitive absorption-based method for early detection and diagnosis of colorectal cancer biomarker carcinoembryonic antigen (CEA) proteins and other biomolecules. Wave mixing offers inherent advantages over conventional methods including zeptomole-level detection and high spatial resolution suitable for single-cell analysis. The wave-mixing signal is a coherent laser-like beam, and hence, it can be collected with excellent signal-to-noise ratios. CEA absorbs in the UV wavelength range in its native form, and it can also absorb in the visible range when labeled with a chromophore. We use a 488/532 nm visible laser when labeled with a chromophore and a 266 nm UV laser to probe label-free native CEA analytes. Since wave-mixing signal has a quadratic dependence on analyte concentration, it is especially effective for monitoring small changes in analyte properties. In order to enhance chemical selectivity, a fused silica capillary (75 or 50 μm i.d.) is used to separate analytes in a custom-built capillary electrophoresis system. Since the wave-mixing probe volume is small (nanoliter to picoliter), it is inherently suitable for interfacing to microfluidics systems.

Acknowledgment: We acknowledge partial support of this work by the NIH (R01), NIH NIHGMS IMSD (2R25GM058906), NSF, DoD, Army, DHS, Lockheed Martin and Johnson and Johnson.

2015 Western Regional Meeting 202

Nickel catalyzed stereospecific cross coupling: Novel approaches to optically enriched triarylmethanes

Luke Hanna, *lucus86@gmail.com*. Department of Chemistry, University of California, Irvine, Irvine, California, United States

Nickel catalyzed cross coupling reactions offer facile access to single enantiomers of known anticancer drug motifs, triarylmethanes. Stereospecific coupling of benzylic carbamates and pivalates with aryl- and heteroarylboronic esters has been developed. The reaction proceeds with selective inversion or retention at the electrophilic carbon, depending on the nature of the achiral ligand. Tricyclohexylphosphine ligand provides products with retention of configuration, while an N-heterocyclic carbene ligand provides the product with inversion.

2015 Western Regional Meeting 203

Disiloxanediols as anion-binding and hydrogen-bonding catalysts

Kayla Diemoz, *kmdiemoz@ucdavis.edu*, Sean Wilson, Annaliese K. Franz. UC Davis, Davis, California, United States

The synthesis and binding studies of disiloxanediols are presented with applications for catalysis. New disiloxanediols have been synthesized in four steps or less including naphthyl-substituted as well as unsymmetrical siloxane structures. These disiloxanediols were tested as anion-binding catalysts in the addition of silyl ketene acetal to acylated-isoquinoline and as hydrogen-bonding catalysts in the Michael addition of indole to *trans*- β -nitrostyrene. In both reactions, the disiloxanediols were found to have greater catalytic activity compared to silanediols with similar substitution. Naphthyl-substituted disiloxanediols demonstrated increased catalytic activity relative to the phenyl-substituted systems. Testing of several derivatives of the disiloxanediols demonstrate the importance of the Si-O-Si connectivity and cooperative hydrogen bonding effects of the scaffold. ^1H NMR binding studies demonstrate the effects of concentration on binding with anions and electrophiles providing insight into the hydrogen-bonding activation and self-association of disiloxanediols. Analytical techniques were investigated to quantify the hydrogen-bonding ability of disiloxanediols and to compare to other classes of hydrogen-bonding catalysts.

2015 Western Regional Meeting 204

Metal-free cationic polymerization of styrene utilizing a boron-rich cluster photo-catalyst

Paul Chong, *paulgates.chong@gmail.com*. Department of Chemistry and Biochemistry, University of California, Los Angeles, Los Angeles, California, United States

Popular methods for polymerization such as ROMP, ATRP, and olefin polymerization require the use of toxic and expensive transition metals. Recently, much progress has been made in replacing metals with organic photo-catalysts. Herein, we report the metal-free, visible light initiated cationic polymerization of styrene monomers using a boron-rich cluster photo-catalyst. These boron cluster photo-catalysts can be synthesized on a gram-scale in two-steps from commercially available precursors and are stable to air and moisture. A variety of electron-rich and -poor styrene substrates were polymerized in quantitative yields ($>90\% \pm 5\%$) utilizing

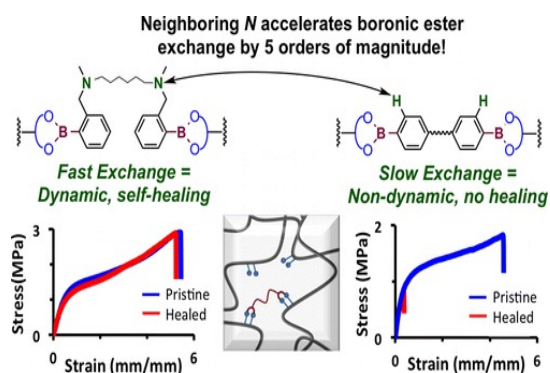
catalyst concentrations as low as 0.005 mol%. Molecular weights (M_n) between 8 and 30 kDa were observed along with dispersities (\mathcal{D}) between 1.2 and 2.2. Our system offers lower catalyst loading over previously developed systems, improved monomer scope, ease of photo-catalyst preparation, and ease of polymer purification as the photo-catalyst is readily soluble in most organic solvents. Current research is aimed at optimizing our chemistry to produce block co-polymer architectures as well as elucidating the precise mechanism governing this unprecedented reactivity.

2015 Western Regional Meeting 205

Malleable and self-healing covalent polymer networks through tunable dynamic boronic ester bonds

Jaeyoon Chung², jaeyooc@uci.edu, **Zhibin Guan**¹. (1) 1102 Nat Sci II, Univ of California, Irvine, California, United States (2) University of California Irvine, Irvine, California, United States

Despite numerous strategies involving dynamic covalent bond exchange for dynamic and self-healing materials, it remains a challenge to be able to tune the malleability and self-healing properties of bulk materials through simple small molecule perturbations. Here we describe the use of kinetically tunable rates of boronic ester transesterification to effectively tune the malleability and self-healing efficiencies of bulk materials. To demonstrate the concept, we used two telechelic di-boronic ester small molecules with variable transesterification kinetics to dynamically crosslink 1,2-diol-containing polymer backbones. We found that the sample crosslinked with fast-exchanging di-boronic ester showed enhanced malleability and accelerated healing compared to the slow-exchanging variant under the same conditions. Our report demonstrates the possibility of transferring small molecule exchange kinetics to malleability and self-healing ability of bulk solid material, and may serve as a guide for the bottom-up rational design of tunable dynamic materials.



2015 Western Regional Meeting 206

Synthesis and electrochemical characterization of oligonucleotide-inspired organic nanowires

Amir Mazaheripour¹, amazaher@uci.edu, **Austin G. Wardrip**¹, **Jonah Jocson**¹, **Nina Hüsken**², **Anthony M. Burke**¹, **Alon A. Gorodetsky**¹. (1) University of California, Irvine, Irvine, California, United States (2) University of Bochum, Bochum, Germany

One-dimensional organic nanowires have emerged as idealized model systems for investigating charge transport mechanisms at molecular length scales. However, there are significant difficulties associated with the synthesis and electrical characterization of well-defined organic nanowires. By drawing inspiration from oligonucleotide synthesis, we have developed a facile strategy for the assembly of organic semiconductor building blocks in predetermined arrangements on a DNA-like backbone. Not only can the resulting constructs be purified/processed under partially aqueous conditions *via* known biochemical techniques, but also they feature many of the advantages of standard oligonucleotides, including a well-defined length, geometry, and sequence context. We have self-assembled monolayers of our nanowires on gold substrates and investigated their charge transport properties with electrochemical techniques. Our findings hold significance both for fundamentally understanding nanoscale charge transport phenomena and for the development of new types of biological and molecular electronic devices.

2015 Western Regional Meeting 207

Chemical compartmentalization for controlling reactivity in kinetically stable molecular capsules

Byron W. Purse, *bpurse@mail.sdsu.edu. Department of Chemistry and Biochemistry, San Diego State University, San Diego, California, United States*

Pyrogallol[4]arene hexamers are self-assembling molecular capsules capable of stably sequestering small molecules within approximately 1300 Å³ of cavity volume. Owing to the highly cooperative nature of the 72 hydrogen bonds stabilizing the assembly and the rigidity of the capsule components, the kinetics and thermodynamics of capsule formation and guest exchange are intimately tied to the complementarity between host and guest. When assembled in solution, these capsules most often are solvent-filled at equilibrium, but here we present solvent-free assembly methods of host and guest using melting-cool cycles or, alternatively, mechanochemistry, giving rise to pre-formed capsules that are not thermodynamically stable in solution but nonetheless have sufficient kinetic stability to persist for years under ambient conditions. The capsules are robust enough for purification by gel permeation chromatography without the exchange of occupants, and their ability to entrap small molecules provides a physical sequestration that can be used to differentiate reactivity between free and encapsulated species, which we demonstrate by the compartmentalization of reactions of alkenes. The design, assembly, and exceptional kinetic stability of these capsules invites future applications in nonequilibrium systems, such as functional polymers.

2015 Western Regional Meeting 208

Unlocking the genome of halogenated polycyclic aromatic hydrocarbons

Bohdan Schatschneider, *bxs54@psu.edu. Department of Chemistry and Biochemistry, California State Polytechnic University Pomona, Pomona, California, United States*

The drive to develop new organic materials for use in optoelectronic devices has created the need to understand the fundamental role functionalization plays concerning the electronic properties of conjugated molecules. Here we utilize density functional theory (DFT) to look at how the HOMO-LUMO gaps of halogenated polycyclic aromatic hydrocarbons are affected as a

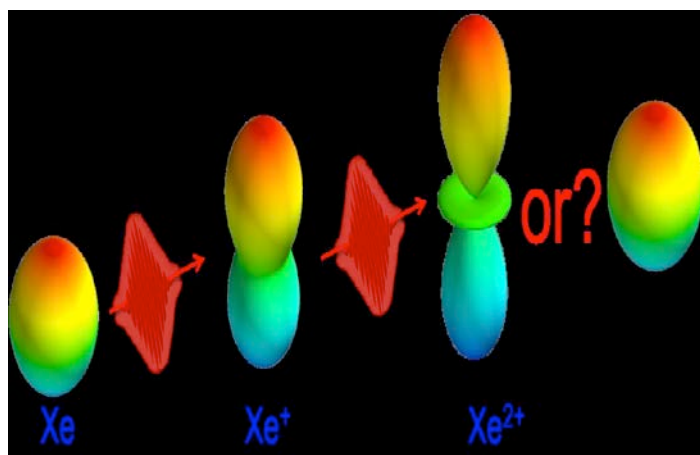
function of substituent size, position, electronegativity, and polarizability. It is shown that the primary physical descriptor governing the HOMO-LUMO gap within halogenobenzenes is the molecular static polarizability. A secondary descriptor controlling the HOMO-LUMO gap in these materials is the aromaticity of halogen substituted benzene rings which was monitored *via* the harmonic oscillator method of aromaticity index (HOMA). Both the molecular polarizability and aromaticity are shown to be a function of substituent size, number, position, and electronegativity. It is ultimately demonstrated that molecules which are most polarizable and least aromatic have the smallest HOMO-LUMO gaps.

2015 Western Regional Meeting 209

Utilizing tabletop XUV spectroscopy to explore how electronic spin influences the alignment from strong-field multiple ionization

Scott G. Sayres, ssayres@asu.edu. Chemistry & Biochemistry, Arizona State University, Tempe, Arizona, United States

Our recent experiments suggest that spin can play an important role during strong-field multiple ionization. Tabletop extreme ultraviolet (XUV) absorption spectroscopy is used to measure the angular distributions of singly and doubly tunnel-ionized xenon atomic states via 4d core to 5p valence shell transitions between 55 and 60 eV [1]. From the angular absorption peak intensities, the orbital alignment is determined and used to explore effects of sequential and non-sequential ionization. The comparison between the orbital alignment measurements and theory reveals new details about electron correlation (electron-electron interaction) during atomic strong-field double ionization that is fundamentally important for understanding light-matter interaction. While triplet states agree well with our theoretical model describing strong-field ionization of independent electrons, the singlet states appear to be unaligned and suggest that correlated electron motion is significant. [1] S.G.Sayres, E.R. Hosler, and S.R. Leone, J. Phys. Chem. A **118**, 8614 (2014).



2015 Western Regional Meeting 210

Non-adiabatic molecular dynamics with spin-symmetry breaking for describing photochemistry of acetaldehyde

Jordan Vincent, jvincent@uci.edu. Chemistry, University of California-Irvine, Irvine, California, United States

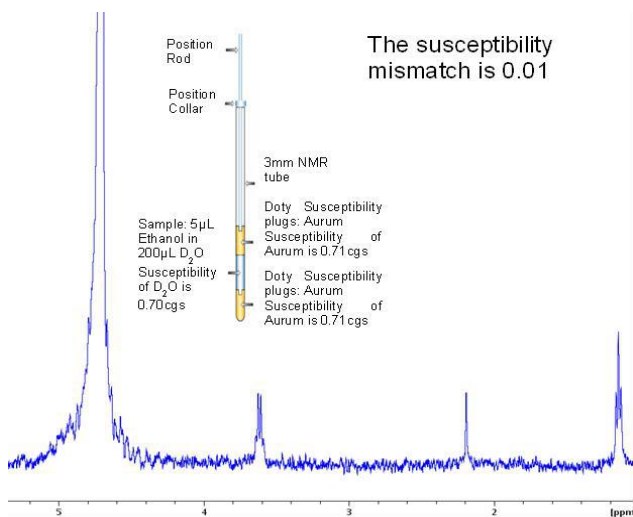
Excited state processes such as photochemical reactions and radiationless decay involve at least two Born-Oppenheimer (BO) potential energy surfaces (PESs). In regions of strong coupling between PESs, the BO approximation breaks down and non-adiabatic methods are needed. This work utilizes a Tully's Fewest Switches Surface Hopping (FSSH) algorithm within TDDFT for non-adiabatic molecular dynamics (NAMD). Within the TDDFT-FSSH framework, a new spin-symmetry breaking method is implemented in the quantum-chemical simulation software suite, Turbomole. Effectiveness of the TDDFT-FSSH method is demonstrated via a benchmarking study on the photochemistry of acetaldehyde.

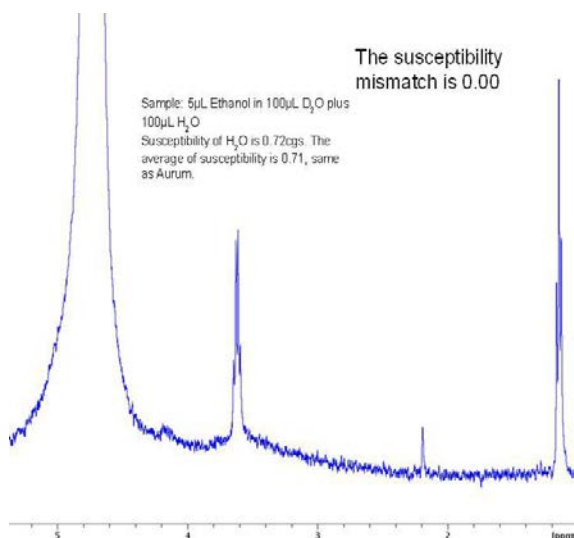
2015 Western Regional Meeting 211

Methods for qNMR: Spin counting in NMR coil volume

Ming Huang, huangmin@mst.edu, Lingyu Chi, Rex E. Gerald, Klaus H. Woelk. Chemistry, Missouri University of Science and Technology, Rolla, Missouri, United States

The methods of quantitative nuclear magnetic resonance (qNMR) include accurate measurements of solute quantity, chemical shifts, J-coupling constants, relaxation time constants, etc. For absolute measurements of solute quantity, a calibration of the NMR spectrometer signal output (spin counting) is needed. We determined the ratio of protons that were placed in the NMR active volume to the absolute integral that is measured by the spectrometer. Doty Susceptibility plugs were used to confine the entire sample in the NMR active volume. Figure 1 shows the low-resolution spectrum of a sample of 5 μL of ethanol in D_2O that is completely contained in the NMR active volume of the probe by Doty susceptibility plugs of machined arum material positioned both above and below the solution sample. Figure 2 shows the high-resolution spectrum of a sample composed of 50% v/v D_2O and H_2O with 5 μL of ethanol in the same configuration used for Fig.1. The high-resolution spectrum of ethanol is necessary to accurately determine the signal-to noise ratio for the ethanol proton's absolute signal integration value for the protons that are completely contained within the NMR active volume. The ratio of the total number of equivalent protons to the absolute signal integral represents the absolute proton sensitivity of the probe for measuring any type of proton.





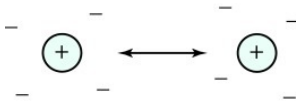
2015 Western Regional Meeting 212

Moderated PEF from transitioning between the micro and macroscopic usage of Coulomb's law

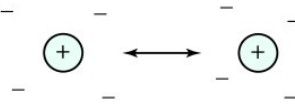
Eve G. Zebisch, zebisich@ripariansoftware.com. Riparian Software, Vista, California, United States

The dielectric constant in Coulomb's Law, D , can quantify an empirical reduction of force. It can also quantify a reduction of electrostatic field as seen in classical electrostatic theory where the induced charge layer is assumed to be infinitely thin. The two approaches exemplify two traditions that have been used in parallel for decades. They produce Potential Energy Functions (PEFs) that differ by a factor of the permittivity, ϵ_r . The classical electrostatic theory result can be incorporated into force field models with an effective dielectric function, D_{eff} , which spans the induced charge layer and accommodates both traditions. The D_{eff} function increases the magnitude of local terms as compared with cumulative long distance terms. It is shown that the D_{eff} function reduces distance dependence of the radial PEF within the induced charge layer and improves computational stability for some systems including substrate in dilute salt solution.

Alternate equations for total force between charges

$$\mathbf{F} = \frac{1}{4\pi\epsilon_0} \frac{q_1 q_2 \mathbf{r}}{Dr_{12}^2}$$


(a)

$$\mathbf{F} = \frac{1}{4\pi\epsilon_0} \frac{(q_1/\epsilon_r)(q_2/\epsilon_r) \mathbf{r}}{r_{12}^2}$$


(b)

$$q_{total} = \frac{q}{\epsilon_r}$$

$$q_{total} = \frac{q}{\epsilon_r}$$

Figure 1. (a) Analysis in chemistry is based on the empirical force between charges; D is frequently set to the permittivity, $D=\epsilon_r$. (b) Physics uses a linear approximation to determine total charge (initial + induced). The force between charges is then calculated using vacuum Coulomb's Law

2015 Western Regional Meeting 213

Ab initio kinetic model for parallel addition reactions of interesting radicals

Pierre Winter¹, pierre.m.winter@gmail.com, Amalia Lopez¹, Andrew L. Cooksy². (1) Chemistry and Biochemistry, San Diego State University, San Diego, California, United States (2) Department of Chemistry, San Diego State University, San Diego, California, United States

We have developed a kinetic model for addition reactions of the acroleinyl ($C_3H_3O^\bullet$), butadienyl ($C_4H_5^\bullet$), and cyclooctatetraenyl ($C_8H_7^\bullet$) radicals each with C_2H_4 , CO, and CH_2O . These radical species exhibit isomers separated by little or no barrier, where the less stable 1,3-dienyl radicals lead to more stable products than the 1,2-dienyl (allylic) radicals. Optimized geometries and vibrational modes were computed with the CCSD/aug-cc-pVDZ level and basis, with the exception of $C_8H_7^\bullet$ which was computed at QCISD/cc-pVDZ. Our findings indicate that the kinetics and thermodynamics both favor reaction along the 1,3-dienyl pathway. However, the difference between the transition state energies of the 1,3 and 1,2 pathways in all reactions are predicted to be much less than the difference in product energies. Analysis based on the Eyring kinetic model predicts that a significant mixture of products will be formed at combustion temperatures.

2015 Western Regional Meeting 214

X-ray spectroscopic characterization of organic semiconductor nanowires

Amir Mazaheripour¹, amazaher@uci.edu, Nina Hüsken⁵, Jonah Jocson¹, Gregor Kladnik², Albano Cossaro³, Luca Floreano³, Alberto Verdini³, Austin G. Wardrip¹, Anthony M. Burke¹, Kelsey Miller¹, Amrita V. Marsukar⁴, Ioannis Kymissis⁴, Dean Cvetko², Alberto Morgante³, Alon A. Gorodetsky¹. (1) University of California, Irvine, Irvine, California, United States (2) University of Ljubljana, Ljubljana, Slovenia (3) Laboratorio TASC/IOM-CNR, Trieste, Italy (4) Columbia University, New York, New York, United States (5) University of Bochum, Bochum, Germany

One-dimensional organic nanowires provide a valuable platform for understanding the emergent electronic phenomena in organic semiconductor materials. We have prepared a class of organic nanowires consisting of stacked pi-conjugated building blocks covalently attached to a solubilizing backbone. We have formed self-assembled monolayers from nanowires of various lengths and sequence contexts on gold substrates and characterized their properties with a range of techniques, including x-ray photoelectron spectroscopy (XPS), near-edge x-ray absorption fine structure spectroscopy (NEXAFS), and resonant photoemission spectroscopy (RPES). These studies have elucidated the nanowires' electronic structure, geometric orientation at solid substrates, and interaction with the surrounding environment. Our experiments may offer improved insight into the design of pi-conjugated materials for organic electronic applications.

2015 Western Regional Meeting 215

Structural disorder and organic solar cell performance: A drift-diffusion study

Benjamin Y. Finck, bfinck@chem.ucla.edu, Benjamin J. Schwartz. Chemistry and Biochemistry, UCLA, Los Angeles, California, United States

Solar cells based on organic materials have garnered an astounding amount of research interest in recent years due to their potential as a low cost, renewable energy technology. Unfortunately, they have yet to see full adoption due to their relatively low power conversion efficiency and sensitivity to processing methodology. This is in part due to the inherent structural disorder of the active components of organic solar cells. In this talk, we discuss the source of this disordered morphology as well as our attempts to model its effect on device performance by employing drift-diffusion model simulations. We utilize two approaches to probe the effects of structural disorder. First we present a 1-D ensemble averaging technique (Finck, B. Y. and Schwartz, B. J. (in press). *Phys. Rev. Appl.*). Subsequently we present full 2-D simulations of OPV morphologies. The 2-D simulations in particular illustrate the role in charge transport of the intermixed region between pure domains of polymer and fullerene that exist in typical OPV devices. Our results show that two of the figures of merit in particular (the short-circuit current and fill-factor) are negatively impacted by the inclusion of structural disorder in a device model. However, another figure of merit for OPV devices (the open-circuit voltage) is nearly impervious to the effects of structural disorder.

2015 Western Regional Meeting 216

Tuning the degree of intermixing in sequentially-processed polymer/fullerene photovoltaics: The role of swelling by solvent additives

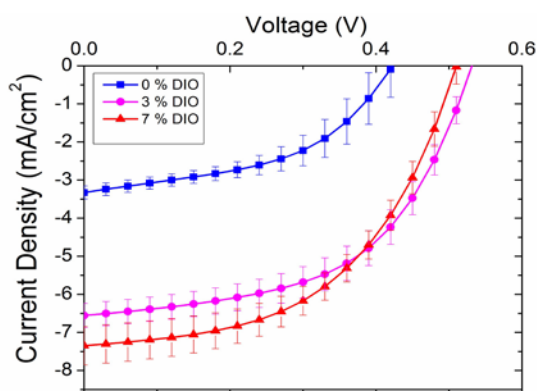
Matthew T. Fontana, fontanam@ucla.edu, Jordan C. Aguirre, Steven Hawks, Guangye Zhang, Patrick Yee, Hyeyeon Kang, Rachel Huber, Laura Schellas, Zongwu Fan, Sarah H. Tolbert, Benjamin J. Schwartz. Chemistry and Biochemistry, University of California, Los Angeles, Los Angeles, California, United States

Solvent additives play a critical, yet mysterious role in the formation of an optimal bulk heterojunction (BHJ) for organic photovoltaics (OPVs). While necessary in almost every high performance solar cell, the role of solvent additives is difficult to elucidate in OPVs fabricated using the traditional "blend-casting" method due to the multiple components present in a single

solution. Here we took advantage of a more recent active layer fabrication route, sequential processing (SqP), to analyze the role of the commonly used solvent additive 1,8-diiodooctane (DIO) on sequentially processed OPVs. The advantage of SqP, which has the polymer donor and fullerene acceptor spin-cast in two separate steps is that this processing technique allows each layer to be controllably formed by removing complicated drying kinetics.¹ Through the addition of DIO to a solution of the polymer P3HT and subsequently casting the film, it is shown by spectroscopic ellipsometry that DIO swells the polymer film while X-ray photoelectron spectroscopy (XPS) results suggest that the swollen film facilitates fullerene intercalation into the polymer during the second processing step, thereby promoting intermixing and moving towards an ideal BHJ. This intermixing supports the observed increased current density with % DIO (Figure 1). Investigation of the device physics using photocurrent spectral response (PSR) and transient photovoltage (TPV)/photocurrent (TPC) support increased intermixing with increased % DIO. Using techniques developed in our lab to fabricate sequentially processed solar cells with high performance polymers, results using the polymer PTB7 will be discussed.²

References:

1. A. L. Ayzner, C. J. Tassone, S. H. Tolbert and B. J. Schwartz, *J. Phys. Chem. C* **113**, 20050-20060 (2009).
2. J.C. Aguirre, S.A. Hawks, A. S. Ferreira, P. Yee, S. Subramanyian, S. A. Jenekhe, S. H. Tolbert and B. J. Schwartz, *Adv. Energy Mater.* 1402020, 1-11 (2015).



J-V data for as cast P3HT:PCBM solar cells fabricated with varying % DIO.

2015 Western Regional Meeting 217

Tracking transplanted cells with paramagnetic fluorinated nanoemulsions

Alexander A. Kislukhin, akscrps@gmail.com. Pharmacology, University of California San Diego, La Jolla, California, United States

Visualization of distinct cell populations *in vivo* is one of the most formidable challenges in biomedical sciences. Clinical translation of cutting-edge therapies that involve administration of live immunotherapeutic or stem cells can benefit from understanding the fate of injected cells *in vivo*. Magnetic resonance imaging (MRI) is emerging as a prime method for non-invasive, longitudinal cell tracking. Fluorine-19 MRI (¹⁹F MRI) involves the use of non-radioactive ¹⁹F label in the form of biologically inert, cytocompatible perfluorocarbons (PFC). Immediately prior to

injection, cells of interest are labeled *ex vivo* with water-based PFC nanoemulsions. ^{19}F MRI yields background-free images of labeled cells in an anatomical context provided by conventional ^1H MRI. Both datasets are acquired on the same scanner in one imaging session. This technology has recently been used to detect immunotherapeutic dendritic cells delivered to colorectal adenocarcinoma patients.

We sought to enhance sensitivity and versatility of ^{19}F MRI by using paramagnetic relaxation agents. Covalent modification of clinically relevant PFCs with metal-binding ligands enabled stable and uniform incorporation of gadolinium and iron in the fluorophilic phase of nanoemulsions. Paramagnetic relaxation enhancement resulted in up to 50-fold reduction in ^{19}F longitudinal relaxation time (T_1) compared to state-of-the-art commercial tracers. The ultralow ^{19}F T_1 of our paramagnetic tracers enabled *in vivo* cell tracking with rapid, three-dimensional, zero time-to-echo (ZTE) ^{19}F MRI pulse sequences in mice bearing subcutaneous allografts of ^{19}F -labeled GL261 cells. Moreover, the high local concentration of paramagnetic metals imparted negative contrast in T_2^* -weighted ^1H images.

Combination of the new agents with conventional ^{19}F tracers comprises a previously unavailable toolbox of ^{19}F contrast agents, selectively detectable by appropriate acquisition methods. This enables “multicolor” ^{19}F MRI tracking of multiple cell populations, *e.g.*, for monitoring the interaction of host immune cells with injected therapeutic cells or cancer xenografts. Overall, the design of biocompatible, fast-relaxing ^{19}F tracers addresses the issue of modest sensitivity of ^{19}F MRI and reduces the barriers to widespread adoption of this powerful imaging technique.

2015 Western Regional Meeting 218

Evaluation of the cellular biocompatibility of collagen- and synthetic polymer-coated gold nanoparticles

Oana T. Truica¹, oanamarisca@gmail.com, Joanna Rejman², Nicolae Leopold¹. (1) Biophysics, Babes Bolyai University, Cluj Napoca, Romania (2) Dr. von Hauner Children's Hospital, Ludwig Maximilians University, Munich, Germany

The development of new biocompatible nano-materials is an exponentially growing field of research. The biocompatibility of NPs not only depends on their physicochemical properties associated with the bulk of the NPs, such as size or shape, but also on properties associated with the type of material used for their surface coating, such as Zeta-potential [1].

In this study, we compared two gold NP systems differing in surface coating in terms to their interaction with cells and culture media. One system was coated with a synthetic polymer, poly(isobutylene-*alt*-maleic anhydride (PMA)[2], and the other with a protein, collagen.

To assess how the surface coating affects cell-NP interactions, internalization and cytotoxicity tests were performed in two cancer cell lines: cervical carcinoma (HeLa) and lung adenocarcinoma (A549) cells. The uptake of Au NPs was quantitatively evaluated by inductive coupled plasma-mass spectrometry (ICP-MS), and intracellular NP localization was visualized with fluorescence microscopy, as seen in figure 1. Cell viability was probed using the MTT assay.

NPs stabilized with collagen were taken up by both cell lines more efficiently than those stabilized with PMA, both in the presence and absence of serum. Concentration dependent toxicity studies further revealed that at short exposure times collagen-coated Au NPs were less toxic to the cells than PMA-coated Au NPs. Importantly, the collagen-coated NPs, which are internalized to a high degree, exhibit lower toxicity.

Cytotoxicity and internalization studies proved that nanoparticles don't present high toxicity to HeLa cancer cells in this range of nanoparticle concentration. There was no cellular viability

under 80 %, and the behavior of the viability is a linear decrease. The results regarding internalization indicate that the GNPs are internalized within the cells in a concentration dependent pattern. Concluding, this type of gold nanoparticles didn't show toxicity for human cervix cellular line which can lead to their further use in biomedical field.

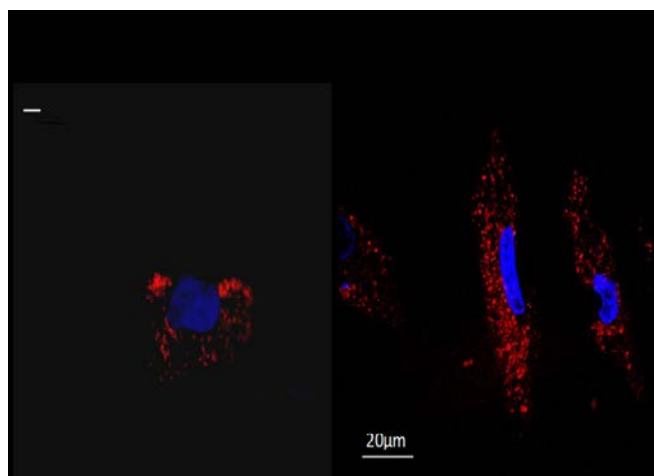


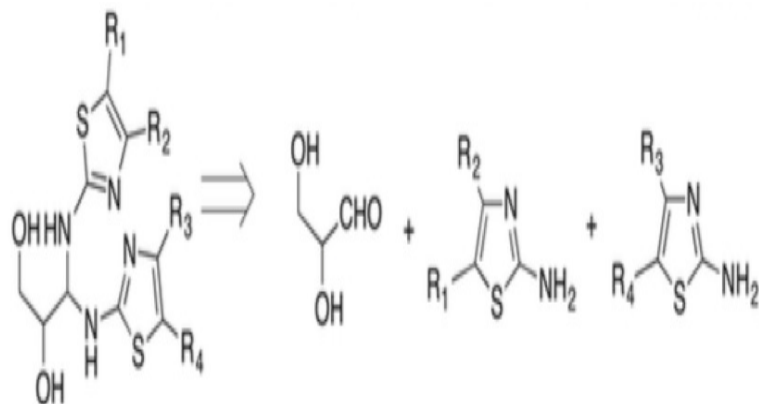
Fig.1 Images of HeLa cells as incubated with fluorescence-labelled Au NPs. A) Collagen-coated Au NPs, the scale bar corresponds to 10 μm . B) PMA-coated Au NPs, the scale bar corresponds to 20 μm .

2015 Western Regional Meeting 219

Prebiotic flow synthesis of bioactive nucleoside precursors

Amanda Evans, amevans@fullerton.edu, Joshua Kading, Jackson Feng. Chemistry & Biochemistry, California State University Fullerton, Fullerton, California, United States

2-Amino-oxazole and -thiazole derivatives have been used to treat both Alzheimer's and other prion-related diseases, and they have also been studied for their anti-inflammatory properties. Chiral oxazole and thiazole derivatives are interesting because of their biological activity and their role as prebiotic genetic precursors. These molecules can be produced under continuous flow conditions in a highly "green" and sustainable manner using only aqueous solvents and chiral additives (such as amino acids) to induce biomimetic asymmetry.



Scheme 1 – Bioactive heterocycle derived from prebiotic precursors.

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Towards a continuous flow synthesis of levomilnacipran

Christian Ayoub², *cayoub1991@gmail.com*, **Matthew Nguyen²**, **Amanda C. Evans¹**. (1) *Chemistry & Biochemistry, California State University Fullerton, Fullerton, California, United States* (2) *California State University, Fullerton, Foothill Ranch, California, United States*

Levomilnacipran is a drug prescribed for fibromyalgia syndrome (FMS) that currently requires over nine days to synthesize. A critical component of this synthesis involves the enantioselective formation of the central cyclopropane ring, which is a common structural scaffold found in many neuroactive molecules. This work demonstrates the utility of a novel five-step continuous flow synthesis of levomilnacipran that employs both chemical and biochemical catalytic strategies to generate the central cyclopropane ring and ultimately produce the drug under efficient and sustainable reaction conditions. The advantages of flow chemistry enable high yields, faster reaction times, reduced waste, and access to chemistry that is previously impossible under batch protocols. The proposed method has the potential to revolutionize production of neuroactive drugs as well as other biologically active molecules.

2015 Western Regional Meeting 221

Flow chemistry enabling safer and novel chemistry

Heather Graehl², *heather@graehl.com*, **Laszlo Kocsis²**, **Richard V. Jones¹**. (1) *Thales Nano Inc, Budapest, Hungary* (2) *ThalesNano, Newbury Park, California, United States*

Flow reactors are being used to enable chemists to perform novel chemistry, tackle traditionally dangerous chemistry, rapidly optimize conditions, and all by an inherently scalable method. Flow reactions involving packed fixed bed catalysts enhances mass transfer, decreases reaction time, and eliminates catalyst handling and filtration. Hydrogenations are the most published and adopted fixed bed flow chemistry, though other heterogeneous chemistry such as carbonylations, oxidations, and carbon-carbon couplings are well demonstrated.

Flow chemistry can expand the available parameter space into higher pressures and temperatures normally available in conventional laboratories. The large surface area to volume ratio of reactor lines allows for heated reactions to rapidly heat and subsequently cool resulting in high selectivity, minimal decomposition, accessing new chemistry not possible in batch, and scaling microwave synthesis.

Conversely for exothermic reactions requiring cooling, flow is ideal for increasing safety, selectivity, and expanding into multi-step reactions with high energy intermediates. Ozonolysis, azide synthesis, lithiations, swern oxidation, and fluorination results are discussed. Interestingly, flow reactors offer such control over mixing and heat transfer that exothermic reactions can be performed at higher temperatures in a flow manner when compared to traditional batch chemistry in which undesirable side products are formed.

2015 Western Regional Meeting 222

Cyclopropane synthesis via stereospecific intramolecular reductive cross-electrophile couplings

Emily Tollefson², etollefs@uci.edu, **Lucas Erickson**², **Elizabeth R. Jarvo**¹. (1) Dept of Chemistry, UC Irvine, Irvine, California, United States (2) University of California, Irvine, Irvine, California, United States

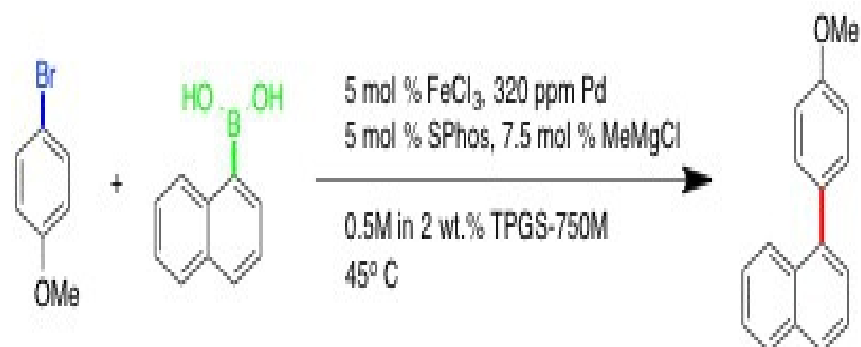
An intramolecular stereospecific reductive cross-electrophile coupling reaction of 2-aryl-4-chlorotetrahydropyrans has been developed. These substrates undergo a nickel-catalyzed ring contraction to afford disubstituted cyclopropanes with excellent stereochemical fidelity at both the alkyl halide and ether bearing stereogenic centers. This new method provides access to stereochemically defined cyclopropanes in two steps from commercially available aldehydes.

2015 Western Regional Meeting 223

Still paying for Pd in your Pd-catalyzed reactions? Why? Use Fe nanoparticles containing naturally occurring ppm Pd, and get it for free!

Sachin Handa¹, **Ye Wang**¹, **Fabrice Gallou**², **Bruce H. Lipshutz**¹, **Evan B. Landstrom**¹, evanlandstrom@umail.ucsb.edu. (1) Chemistry and Biochemistry, University of California, Santa Barbara, Santa Barbara, California, United States (2) Novartis AG, Basel, Basel-Stadt, Switzerland

Notwithstanding all the virtues of Pd associated with cross-coupling reactions, the reality is that it is an endangered metal, oftentimes requires a proprietary ligand, is typically utilized in the 1-5 mol % range, and as a result, is virtually always found as residual metal in each product at levels that require further purification. Moreover, such couplings are run in organic solvents, adding significantly to both the organic and aqueous waste generated. In this presentation, new technology that addresses all of these issues will be discussed. Based on an inexpensive iron salt, found to have sufficient ppm levels of Pd such that its processing (in a single step at RT) leads to very active Fe/ppm nanoparticles (NPs) that catalyze Suzuki-Miyaura couplings. These are performed in water containing a designer surfactant, in which the substrates are housed, where the PEG component of each functions as a delivery mechanism to the Fe/ppm Pd NPs. Several new and unpublished aspects to this work will be revealed, including the choice of ligand involved, applications to other “name” reactions, and use in reductions of considerable synthetic value, especially to the pharmaceutical industry.



2015 Western Regional Meeting 224

Nickel-catalyzed activation of amides and simple esters

Liana Hie², lhie@chem.ucla.edu, Neil K. Garg¹, Noah F. Fine Nathel⁴, Tejas Shah⁵, Emma Baker², Xin Hong⁶, Yun-Fang Yang², Peng Liu³, Kendall N. Houk⁴. (1) UCLA Chemistry, Los Angeles, California, United States (2) Box 951569, UCLA Dept of Chem BioChem, Los Angeles, California, United States (3) Department of Chemistry, University of Pittsburgh, Los Angeles, California, United States (4) UCLA, Los Angeles, California, United States

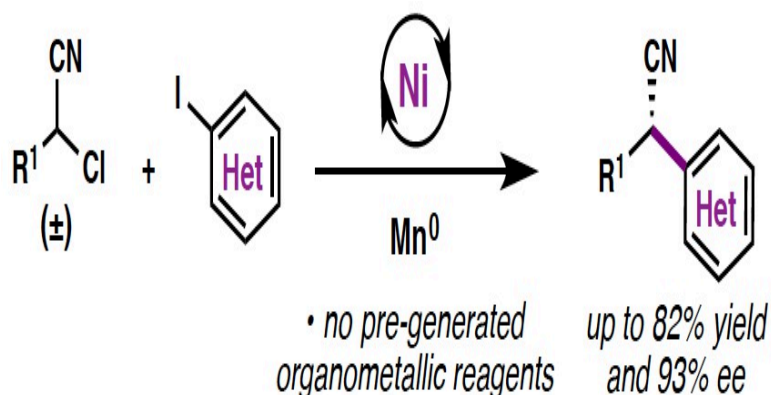
This presentation will focus on our recent efforts to develop reactions of acyl electrophiles using nickel catalysis. The methodologies proceed under mild reaction conditions and allow for the interconversion of amides and esters. These studies are expected to fuel the further use of non-precious metal catalysis for the construction of C–heteroatom and C–C bonds.

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Nickel-catalyzed asymmetric reductive cross-coupling between heteroaryl iodides and α -chloronitriles

Nathaniel T. Kadunce, nkadunce@caltech.edu. Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, California, United States

Ni-catalyzed asymmetric reductive cross-coupling provides an attractive and powerful means to access tertiary stereocenters. However these methods had previously been limited to benzylic alkyl partners and were not amenable to heterocyclic substrates. To expand the utility of this class of reactions, the Ni-catalyzed asymmetric cross-electrophile coupling of heteroaryl iodides and α -chloronitriles has been developed. This method furnishes enantioenriched α,α -disubstituted nitriles from simple organohalide building blocks. The reaction tolerates a variety of heterocyclic coupling partners, including pyridines, pyrimidines, quinolines, thiophenes, and piperidines under mild conditions enabled by a novel ligand scaffold. The products can be derivatized to a range of synthetically useful functionality.



2015 Western Regional Meeting 226

Review of biofuels and biofuels-related technology patents and patent applications

Sandra P. Thompson, *thompsoniplaw@cox.net. Slater Hersey & Lieberman LLP, Irvine, California, United States*

This presentation will outline the innovation in the field of biofuels and biofuels-related technology by providing a review of recent US, European, and Japanese patents and patent applications.

2015 Western Regional Meeting 227

Mesoporous MoS₂ as a transition metal dichalcogenide exhibiting pseudocapacitive Li and Na-ion charge storage

John B. Cook¹, *jbcliberty@yahoo.com*, **Hyung-Seok Kim**², **Yan Yan**¹, **Jesse Ko**², **Bruce Dunn**², **Sarah H. Tolbert**^{1,2}. (1) *Department of Chemistry and Biochemistry, University of California, Los Angeles, California, United States* (2) *Department of Materials Science and Engineering, University of California, Los Angeles, California, United States*

The ion insertion properties of MoS₂ continue to be of widespread interest for energy storage. While much of the current work on MoS₂ has been focused on the high capacity four-electron reduction, this reaction is prone to poor reversibility. In this study we instead focus on traditional ion intercalation reactions and demonstrate that ordered mesoporous thin films of MoS₂ can be utilized as pseudocapacitive energy storage material with a specific capacity of 173 mAh g⁻¹ for Li-ions and 118 mAh g⁻¹ for Na-ions. Utilizing synchrotron grazing incidence X-ray diffraction techniques we have correlated fast electrochemical kinetics with the ordered porous structure and with an iso-oriented crystal structure. When Li-ions are utilized, the material can be charged and discharged in 20 seconds while still achieving a specific capacity of 140 mAh g⁻¹. Moreover, the nanoscale architecture of mesoporous MoS₂ retains this level of lithium capacity for 10,000 cycles. A detailed electrochemical kinetic analysis indicates that energy storage for both ions in MoS₂ is due to a capacitor-like mechanism.

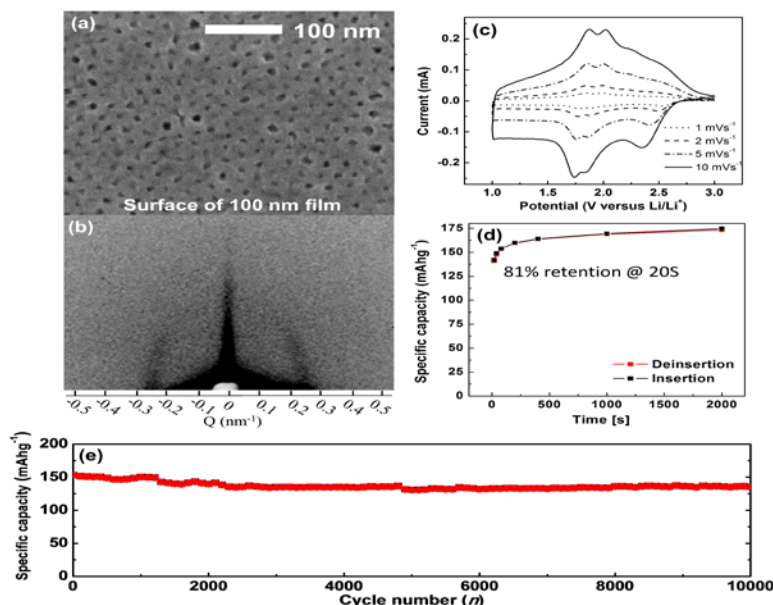


Figure (a) Scanning Electron Microscope image of the surface of a 100 nm thick mesoporous MoS₂ thin

film. (b) Synchrotron grazing incidence small angle x-ray scattering image of MoS₂ showing the ordered nature of the mesoporous framework. (c) Cyclic voltammograms from 1-10 mVs⁻¹ of mesoporous MoS₂ in Li-ion electrolyte. (d) Capacity versus charge time showing that over 80% of the capacity observed at slow rates is achieved in only 20 seconds. (e) Capacity versus cycle number for 10,000 cycles.

2015 Western Regional Meeting 228

Photochemical charge transfer observed in nanoscale hydrogen evolving photocatalysts using surface photovoltage spectroscopy

Jiarui Wang, wjrwang@ucdavis.edu. Department of Chemistry, University of California, Davis, Davis, California, United States

Abstract:

The application of inorganic nanostructures for solar water splitting is currently limited by our understanding of photochemical charge transfer on the nanoscale, where space charge layers are less effective for carrier separation. Here we employ surface photovoltage spectroscopy to measure the internal photovoltages in single crystalline platinum/ruthenium-modified Rh-doped SrTiO₃ nanocrystals for the first time. Voltages of 0.88 V and 1.13 V are found between the absorber and the Ru and Pt cocatalysts, respectively, and a voltage of 1.48 V for a Rh:SrTiO₃ film on an Au substrate. This shows that the Pt and Ru cocatalysts not only improve the redox kinetics but also aid charge separation in the absorber. Voltages of +0.4 V, +0.6 V, and +1.2 V are found for hole injection into KI, K₄[Fe(CN)₆], and methanol, respectively, and a voltage of 0.7 V for electron injection into K₃[Fe(CN)₆]. These voltages correlate well with the photocatalytic performance of the catalyst; they are influenced by the built-in potentials of the donor-acceptor configurations, the physical separation of donors and acceptors, and the reversibility of the redox reaction. The photovoltage data also allowed the identification of a photosynthetic system for hydrogen evolution (80 mmol/g/h) under visible light illumination (4400 nm) from 0.05 M aqueous K₄[Fe(CN)₆].

2015 Western Regional Meeting 229

Numerical and experimental study of a reactive flow with a perovskite catalyst

Juan Arbelaez¹, juanmateo.arbelaez@upb.edu.co, Cesar Nieto², Wilber Silva³. (1) Master's Degree Student on Chemical Engineering, Universidad Pontificia Bolivariana, Medellin, Antioquia, Colombia (2) Research Group on Aerospace Engineering, Faculty of Aeronautical Engineering, Universidad Pontificia Bolivariana, Medellin, Antioquia, Colombia (3) Research Group on Energy and Thermodynamics, Faculty of Nanotechnology Engineering, Universidad Pontificia Bolivariana, Medellin, Antioquia, Colombia

The development of microreactors for catalytic combustion requires the implementation of suitable catalysts coupled microchannel designs. For the use of methane gas on these devices, a series of perovskite catalyzers were evaluated. Catalytic tests consist of subjecting the catalyst to a heating program in which the temperature increases at a rate of 5 °C/min until it reaches 600 °C under an atmosphere of 10% methane, 20% oxygen and argon, where combustion products were analyzed by mass spectrometry. Based on these catalytic activity and stability tests, Figure 1, it is selected a based Iron and Lanthanum solid. On the selected the catalyst, we proceed to determine the most relevant kinetic parameters of

the methane combustion reaction. These parameters were feed to FLUENT's software subroutine, allowing the simulation of reactive flows. Throw the computational fluid dynamics (CFD) tests were performed using the kinetic parameters of the database of the subroutine, which correspond to gas phase reactions (uncatalyzed) and kinetic data determined for the catalyst, the first one is made as a reference (blank) and the second to simulate the reaction under the catalyst conditions. With this simulation different geometries of microchannels can be tested aimed at maintaining and improving the combustion and heat transfer.

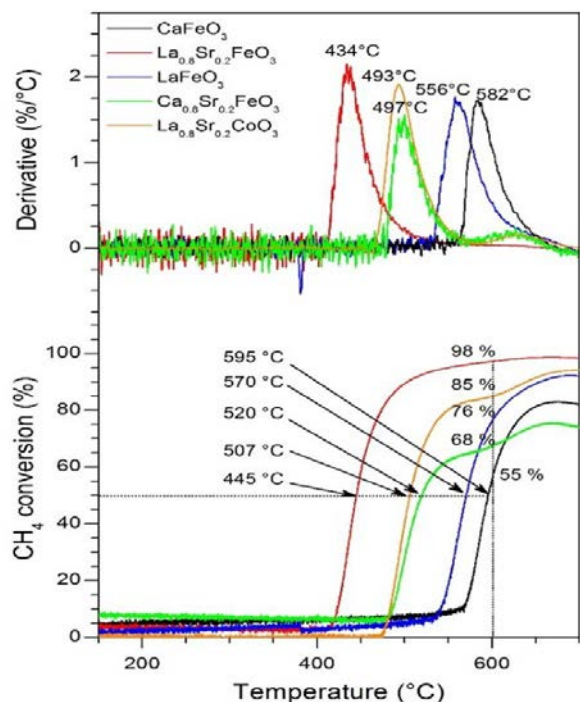


Figure 1. Percentage of methane conversion profiles of the selected perovskites.

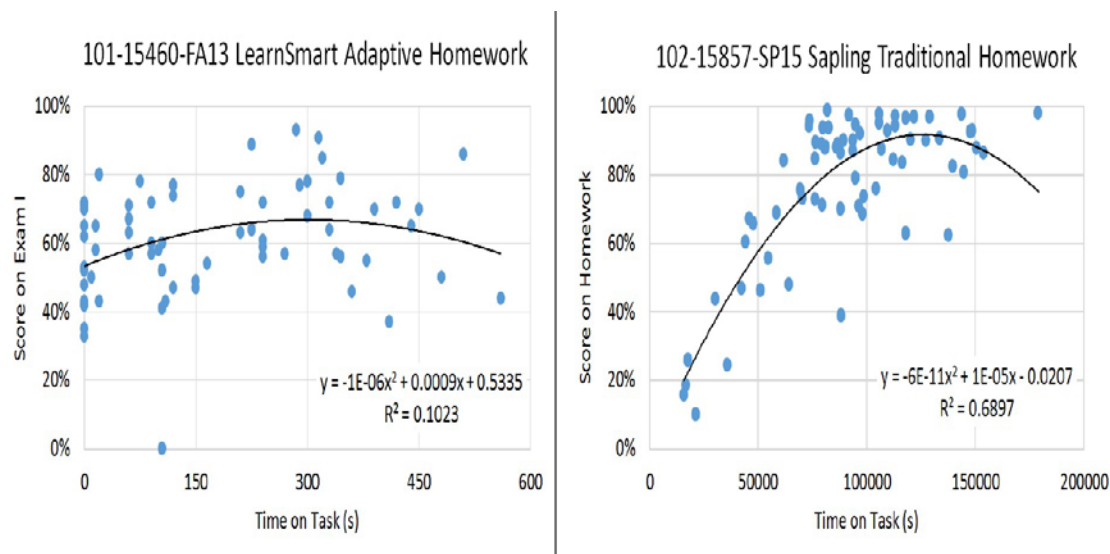
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Effectiveness of socially-mediated and online learning tools in general chemistry

Kayla A. Kaiser, hamerk02@hotmail.com. Chemistry and Biochemistry, California State University at Northridge, Northridge, California, United States

For the general chemistry teacher, it is useful to have qualitative and quantitative metrics of the effectiveness of assignments. Activities categorized as socially-mediated were compared to two online learning platforms. Analysis of 600 students' participation in general chemistry courses at California State University, Northridge revealed that discussion activities were a positive predictor in the final exam score ($p = 0.0030$) whereas online homework was not ($p = 0.43$). Adaptive homework (LearnSmart) showed positive correlation with final exam scores, while a more traditional program (Sapling) showed negative correlation. A polynomial fit was observed when correlating individual students' time on task and grades. One possible reason is that students spend time on the internet searching for a solution instead of working the problems. Survey data from General Chemistry II revealed that 41% of the time students use an online service called Chegg. Students using Chegg circumvent their learning by paying for solutions to

problems. By contrast, our general chemistry lectures are accompanied by discussions where students engage in socially-mediated learning. Discussions were found to be beneficial for students who make a serious effort at solving problems, whereas attendance was not significantly correlated with final exam scores ($p = 0.37$). General Chemistry I (CHEM 101) students when surveyed found discussion activities to be less valuable than the textbook ($p = 0.22$) and reported that the LearnSmart online homework was their least favorite part of the course by a significant margin ($p = 0.034$). General Chemistry II students (CHEM 102) reported that discussion activities and Sapling online homework to be significantly more valuable than the textbook ($p < 0.01$). Taken together these results suggest that Process-Oriented Guided Inquiry Learning (POGIL) socially-mediated discussion activities are valuable for students, even though students do not believe discussion is helpful. Additionally, students report liking online homework when the solutions are easy to find. Even without paying for Chegg, 24% of the time students use Google and Yahoo Answers to sabotage learning from online homework.



Students who spend the most time in online homework programs do not achieve the highest scores.

2015 Western Regional Meeting 231

Development of specific, irreversible inhibitors for a receptor tyrosine kinase EphB3

Alvin Kung, alvink19@yahoo.com, Chao Zhang. Chemistry, University of Southern California, Baldwin Park, California, United States

As the largest family of receptor tyrosine kinases in human, Eph receptors regulate a variety of dynamic cellular events including cell protrusion, migration, proliferation and cell-fate determination. A number of Eph receptors have been implicated in human diseases such as cancer. Small-molecule inhibitors of Eph kinases are valuable tools for dissecting the physiological and pathological roles of Eph. However, there is a lack of small-molecule inhibitors that are selective for individual Eph isoforms due to the high homology within the family. Herein, we report the development of the first potent and selective inhibitors of one Eph receptor, EphB3. Through structural bioinformatic analysis, we identified a cysteine in the hinge region of the EphB3 kinase domain, a reactive feature that is not shared with any other human kinases. We have synthesized and characterized a series of electrophilic quinazolines to target the nucleophilic thiol group in this unique cysteine in EphB3. Some of the electrophilic quinazolines

selectively and potently inhibited EphB3 both *in vitro* and in cells. Finally, we demonstrate that our quinazolines could be also utilized to block other Eph kinases in a chemical-genetic fashion through introduction of a cysteine in their active sites.

2015 Western Regional Meeting 232

DFT calculations relating hydricities, pK_a , and redox potentials in coordination and organometallic iridium(III) complexes

Robert Adams¹, rma824@socal.rr.com, **Antonio Lopez**⁴, **Sarina Bellows**², **Thomas Cundari**³. (1) Chemistry and Biochemistry, California State University Dominguez Hills, Carson, California, United States (2) Chemistry, University of Rochester, Rochester, New York, United States (3) Chemistry, University of North Texas, Denton, Texas, United States (4) Chemistry and Biochemistry, St. Marys University, San Antonio, Texas, United States

Hydricity is the potential for a metal complex to donate a hydride, which has been shown to be important in determining the activity and selectivity of several catalysts such as the Aldehyde Water Shift reaction. Unlike other thermodynamic processes, such as redox potentials and pK_a , hydricity cannot be directly measured in water due to the instability of the hydride in aqueous media. It is also difficult to accurately calculate it via computational chemistry methods with water as a solvent. The solvent most widely used to model hydricity has been acetonitrile, because water causes complications arising from specific and non-specific solute-solvent interactions. However, hydricity, redox potentials, and the pK_a of a complex are related by Hess' Law. To develop accurate methods to calculate hydricity in water, electrochemical potentials of several iridium(III) complexes were analyzed. The potentials for coordination complexes were calculated with a root mean square deviation (RMSD) of 0.5 V versus experiment. Organometallic Ir(III) complexes were calculated with higher confidence, RMSD ~ 0.1 V.

2015 Western Regional Meeting 233

Alkylation of amino acids by anticancer drug, chlorambucil

Tieli Wang, tieli.wang@gmail.com, **BreAna Brook**, bbrooks4@toromail.csudh.edu. Chemistry and Biochemistry, CSU Dominguez Hills, Carson, California, United States

Chlorambucil (CB) is an alkylating agent used for clinical treatment of a variety of cancers such as lymphoma and ovarian cancer. It has been reported that the therapeutic benefit of CB involves reactions with crosslinking DNA. This DNA alkylation in turn inhibits the correct utilization by DNA base pairing, prevents cells from dividing and triggers the tumor cell death. However, the interaction of CB with amino acid residues in proteins is not well documented. Like phosphorylation, ubiquitylation and acetylation of proteins which have been extensively studied, alkylation of amino acid residues in proteins is an important posttranslational modification. It plays essential roles in regulating structure and function of a protein. In the present study, we examined the alkylation reaction of amino acids by CB using proteomic technology. Our results showed that the CB alkylates amino acids at physiological pH. This study provided a direct evidence of alkylation of amino acids by CB at molecular level. It is likely that CB exerts its anticancer activity not only through its interaction with DNA but also its interaction with amino acid residues in the proteins. Alkylation of amino acid residues in proteins will increase functional diversity of the proteome and have effects on all aspects of cellular survival pathways.

Identification and understanding of this type of modification is critical in the study of cancer treatment and prevention.

2015 Western Regional Meeting 234

A historical perspective of the STS (science-technology-society) movement and an application of STS teaching approach in the community college chemistry classroom

Gita Perkins, *gitaperkins@gmail.com. Science/Chemical Education, PhD Alumna, Arizona State University, Tempe, Arizona, United States*

Hurd is often credited for advocating science education for students so that it would enhance their daily lives and enable them to recognize its value to themselves and society, utilizing the phrases “science for life and living” or “science enlightenment”, “science and technology in society” to get his message across (Totten & Pedersen, 2007). The STS movement will be discussed from a historical perspective, beginning with how it emerged as a grass roots movement, then take the audience through the 70-90s when social issues formed the heart of STS. Such a humanistic perspective promotes practical utility and human values in the science curriculum, note Abell and Lederman (2007). An application of STS teaching in the Community College chemistry classroom will be provided. Students were instructed to conduct research in order to find evidence supporting their responses to a set of six discussion questions on a socioscientific scenario. The responses given by students were analyzed qualitatively in order to identify themes in regard to the focus of their discussion. Utilizing the rubric by Sadler, Barab, and Scott (2007), the themes that emerged in regard to the most significant practices for decision-making in the context of socioscientific inquiry will be presented. Four levels of response in relation to complexity could be found regarding both the inherent complexity of socioscientific inquiry, the examination of the issue from multiple perspectives, the appreciation that socioscientific inquiry is subject to ongoing inquiry, and the exhibiting of skepticism when presented with potentially biased information.

2015 Western Regional Meeting 235

Synthesis of alkanethiolate-capped platinum nanoparticle catalysts with enhanced activity using alkylthiosulfate ligand precursor

Khin Aye San, *khinsan18@gmail.com, Young-Seok Shon. Department of Chemistry and Biochemistry, California State University, Long Beach, Long Beach, California, United States*

Research on platinum nanoparticles (Pt NPs) is starting to gain more interests in recent years due to their potential as active catalyst. These Pt NPs are stabilized against aggregation and oxidation by using various organic ligands such as alkanethiol ligands. Cliffel group has synthesized alkanethiolate-capped Pt NPs for catalysis but the catalytic activity of their Pt NPs was fairly low. In our research group, alkanethiolate-capped palladium nanoparticles prepared using alkylthiosulfate ligand has shown enhanced catalytic activity and excellent selectivity towards isomerization of allyl alcohol over hydrogenation process. This poster presents the synthesis of alkanethiolate-stabilized platinum nanoparticles using the modified two-phase Brust-Schiffrin method with alkylthiosulfate as ligand precursor. The mechanistic formation of alkanethiolate-capped Pt NPs from both S-octylthiosulfate and 1-octanethiol ligands is investigated. The synthesis using S-octylthiosulfate produces Pt NPs in higher yields than that

using 1-octanethiol ligand. The obtained nanoparticles are characterized by ^1H NMR, UV-vis spectroscopy, thermogravimetric analysis (TGA), and transmission electron microscopy (TEM). The results obtained from ^1H NMR and UV-vis spectroscopy are consistent with the formation of nanoparticles. Based on the TGA data, the Pt NPs contain about 30 wt % organic ligand content. They are characterized for further use as selective catalysts for hydrogenation of various organic compounds including styrene, allylbenzene, 3-nitrostyrene, acrolein and allyl alcohol.

2015 Western Regional Meeting 236

C-H amination of tetrahydroisoquinoline

Katherine Bay², *katherine.bay@laverne.edu*, **Seojung Han**¹, **Brian M. Stoltz**¹. (1) MC 101-20, California Inst of Technology, Pasadena, California, United States (2) Chemistry, University of La Verne, Arcadia, California, United States

Cyanocycline A is a member of the tetrahydroisoquinoline (THIQ) alkaloids, a class of natural products that display potent biological activity as antitumor antibiotics. Isolated from the fermentation broth of *Streptomyces flavogriseus*, cyanocycline A is a potent, broad-spectrum cytotoxin effective against mammalian and bacterial cells. We envisioned a total synthesis of cyanocycline A involving late-stage C–H activation as a key step. The chemistry of C–H amination offers powerful methodology for the synthesis of amine-derived materials through intramolecular C–H oxidation. Progress was made towards producing a benzo-fused oxathiazinane heterocycle from an *ortho*-substituted phenolic sulfamate through C–H amination using a Rhodium-tetracarboxylate catalyst. The preparation of this novel substrate contributes to the total synthesis of Cyanocycline A.

2015 Western Regional Meeting 237

Plant growth and soil chemistry: Standard solution models and measurement errors

Paul Johnson¹, **Ling Huang**², *Lghuang@ucdavis.edu*. (1) Consultant, Software Development, Davis, California, United States (2) Chemistry, Sacramento City College, Sacramento, California, United States

What effect does the introduction of plants and their growth have on soil composition? Lab spectrophotometer and atomic absorption spectroscopy were used to determine soil composition for plants grown in pots in controlled environments. The controls contain the original soil exposed to the same elements (weather, sunlight, water etc.) as the other plants. Concentration values were compared to the original soil and to that of the control. The effects of plant growth on soil composition will be examined. An example is given based upon controlled standard measurements. Model error simulations are used to compare least squares, least median squares and least absolute differences. Raposo et al. (2008) combine least-squares background correction and internal standardization techniques to eliminate spectral interferences. Johnson and Huang in this paper provide bootstrap estimates of the least-squares model coefficients to examine experimental and measurement bias. A question of interest: Which model provides the 'best' comparison when measurement errors, artificially generated from known parametric distributions, are introduced? Multiple Imputation methods will be used for the estimation of any missing values introduced to illustrate procedure. This work

will provide a framework for investigating plant growth on soil chemistry; and improving the fit of standard solution models when the effects of measurement errors are known. SYSTAT and STATA are used in the data analysis.

Keywords: chemistry, plants, soil, analytic methods, statistical analysis

2015 Western Regional Meeting 238

The effects of high leverage on the optimum product yield of oxazoline

Paul Johnson¹, Ling Huang², Lghuang@ucdavis.edu. (1) Consultant, Software Development, Davis, California, United States (2) Chemistry, Sacramneto City College, Sacramento, California, United States

Oxazoline is a heterocyclic organic compound. Oxazolines have recently been used as ligands in asymmetric catalysis (Hargaden and Guiry, 2009); and as a protecting group for carboxylic acids. Maheswari, Kumar and Venkateshwar (2014) comment on the synthesis of optically active 2-oxazolines, which can act as useful chiral auxiliaries and as ligands. The product yield of oxazoline (in %) was measured in experiments that were carried out at various levels of two independent variables: temperature (oC) and concentration of amino alcohol (mMolar concentration) [see Huang, 1998]. In this paper simulations were carried out where a point with high leverage was artificially introduced to the data set. An outlier analysis was performed to examine this high leverage point. Cook's D distances were used to measure the influence of the data points. Robust regression estimators were obtained from least trimmed square estimates (LTS). Response surface analysis (RSA) methods were used to compute the ridge of optimum yield of oxazoline. The effect of the high leverage point was examined as it pertained to optima yields. Toluenesulfonic acid acts as a catalyst. Oxazolines were synthesized from the condensation between an amino alcohol and carboxylic acid. The concentration of carboxylic acid was fixed at a constant in order to measure the effects of temperature and the concentration of amino alcohol. SAS, SYSTAT and SIGMAPLOT were used to perform the data analysis and for the production of graphical displays.

2015 Western Regional Meeting 239

Get involved with the ACS Division of Chemical Education

Jerry L. Sarquis, sarquijl@miamioh.edu. Chemistry, Miami University, Healdsburg, California, United States

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2015 Western Regional Meeting 240

Characterizing the Rubisco / Rubisco activase interaction via assembly studies

Andrew J. Serban^{1,2}, ajserban@asu.edu. (1) Chemistry & Biochemistry, Arizona State University, Avondale, Arizona, United States (2) Biodesign, Arizona State University, Tempe, Arizona, United States

In addition to being one of the most abundant proteins on Earth, Ribulose 1,5-Bisphosphate Carboxylase/Oxygenase (Rubisco) is responsible for fixing atmospheric CO₂ in plants and generating the necessary precursors for sugar production, a function critical in biomass accumulation. Although Rubisco has such a pivotal role in plants, it is not without its setbacks. One such limitation is Rubisco's propensity to bind O₂ in place of CO₂, as well as being prone to inhibition via a variety of substrate analogs, including its own, under certain conditions. An activator protein discovered in the late 80's, termed Rubisco Activase (Rca), has been shown to reactivate Rubisco via ATP hydrolysis. Rca is a chemo-mechanical motor protein belonging to the AAA+ protein superfamily, which is thought to remove the inhibitor by modifying the conformational state of Rubisco via ATP hydrolysis. The main goal of this research is to characterize this loosely understood interaction between Rubisco and Rca. In order to properly characterize this interaction, it was first necessary to characterize the assembly of Rca, to better relate its function to its oligomeric state. By using Fluorescence Correlation Spectroscopy (FCS), former colleagues discovered that Cotton Rca forms continuous spiraling oligomers at higher concentrations when in the presence of ADP. Our recent work indicated that Cotton Rca favored the hexameric state when in the presence of ATP- γ -S, a non-hydrolysable ATP analog. This same hexameric species was observed when working with a Cotton Rca mutant, termed D173N, chosen because it lacks the ability to hydrolyze ATP but still retains the ability to bind it. By using this mutant, assembly studies could be performed in the presence of ATP, without fear of ADP generation. Assembly studies, thus far, have been performed solely on Cotton Rca. Therefore, the next phase of this research is geared at understanding the assembly of Rca from different species, as well as, understand how the assembly of Rca varies when in the presence of Rubisco.

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Novel peptidomimetic inhibitors for the West Nile virus NS2B-NS3 protease

Julianne Truong, juliannetruong@csu.fullerton.edu, Bianca Espinosa. Chemistry and Biochemistry, California State University, Fullerton, Corona, California, United States

The West Nile virus (WNV), a flavivirus, has rapidly spread throughout the United States and has been a global epidemic since the early 1990's. The virus is spread to humans via infected mosquitoes blood meals. Severe WNV infections attack the central nervous system resulting in meningitis which can be fatal. Currently there are no approved therapeutic treatments for WNV infections, only the symptoms can be managed. A therapeutic target for WNV infections is the viral NS2B-NS3 protease, which is responsible for viral replication and assembly in infected host cells. Inhibition of the NS2B-NS3 protease has been reported to halt viral replication in cells, thereby ending the infection. The goal of this project is to identify small molecule inhibitors for the NS2B-NS3 protease. With the ultimate goal of developing a viable therapeutic treatment for WNV infection.

Peptides have been identified to inhibit the NS2B-NS3 protease, but have poor bioavailability, which is undesirable for therapeutic applications. Peptidomimetics are small molecules that mimic peptide interactions but with improved bioavailability. In this study, a library of peptidomimetics was synthesized and evaluated for inhibition of the NS2B-NS3 protease, via competitive FRET-based protease assay. The screen resulted in several novel peptidomimetic inhibitors for the NS2B-NS3 protease.

2015 Western Regional Meeting 242

Thin film crystallization

Kory Ulle, *koryulle@gmail.com*. Chemistry, California State University San Marcos, Escondido, California, United States

It is now widely accepted that many crystallization processes, such as biomineralization, proceed by "non-classical" mechanisms. These may involve aggregation of nanometer- to micron-size amorphous or crystalline precursors. One model system for biomineralization has been shown to result in thin (~0.5 micron) crystalline films, which have rhombohedral outlines under some conditions, and irregular outlines under other conditions. One hypothesis is that these films are formed through two-dimensional diffusion of 0.5 micron-sized precursor particles. These thin films are grown through the use of a polymer-induced liquid-precursor process (PILP) using polyaspartic acid. One important goal was to determine whether the different outline shapes could be explained by different supersaturations or relative rates of diffusion and crystallization. When the conditions of crystallization are varied, different outline shapes can be created. By measuring the apparent angles of the resulting rhombohedral films and comparing them to computer models, information regarding the "non-classical" mechanisms of biomineralization can be attained.

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Activity and selectivity of Pd nanoparticle catalysts for alkyne hydrogenation in water: Effects of graphene oxide supports and thiolate surface ligands

Vivian Chen¹, *xalitalisx@gmail.com*, Young-Seok Shon². (1) Chemistry, California State University Long Beach, San Juan Capistrano, California, United States (2) Chemistry and Biochemistry, California State University Long Beach, Long Beach, California, United States

This poster presents the influence of graphene oxide supports and thiolate surface ligands on their catalytic activity and selectivity for alkyne hydrogenation in water. In this study, the preformed Pd nanoparticle catalysts are assembled on the surface of graphene oxide and then annealed at 300 °C to activate catalytic surfaces. The studies show that unsupported, water-soluble thiolate-capped Pd nanoparticles (PdNP) favor the generation of semi-hydrogenated product, dimethyl maleate, over fully hydrogenated product from the reaction of dimethyl acetylene dicarboxylate (DMAD). Pd nanoparticles supported on graphene oxide (PdNP-GO) exhibit a similar activity for the hydrogenation of DMAD despite being kinetically confined, but they show an improved long-term stability by maintaining a high solubility in aqueous solution even after multiple catalytic cycles. After the heat treatment at 300 °C, the Pd nanoparticle-graphene oxide hybrids (heated PdNP-GO) exhibit an enhanced catalytic activity with an increase in reaction rate along with an alternating selectivity towards the fully hydrogenated

product, dimethyl succinate. Testing of the PdNP and PdNP-GO catalysts on acetylene dicarboxylic acid has shown similar results to those of DMAD tested for PdNP and PdNP-GO. However, the heated PdNP-GO catalysts also generated the semi-hydrogenated product, maleic acid, as the main product instead of the fully-hydrogenated product, succinic acid. This indicated that the additional hydrogenation of maleic acid might be hindered by the strong chelating hydrogen bonding interaction of graphene oxide with maleic acid. The hydrogenation of the terminal alkyne, 2-methyl-3-butyne-2-ol (dimethyl ethynyl carbinol), has shown an increased tendency to produce the full hydrogenation product rather than the semi hydrogenation product for both PdNP and heated PdNP-GO catalysts. Overall, the studies suggest large influences of graphene oxide supports and thiolate surface ligands on both activity and selectivity of Pd nanoparticle catalysts.

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TNA protects DNA and RNA from nuclease digestion under simulated physiological conditions

Michelle Culbertson¹, mcculber@asu.edu, Kartik W. Temburnikar², Sujay Sau¹, Jen-yu Liao¹, Saikat Bala¹, John C. Chaput¹. (1) Biodesign Institute, Arizona State University, Tempe, Arizona, United States (2) Univ of Maryland, Baltimore, Maryland, United States

Oligonucleotides and their chemically modified derivatives are routinely used to control gene expression and probe biologically relevant interactions. However, clinical applications of therapeutic oligonucleotides have been hindered by poor intracellular and extracellular stability. Here we examine the biological stability of α -L-threofuranosyl nucleic acid (TNA), an unnatural genetic polymer composed of repeating units of α -L-threofuranosyl sugars linked by 2',3'-phosphodiester bonds. We show that TNA homopolymers remain undigested when assayed under relevant biological conditions that include incubation for 7 days in human serum and human liver microsomes. We further show that DNA is resistant to nuclease degradation when incorporated into mixed backbone TNA-DNA heteropolymers or targeted by Watson-Crick base pairing with complementary strands of TNA. Taken together, these results suggest that TNA is a biologically stable nucleic acid mimic that could be used in future therapeutic and diagnostic applications.

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Antioxidant activity, total phenolics and total flavonoids content study of *Yucca whipplei* blossoms

Conscience Bwiza¹, MyThank Quach¹, America Hidalgo¹, Timothy Yoon¹, Diana Paez², Joan Kalimba¹, John Luong¹, Daniel McCarthy³, Margaret Barth², **Ying Hu¹**, yhu@calbaptist.edu. (1) Natural & Mathematical Sciences, California Baptist University, Riverside, California, United States (2) Department of Health Sciences, California Baptist University, Riverside, California, United States (3) Cultural Resources Management Department, San Manuel Band of Mission Indians, Highland, California, United States

Plant derived foods such as fruits and vegetables reduces the risk of cardiovascular disease, cancer and diabetes due in part to the action of phytonutrients that are capable of neutralizing free radicals and reducing oxidative damage. Native American edible plants are thought to be

good contributors of antioxidants; however there are few research reports on this topic. Thus, the objective of this research was to study the antioxidant activity, total phenolics and total flavonoids content in blossoms of *Yucca whipplei*, a traditional Native American plant from Southern California. The blossoms were harvested from a reservation close to Riverside, California in April 2015. The Moisture content result showed that the blossoms had relatively high moisture level 90.48%. The blossoms were slightly acidic with a pH of 5.430. The 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging activity assay was used for the antioxidant method with ascorbic acid as the reference. DPPH was allowed to react with plant extracts of different concentrations for 30 min in dark (5°C). The absorbances of aliquots of the extracts were measured at 517 nm. The blossoms gave an IC₅₀ 21.85 mg/ml. The total phenolics content was measured by using the Folin-Ciocalteu method. The phenolics content was 245.8 mg gallic acid equivalents/g of dry weight. The aluminum chloride colorimetric method was applied to test the total flavonoid content. The total flavonoid content of blossoms was 8.954 mg quercetin equivalents/g of dry weight.



2015 Western Regional Meeting 246

Dye-sensitized solar cell based on the natural dye extract from elderberry leaves

Joan Kalimba, John Luong, **Ying Hu**, yhu@calbaptist.edu. Natural & Mathematical Sciences, California Baptist University, Riverside, California, United States

The large energy demand has caused a big concern around the world. Due to the simple fabrication and the use of natural pigments as sensitizing dyes, the dye-sensitized solar cells (DSSC) provides a technically and cost-effective alternative concept to the more used photovoltaic cells. In our study, we used a dye extracted from elderberry leaves (*Sambucus nigra*), which have a characteristic black color after complexes with Fe. The black dye has been used by Native Americans for making their royal black color for ages and has never been studied in DSSC. The purpose for our research was to investigate the potential application of this dye in producing DSSC. The cell was fabricated according to the literature reported procedure. The dye was absorbed by a TiO₂ layer which was coated on a transparent fluorine-doped tin oxide (FTO) glass as the anode, A LiI and I₂ acetonitrile solution was used as the electrolyte solution. The counter electrode was carbon coated on a piece of FTO glass. A cell

base on the pink dye in Bougainvillea flower served as a reference and gave a V_{oc} 0.551 V under the direct sunlight. The V_{oc} of the cell based on the black dye from elderberry leaves is 0.596 V. The current and efficient of the DSSCs are currently under study.

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Effects of steric hindrance near the metal surface of unsupported palladium nanoparticle catalysts for alkene isomerization

Peter Tieu, *shadowsbind@gmail.com*, Young-Seok Shon. Chemistry, California State University, Long Beach, Long Beach, California, United States

Evaluation of metal nanoparticle catalysts functionalized with well-defined small organic ligands can be potentially important, because such systems can provide a spatial control in the reactivity and selectivity of nano-catalysts. Our group recently discovered a synthetic method utilizing Bunte salts (sodium S-alkylthiosulfates) to generate catalytically active Pd nanoparticles (PdNP) capped with a low density alkanethiolate ligands. These unsupported PdNP catalyst were successful in selective isomerization of allyl alcohols to carbonyls in organic solvents. These PdNP were also found to be selective for alkene hydrogenation and/or isomerization of various alkenes and dienes. Herein, this poster describes the synthesis and catalytic property evaluation of five different PdNPs capped with constitutional isomers of pentanethiolate ligands that have one or two methyl groups at different locations (α , β , or γ from the surface-bound sulfur). The PdNPs were characterized by thermogravimetric analysis (TGA), proton NMR, transmission electron microscopy (TEM), and gas adsorption using the Brunauer-Emmett-Teller (BET) model. The hydrogenation and/or isomerization of simple terminal pentene isomers were monitored over the course of 24 hours for each combination of ligand and substrate. To compare the catalytic rates among the various PdNPs, the rates were calculated by constructing conversion percentage versus time curves using *in situ* proton NMR data. Since the hydrogenation versus isomerization process is a regioselective process involving a Pd-alkyl intermediate, the steric interactions between surface ligands and alkene substrates near the active sites greatly influence the selectivity between these two products and the overall reactivity of terminal alkenes.

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Elucidating molecular pathways of prostate field cancerization: Potential role of EGR-1 as a master regulator

Kristin Gabriel, *gabri110@mail.chapman.edu*, Marco Bisoffi. Schmid College of Science and Technology, Chapman University, Orange, California, United States

Field cancerization describes the presence of molecular alterations (genetic, epigenetic, biochemical) in structurally intact cells residing in histologically normal tissues adjacent to tumors. Markers of field cancerization have the potential to detect the presence of cancer, leading to improved diagnostic methods. For example, in prostate cancer, markers of prostate field cancerization can increase the clinically informative area surrounding biopsy cores even in the absence of cancerous tissue in the cores, thereby minimizing potential side effects from repeated biopsies. However, it is necessary to gain a detailed understanding of the functional pathways underlying field cancerization in order to use markers to improve diagnostic methods.

We have identified four protein factors as markers of prostate field cancerization: key transcription factor early growth response 1 (EGR-1), lipogenic enzyme fatty acid synthase (FAS), macrophage inhibitory cytokine 1 (MIC-1), and secreted growth factor platelet derived growth factor A (PDGF-A). Using a comprehensive comparison of expression levels of these four factors in human prostate cell models and human tissues, we determined that molecular mechanisms of field cancerization are consistent between cell models and tissues. In particular, we identified a possible regulatory role for EGR-1 in controlling the expression of FAS and MIC-1 (down-regulation) and PDGF-A (up-regulation) in both prostate cell models and human tissues. In summary, our study describes a novel functional pathway of prostate cancerization with a central regulatory role for EGR-1. Knowledge of this pathway could be used in the early and improved detection of prostate cancer in false-negative specimens after initial or repeated biopsies from patients with low risk disease.

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Computational study of butyrylcholinesterase inhibition by dialkyl phenyl phosphate derivatives

Sean G. McCoy¹, *smccoy0392@gmail.com*, **Walter Alvarado²**, **Analisa Garcia¹**, **Eric J. Sorin¹**.
(1) *Chemistry and Biochemistry, California State University, Long Beach, La Palma, California, United States* (2) *Physics, California State University, Long Beach, Long Beach, California, United States*

Acetylcholine (ACh) is a neurotransmitter that allows for communication between nerve and muscle cells. While acetylcholinesterase (AChE) is the primary enzyme responsible for the breakdown of ACh to regulate intercellular communication, butyrylcholinesterase (BChE), an AChE-like scavenger enzyme, also breaks down both ACh and larger choline derivatives. In persons suffering from Alzheimer's disease (AD), BChE activity has been found to gradually increase over time and increased BChE activity is believed to significantly decrease synaptic ACh levels, thereby disrupting intercellular communication. It is therefore of interest to explore BChE-specific inhibitors as potential pharmaceutical approaches to the treatment of AD. Dialkyl phenyl phosphate (DAPP) derivatives are organophosphates that mimic the ester moiety of ACh. As such, DAPP derivatives are expected to interact with the BChE binding pocket in a manner similar to that of natural physiological substrates. This study employs massive flexible-inhibitor docking calculations to predict the relative binding affinity between the enzyme and a number of DAPP derivatives, as well as the optimal binding orientation of each DAPP derivative within the BChE active site. Our results reproduce experimental trends in binding affinity and indicate that DAPP derivatives with substitutions at the ortho- and meta- positions of the phenyl ring will show increased inhibitory strength, while para- substitutions will generally be detrimental due to steric clash with active site residues. These findings provide insight into the structural preference of BChE for specific DAPP derivatives and provide a framework for future inhibitor design and testing.

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Computational study of the addition of ammonia, methylamine, and dimethylamine to acetaldehyde catalyzed by a single water molecule: Energetics for carbinolamine formation

Josue E. Perez, perezjosue91@gmail.com, Matthew K. Louie, Amitabha Sinha. Univ of California San Diego, La Jolla, California, United States

Ammonium and its organic derivatives, methylamine and dimethylamine are common atmospheric species that play an important role in the formation of atmospheric aerosols. In this poster we present data comparing the relative energetics associated with carbinolamine formation resulting from the addition of respectively ammonia, methylamine and dimethylamine to acetaldehyde catalyzed by a single water molecule. At the CCSD(T)/6-311++G(3df,3pd)//MP2=Full/6-311++G(3df,3pd) level, we find that the reaction involving dimethylamine has the lowest barrier with the transition state being 2.6 kcal/mol below the $(\text{CH}_3)_2\text{NH} + \text{CH}_3\text{CHO} + \text{H}_2\text{O}$ separated reactants. The reaction involving ammonia and methylamine have significantly higher barriers. The low barrier associated with the dimethylamine addition reaction suggests it can potentially contribute to secondary organic aerosol formation under atmospheric conditions.

2015 Western Regional Meeting 251

β -hairpins: Molecular accessories for helical peptide expression

Melissa E. Lokensgard¹, m.e.lokensgard@gmail.com, John J. Love². (1) Chemistry & Biochemistry, San Diego State University, Poway, California, United States (2) Chemistry & Biochemistry, San Diego State University, San Diego, California, United States

One barrier to recombinant production of proteins is that small peptides and domains are often degraded or otherwise unstable or insoluble in some expression systems. Often the solution to this problem when large quantities of material are needed, is to fuse the peptide to the C-terminus of a larger or more well-folded domain, such as Ubiquitin, SUMO, MBP, G β 1, and others. This frequently improves the yield of recombinant protein and can additionally benefit solubility or aid in purification. G β 1 and other tags can improve not only yield, but also solubility and folding of the target protein, and some can double as handles for chromatographic purification and crystallization. We are developing methods to employ smaller tags to accomplish similar expression and solubility enhancement without complicating purification of the target peptide. We describe a method for stabilizing a helical protein for recombinant over-expression by adding a short sequence thought to adopt a beta-hairpin structure. The twelve or seventeen amino acid fusion tag is derived from the amino-terminal beta-hairpin of either G β 1 or Ubiquitin and can be fused to either terminus of a helical protein recalcitrant to over expression in *E. coli*. We observe high yields of the chimeric protein. Moderate destabilization of the helical peptide does not significantly diminish the expression enhancement effect. Spectral analysis indicates that helical content and thermal stability are neither perturbed nor enhanced by the addition of the beta-hairpin. While the biochemical origins of the expression enhancement are still not clear, we suspect that this tag reduces interactions with host degradation factors. Thus, in addition to an application as a biotechnological tool, this system may represent a way to study fundamental protein recycling questions in biology.

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Sensitive detection of proteins and cancer markers by nonlinear laser wave-mixing detection and capillary electrophoresis

Mya Brown¹, *myamarie1991@yahoo.com*, **Jean S. Pradel**², **Sashary Ramos**², **William G. Tong**². (1) Chemistry, San Diego State University, San Diego, California, United States (2) San Diego State University, San Diego, California, United States

Ultrasensitive detection of proteins and small molecules is important for the diagnosis of diseases as well as the evaluation of treatment progress. However, current detection methods do not offer adequate sensitivity and specificity levels. In this work, we introduce a novel nonlinear laser method, coupled with capillary electrophoresis, for the separation and detection of proteins, small molecules and other biological samples. In a typical laser wave-mixing setup, the signal is generated when two laser beams intersect inside the capillary containing the analyte of interest. The wave-mixing signal is a coherent laser-like beam and can be collected with virtually 100% efficiency and minimal background noise. The signal has a cubic dependence on laser power and a quadratic dependence on analyte concentration, and hence, it is inherently suitable as a chemical sensor. NBDX-labeled beta-lactoglobulin is first detected by a visible laser to optimize the wave-mixing setup. A standard protein ladder labelled with NBDX is also separated and detected using capillary electrophoresis and wave mixing. A breast cancer prognostic marker, CA 15-3, labeled with NBDX, is also detected using laser wave mixing. We have also demonstrated femto-mol or zepto-mole detection levels for other proteins and small molecules such as neurotransmitters.

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Triplet state dynamics in the visible light absorbing zinc chlorodipyrin

William Thornbury⁵, *wthornbu@gmail.com*, **Saptaparna Das**¹, **Andrew Bartynski**², **Mark E. Thompson**³, **Stephen E. Bradforth**⁴. (1) USC, Los Angeles, California, United States (2) Chemical Engineering, University of Southern California, Los Angeles, California, United States (3) Department of Chemistry, University of Southern California, Los Angeles, California, United States (4) Chem Dept SSC 726, Univ of Southern California, Los Angeles, California, United States (5) University of Southern California, Los Angeles, California, United States

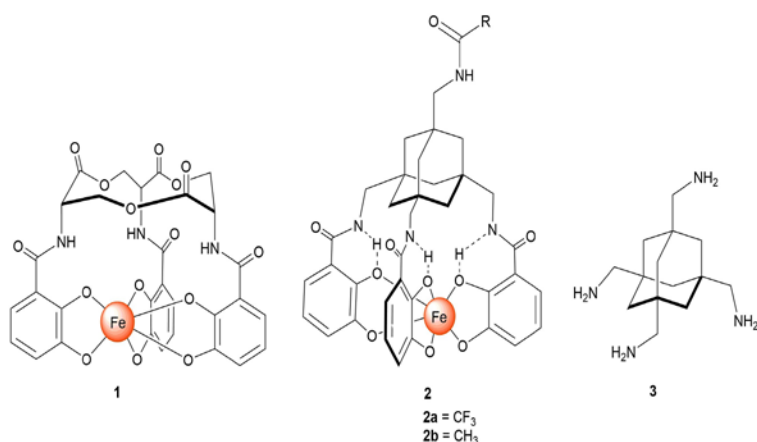
An organic photovoltaic device's constituent materials are of great importance to the device's power conversion efficiency (PCE): the energetic offset between the donor material HOMO and acceptor material LUMO define the device's open-circuit voltage (V_{oc}) and subsequent PCE. Tetraphenyl-dibenzoperylfuran/zinc chlorodipyrin (DBP/ZCl) donor acceptor systems have shown significantly larger V_{oc} 's than the conventional DBP/C₆₀ devices. Although the excited state dynamics of ZCl have been explored in the femto/picosecond range, where symmetry breaking charge transfer (SBCT) occurs in all but non-polar solvents, the extended excited state behavior has not been characterized in the ns - μ s regime where the triplet state photophysics dominates. Analysis using nanosecond transient absorption spectroscopy reveals that in non-polar cyclohexane, ZCl undergoes intersystem crossing with a triplet appearance time of 1 – 5 ns. In the more polar solvents, toluene and acetonitrile, the triplets had been shown to form within 1 ns via recombination from the SBCT state. The triplets in all three solvents were found to decay to the ground state in 0.6 – 2 μ s.

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A synthetic siderophore as a molecular shuttle

Arabo A. Avanes, AraboAvanes@gmail.com, Jonathan Saboury, Armen Davidian, Carla Bezjian, Brittany Ulloa, Miguel Pinto, Carlos G. Gutierrez. Chemistry & Biochemistry, California State University, Los Angeles, Los Angeles, California, United States

We designed and synthesized compounds **2** as molecular shuttles for the deliberate transport of small exogenous molecules into *E. coli*. The inspiration is the *E. coli* siderophore enterobactin (**1**) that is recognized and actively transported into the bacterial cell through the FepA cell surface receptor. Shuttle **2** employs 1,3,5,7-tetrakis(aminomethyl)adamantane (**3**) as a core on which we have elaborated bifunctional enterobactin analogs. Three of the aminomethyl groups in **3** are used to build the triscatecholamide motif that is a close spatial mimic of the enterobactin iron-binding domain; cargo R is coupled to the fourth aminomethyl unit, deliberately 180° away from the iron-binding domain as to not interfere with recognition at the FepA receptor. We have selectively discriminated among the four equivalent amines in T_D symmetric polyamine **3** to produce the C_{3v} polyamide pattern required in **2** by taking advantage of pKa differences among the four ammonium ions in tetrahedral **3**•4HCl. It was monodeprotonated and acylated with either trifluoroacetyl (**2a**, R = CF₃) or acetyl (**2b**, R = CH₃). The three remaining ammonium ions were deprotonated and then acylated with dihydroxybenzoyl units. Compounds **2a** and **2b** will test the hypothesis that such enterobactin mimics will be transported into the bacterium.



2015 Western Regional Meeting 255

Crystallization processes modeled by Monte-Carlo simulation of two-dimensional surface diffusion

Michelle Salem, salem005@cougars.csusm.edu, Michael Schmidt. Chemistry and Biochemistry, California State University San Marcos, San Marcos, California, United States

It is now widely accepted that many crystallization processes, such as biomineralization, proceed by “non-classical” mechanisms. These may involve aggregation of nanometer- to micron-size amorphous or crystalline precursors. One model system for biomineralization has been shown to result in thin (~0.5 micron) crystalline films, which have rhombohedral outlines under some conditions, and irregular outlines under other conditions. One hypothesis is that these films are formed through two-dimensional surface diffusion of 0.5 micron-sized precursor

particles. We investigated this hypothesis by constructing two-dimensional Monte-Carlo simulations. One important goal was to determine whether the different outline shapes could be explained by different supersaturations or relative rates of diffusion and crystallization. To this end, we have constructed models on both square and hexagonal grids and allowed for the variation of temperature, binding energy, anisotropy of interactions, and surface concentration of particles. Preliminary results of these simulations will be presented.

2015 Western Regional Meeting 256

A poster session demonstrating graduate student teaching assistants' competence in the design and implementation of a student-centered lesson plan

Mark A. Boerneke, *markb2u@hotmail.com*, Holly Dembinski, Stacey Brydges. Chemistry & Biochemistry, University of California, San Diego, La Jolla, California, United States

Graduate teaching assistants (TAs) play an integral role in undergraduate teaching and learning at research universities. The Department of Chemistry and Biochemistry at UC San Diego has instituted a professional development program for its TAs that combines in parallel training, practice, and critical reflection through apprentice teaching and a required, for-credit 10-week course (CHEM 509). The goals are: (1) to prepare new M.S./Ph.D. candidates for immediate and future TA responsibilities, by developing their proficiency in evidence-based teaching practices that foster student learning in chemistry lecture and lab settings; (2) to build a strong and supportive peer network in the first year of graduate studies; and (3) to cultivate transferrable skills relevant to both research and future careers. Here we describe the design and implementation of a capstone project in which the graduate TAs apply what they have learned in CHEM 509 to develop and carry out a "backwards by design" lesson plan that includes learning goals, assessments, and active-learning strategies and activities for lectures and labs. The TAs share their teaching projects and exchange ideas and resources with peers and colleagues at a department-wide poster session hosted at the end of the academic term.

2015 Western Regional Meeting 257

Relationship between speech and gesture to support molecular-level explanations of macroscopic phenomena in the context of acid-base titration

Amy Lien², *Aamylienn@gmail.com*, Barbara L. Gonzalez¹. (1) Chemistry and Biochemistry, California State University Fullerton, Rancho Palos Verdes, California, United States (2) Biochemistry, California State University, Fullerton, Fullerton, California, United States

Understanding acid base chemistry can be challenging for learners, because of different acid base models, such as Arrhenius, Bronsted-Lowry and Lewis, and the dynamic molecular mechanistic aspects of acid-base behavior. In this study, an instructor's use of visual representations and gestures used to explain the governing principles of acid base titration were analyzed. The research questions probed were: What are the aspects of molecular mechanistic explanations in acid base chemistry that an experienced instructor uses in 1) speech? 2) gesture? and 3) Is there a correlation between them? To explore these questions, a lesson on acid-base titration taught by an experienced college instructor was video recorded. The lesson was transcribed, divided into clips by conceptual topics, and gestures captured by watching the video without sound. For each clip, both the speech and gestures were coded using a binary

coding scheme that consisted of nine categories of molecular mechanistic explanations: entities, states, interactions, hierarchical organization, spatial organization, temporal change, research methods, context/relevance, and analogies/modalities/representation. Preliminary analyses indicate that over three intervals in a lesson on acid-base titration, entities, states and interactions were mentioned in speech. Spatial organization and temporal change occurred in speech less frequently and during the middle or end of the lesson, only. The findings in this study contribute to development of best practices in the use of visualizations and the role of gesture in instruction on titration.

2015 Western Regional Meeting 258

Synthesis of homochiral metal-organic frameworks using tetradentate ligands

Edward Nguyen, *edtnghuyen@gmail.com*, Xiang Zhao, Xianhui Bu. Chemistry and Biochemistry, CSU Long Beach, Long Beach, California, United States

In-situ solvothermal synthesis of organic ligands, specifically tetradentate 1,2,4,5-tetra(4-pyridyl)benzene (TPB), is an interesting aspect in the synthetic design of porous metal-organic framework materials. TPB was previously observed in the in-situ synthesis involving 4,4'-trimethylenedipyridine (TMDPy) with enantiopure D-Camphorate and tetrahedrally coordinated Zn^{2+} . In a comparative study presented here, the use of the pre-synthesized TPB ligand with Zn^{2+} results in a novel previously unobserved material, $Zn_2(D-Cam)_2(TPB)$. This crystalline porous material (CPM) features high symmetry with large pore size. This presentation will give a detailed comparison between self-assembly processes involving in-situ formed ligands and pre-synthesized ligands.

2015 Western Regional Meeting 259

Photoelectrochemical characterization CuGaSe hotocathodes

Benjamin Bachman¹, *bbachman@uoregon.edu*, Todd G. Deutsch², James Young^{2,3}. (1) Chemistry and biochemistry, University of Oregon, Eugene, Oregon, United States (2) MS 1613, National Renewable Energy Lab, Golden, Colorado, United States (3) Physics, University of Colorado Boulder, Boulder, Colorado, United States

Copper Gallium DiSelenide (CGS) has shown promise as a potential material for photoelectrochemical hydrogen generation through water-splitting. We seek a better understanding of CGS compounds for their use as top-junction absorbers in PEC systems. A photoelectrochemical (PEC) cell optimized for water-splitting has the capability of generating hydrogen more cost effectively than solar photovoltaics coupled to a separate electrolyzer. To characterize these compounds, we utilized cyclic voltammetry, photo-current spectroscopy, Incident photo-to-current spectroscopy (IPCE), transmissions, and UV-Vis spectroscopy. The CGS compounds showed bandgaps well optimized for water-splitting (at 1.6 eV or greater) and high photocurrent. Durability analysis shows that these compounds are stable for up to 45 hours in 0.5 M sulfuric acid without a protecting layer before significant degradation occurs. Paired with a small bandgap bottom junction and an active catalyst, we predict these CGS compounds would be well suited for PEC water-splitting.

2015 Western Regional Meeting 260

Spectroelectrochemical characterization and solvent effect on the tautomerism of free-base corrole

Forrest Kohl, *forrestkohl@gmail.com*, Guadalupe N. Calvillo, Silvia Klein, Anthony Loogman, Stephanie Becerra, Elvin A. Aleman. Chemistry, California State University Stanislaus, Turlock, California, United States

Corroles are aromatic compounds consisting of four pyrrole-like subunits connected in a ring via three methane bridges and one direct bond between the alpha carbons of two of the subunits. Similar to porphyrins, corroles demonstrate exceptional photophysical properties in regards to their absorbance of light and fluorescence. Corroles differ from porphyrins in that they can exist in two separate tautomeric states causing them to exhibit noticeably different photophysical behaviors in different solvents. Corroles, like porphyrins, have potential as photosensitizers in photodynamic therapies and solar cells.

In order to fully understand the role of solvents in corroles tautomerization and how they can influence its absorptive and electrochemical properties, we have investigated the spectroelectrochemical properties of free-base triphenylcorrole (H_3TPCor). We have characterized corroles light absorbing behavior in various solvents across various concentrations. The efforts of these studies are being used in the analysis of H_3TPCor 's photophysical properties in its reduced & oxidized states and how solvents can affect their stability. A proper understanding of corroles interaction with solvents and how they affect corroles light absorbing & emitting capabilities are necessary to develop potential uses of corrole in solar energy, cancer diagnosis, and tumor treatment.

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Visualization of organic molecules: An analysis of students' visual-spatial ability at a large primarily undergraduate institution

Arman Garcia, *arman.garcia@gmail.com*, Leslie Perez. Chemistry, California State University of Fullerton, La Habra Heights, California, United States

Organic chemistry requires students to visualize two dimensional molecules in three dimensions. However, many students lack a strong foundation in three dimensional visualization.³ The goal of this project is to test the effectiveness of Jmol, a 3D molecular modeling program on students' performance on organic chemistry tasks that require a high degree of visual-spatial ability. We hypothesize that Jmol will be an effective tool to aid in the performance of visual-spatial problems on an organic chemistry assessment opposed to allowing students to perform ineffective mental rotations.

This study showed that students who were allowed to use Jmol outperformed their 2D counterparts on visual-spatial tasks in organic chemistry. The overall mean for the two dimensional participants was 10.45 whereas the mean for the three dimensional participants was 12.15 with standard deviations of 3.706 and 3.609 respectively. Using a One-Way Analysis of Variance to compare these means, provided an overall significant result ($F=4.409$, $p=0.39$). Previous literature has shown that when students interact with a 3D molecular modeling program to answer visual-spatial questions they outperform all groups. Using eye-tracker technology this study wanted to examine: What cognitive strategies participants of different

visual-spatial ability use to answer organic chemistry problems when using 2D vs. 3D resources. The results show that Jmol was an effective tool for most participants in that they were able to develop a cognitive strategy.

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Novel synthesis of modified nucleic acids and nucleoside analogs for solid phase synthesis of ribonucleic guanidine (RNG)

Alicia Chavez, *alicia.chavez576@myci.csuci.edu. Chemistry, California State University Channel Islands, Ventura, California, United States*

Nucleic acids, nucleosides and nucleotides have the profound capability to serve as therapeutic agents in antisense and RNA interference (RNAi) technology. Antisense and RNAi drugs are short, synthetic oligonucleotides designed to silence gene expression by targeting mRNA. The current focus of our research is the efficient synthesis of RNG, which entails replacing the phosphodiester linkages of RNA with positively charged guanidium linkages. The highly efficient synthetic methods of 5'-amino-5'-deoxyribonucleoside is recorded for uridine, and guanosine. After protection of the 2'- and 3'- hydroxyl groups of the sugar, the 5'-amine was introduced to uridine by Mitsunobu reaction. Despite several condition changes, the Mitsunobu approach was proven to be an ineffective route for amination when applied to the 2'-3'-hydroxyl protected N2-isobutyryl-guanosine. The alternative approach utilizes the synthesis of a 5'-azido derivative. Protecting groups on the newly introduced amine and the remaining hydroxyl groups are adjusted to make them compatible with the solid phase synthesis of RNG. The designed compounds are purified by silica gel chromatography, and the structures are confirmed via proton Nuclear Magnetic Resonance and high resolution Mass Spectrometry. Protocol for the efficient synthesis of all desired monomers is currently being developed.

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Systematic structure modifications of imidazo[1,2-a]pyrimidines to reduce and predict aldehyde oxidase-mediated metabolism

Martha A. Ornelas, *martha.ornelas@pfizer.com. Pfizer, San Diego, California, United States*

Over 93% of small molecule drug candidates fail in phase I-III clinical trials and around 30% of these failures are due to unpredictable toxicity or clinical safety. The metabolism of heteroarenes by aldehyde oxidase (AO) is increasingly being recognized as an important factor. Thus, improved medicinal chemistry strategies to avoid AO-mediated oxidation and the rapid detection of potential liabilities are critical in early discovery programs. The imidazo[1,2-a]pyrimidine ring system has been identified as a representative example of heteroaryl systems that are substrates for AO-mediated metabolism. Multiple medicinal chemistry approaches were employed to reduce the AO liability, and our investigation suggests that alternative heterocycles or direct blockade of the reactive site are two of the more effective strategies. The potential reactive site(s) may be predicted by the AO protein structure-based model or in a quick and effective manner by the use of the "litmus test" using the nucleophilic radical source DFMS. Moreover, DFMS can be employed to prepare metabolically stable analogs for further testing. The approaches described herein may be applicable to other drug discovery programs in which similar AO metabolism problems are encountered.

2015 Western Regional Meeting 264

Synthesis and investigation of soluble PyQuin gold(III) complexes

Enrique Roman, *eroma003@ucr.edu*, Michael D. Sterling, Catharine H. Larsen. University of California, Riverside, Riverside, California, United States

The Larsen chemistry group accesses small nitrogen-containing molecules by finding new ways to catalyze multicomponent reactions of inexpensive starting materials. To this end, a green, catalytic three-component coupling of pyridine carboxaldehyde, phenylacetylene, and any number of anilines forms complex 4-phenyl-2-(2'-pyridyl)quinoline (PyQuin) ligands in a single step. These PyQuins have been shown to act as bidentate ligands for the formation of gold(III) complexes. The goals of this project are twofold: 1) synthesize PyQuins that make more soluble gold complexes and 2) synthesize and characterize the first PyQuin gold(III) bromide complexes.

2015 Western Regional Meeting 265

Real-time reaction kinetics by quantitative nuclear magnetic resonance spectroscopy

Jaideep Singh¹, *jdeeptheegreat@gmail.com*, Cheenou Her¹, Krish V. Krishnan^{1,2}. (1) Department of Chemistry, California State University, Fresno, Fresno, California, United States (2) Department of Pathology and Laboratory Medicine, School of Medicine, University of California, Davis, Davis, California, United States

Nuclear magnetic resonance (NMR) spectroscopy is a powerful analytical tool used to determine the structure and dynamics of molecules. The objective of this research is to develop and apply comprehensive real-time quantitative NMR methods to measure real time kinetics. As an example we demonstrate the use of NMR in measuring the enzyme kinetics of invertase in conversion of sucrose to glucose. We provide an optimized approach that uses a real-time monitoring of the kinetics and a direct analysis of the time course data using Lambert-W function. We further extend this approach to other enzymes such as b-galactosidase that catalyzes the hydrolysis of β -galactosides into monosaccharides. Thus the combination of NMR experimental time-course data with progress curve analysis is demonstrated in the case of enzyme catalyzed hydrolysis reactions, providing direct and simple estimations of Michaelis-Menten kinetic parameters. Complete details on how to implement the experiment and perform data analysis will be provided.

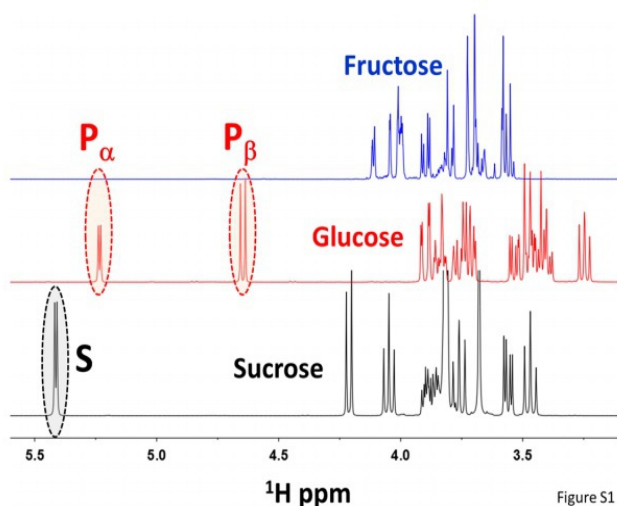


Figure S1

Figure S1: Reference 400 MHz ^1H NMR spectra of sucrose, glucose and fructose. Approximately 40 mM of the samples were used in 99.9 atom % D D_2O and the peaks are references with respect to TSP.

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Revolutionary view on third-hand smoke by NMR spectroscopy: A chemometric approach

Justin Vang¹, yasxayas@mail.fresnostate.edu, Krish V. Krishnan^{1,2}, Alam Hasson¹. (1) California State University Fresno, Fresno, California, United States (2) Department of pathology and medicine, School of Medicine, University of California, Davis, Davis, California, United States

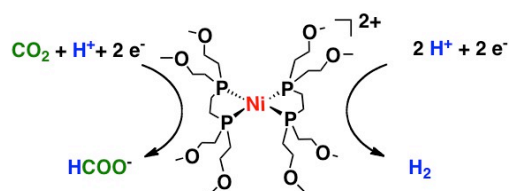
On an average 14.1 cigarettes are smoked by smokers each day and a generic cigarette contains as much as 4000 different chemicals. The smoke from the cigarette contains potentially harmful chemicals and is classified by first-hand, second-hand, or third-hand smoke. A developing hypothesis suggests that third-hand smoke is more dangerous than first-hand or second-hand smoke. Third-hand smoke occurs when second-hand smoke attaches to the environment, but once released the compound will react with ozone or other airborne contaminants creating gaseous volatile organic compounds (VOCs) and unknown harmful chemical. The interest of this research is to study the chemometrics of third-hand smoke effects *in vitro* (molecular composition) and *in vivo* (on cellular systems when exposed). Nuclear Magnetic Resonance (NMR) spectroscopy is a powerful technique used for structural analysis along with the capacity to perform chemical kinetic reactions and identification of chemical composition and molecular structure. With the NMR data collected through *in vitro* experimentation, the unknown chemicals will be identified. The results from this research will establish a chemical data base for possible third-hand smoke contaminant identification. The data collected will help bring to light unknown probable reactions, which will be tested onto cells for *in vivo* testing.

2015 Western Regional Meeting 267

Thermodynamic and electrochemical studies of a $[\text{Ni}(\text{bisphosphine})_2]^{2+}$ complex in water and organic solvents

Bianca M. Ceballos, bceballo@uci.edu, Jenny Y. Yang, Charlene Tsay. Chemistry, University of California Irvine, Irvine, California, United States

Metal hydrides are important intermediates in the catalytic cycle for the heterolytic production of H_2 and reduction of CO_2 . Understanding the thermodynamic and kinetic properties associated with metal hydride transfer is important for the rational design of catalysts. Herein, we report the synthesis and characterization of a $[\text{Ni}(\text{tmepe})_2](\text{BF}_4)_2$ complex (tmepe=1,2-Bis[bis(methoxyethyl)phosphino]ethane) for the investigation of fundamental thermodynamic properties of hydride donor ability at various pH values in water as well as in organic solvents. Electrocatalytic properties and reaction intermediates have been studied using cyclic voltammetry as well as ^1H and ^{31}P NMR spectroscopy.



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Fragmentation studies of flubendiamide under various atmospheric conditions

Erik Rangel, Logan_rangel@yahoo.com. CSU Fresno, Fresno, California, United States

Flubendiamide belongs to a chemical family of benzenedicarboxamides, or phthalic acid diamides, with insecticidal activity through the activation of the ryanodine-sensitive intracellular calcium release channels, leading to the cessation of feeding immediately after ingestion of the compound¹. Flubendiamide is registered for use on corn, cotton, tobacco, pome and stone fruit, tree nut crops, grapes and vegetable crops. Flubendiamide acts against various lepidopterous insect pest such as army worms, bollworms, corn borers, cutworms, diamondback moths, fruit worms, and loopers.

2015 Western Regional Meeting 269

Novel biomarkers for HIV-1 disease progression

Tracey Taylor¹, traceyeltaylor@yahoo.com, **Anjani Pandya**², **Kathleen Borgmann**², **Anuja Ghorpade**³. (1) Chemistry, Texas Southern University, Houston, Texas, United States (2) UNT Health Science Center, Forth Worth, Texas, United States (3) The Brain Bank, UNT Health Science Center, Forth Worth, Texas, United States

Approximately forty million people worldwide live with the human immunodeficiency virus-1 (HIV-1), which can progress into HIV-1-associated neurocognitive disorder (HAND). The most severe form of HIV-1 Central Nervous System (CNS) Disease is HIV-1-associated encephalitis (HIVE) or dementia (HAD), which is a defining condition of acquired immune deficiency syndrome (AIDS). Research suggests that pro-inflammatory proteins and other biomarkers may correlate with the level of neurological impairment in seropositive patients. The purpose of the study is to identify biomarkers that may correlate with neurocognitive decline in patients of varying gender, race, age, and disease progression. A cohort of HIV-1 seropositive patients is currently being recruited from the University of North Texas Health Science Center (UNTHSC) infectious disease clinic. A study visit includes a review of HIV-1 relevant patient history, a socio-demographic survey, a neurocognitive assessment, and a donation of 30-40 milliliters (ml) of blood. Plasma samples, isolated from patient blood, were analyzed by ELISAs specific to human soluble CD40 ligand (sCD40L), Interleukin (IL)-6, CCL2 or monocyte chemoattractant protein (MCP)-1 and tissue inhibitor of metalloproteinase (TIMP)-1. Biomarker levels were correlated to neurocognitive assessments, socio-demographic responses, and relevant measures of HIV-1 infection medical history. The inflammatory biomarkers, CCL2 and TIMP-1, were elevated in the HIV-1 seropositive cohort as compared to non-infected controls. Further, as the neurocognitive abilities of the patient cohort declined, levels of CCL2, IL-6, and TIMP-1 were correspondingly elevated. While sCD40L demonstrated no significant correlations between infection status, longevity, or neurocognitive score, the inflammatory protein showed consistent, positive trends. Although patient T-cell counts did not correlate significantly with inflammatory biomarkers, trends were seen that may improve upon analyzing of the entire cohort. Our data shows that inflammatory biomarkers may play an important role in predicting HIV-1 disease progression through the comparison of plasma samples within the HIV-1 seropositive population.

2015 Western Regional Meeting 270

Small molecule activation using transition metal-Si complexes

Amy Bartrom, abart003@ucr.edu, **Hill Harman**. Department of Chemistry, University of California, Riverside, Riverside, California, United States

In contrast to N-heterocyclic carbene complexes, metal complexes of N-heterocyclic silylenes are a relatively unexplored. One potential difference is the increased electrophilicity of silylenes and the possibility that this might lead to cooperative reactivity with a metal center in activating a small molecule substrate. Here we report progress towards this goal in the synthesis and characterization of an unusual asymmetric nickel (0) silylene dimer and its reactivity with a range of small molecules to afford nickel(I) silyl dimers via E–H bond activation (E = H, O).

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Carbon dioxide reduction to formate by a multi-functional, redox-active borane

Jordan Taylor, *jt_wayne@Hotmail.com*, Alexander McSkimming, Hill Harman. Chemistry, University of California-Riverside, Riverside, California, United States

The capture of CO₂ and its conversion into fuels is a promising strategy for remediating unprecedented atmospheric CO₂ levels. Driven by a solar-derived electrical current, such a process would constitute artificial photosynthesis and would be a carbon neutral source of energy. For this approach to be feasible, electrocatalysts for the efficient combination of CO₂ with H⁺ and e⁻ must be developed. Owing to their redox flexibility, transition metals have been long been targeted in this role. Recently, interest has re-emerged in the reaction of CO₂ with boranes and silanes, in some cases catalyzed by non-metal systems. While potentially useful, the stoichiometric reaction of CO₂ with these hydridic reagents is not directly relevant to the electrochemical conversion of CO₂ into energy dense products. For CO₂ reduction by main group hydrides to be applicable to renewable fuels synthesis, these main group hydrides must be generated catalytically from H⁺ and e⁻. The p-block elements generally do not possess the redox flexibility of the transition metals, rendering this a substantial challenge. We have developed a gold-stabilized 9,10-diboraanthracene system capable of accepting H⁺ and e⁻ to give a reactive borohydride/borane species capable of reducing CO₂ to formate. Formate liberation regenerates the initial complex, closing a synthetic cycle for CO₂ reduction to formate mediated by a multifunctional, redox-active borane.

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Automatic classification of surface-bound bacteria cell motion by image analysis and tracking algorithms

Simon Shen, *sshens8@gmail.com*. Center for Bioelectronics and Biosensors, Arizona State University, Tempe, Arizona, United States

Immobilization of live bacteria cell to surfaces is a prerequisite for micro- and nano-level studies of fundamental cellular processes using powerful imaging techniques such as atomic force microscopy (AFM) and surface plasmon resonance (SPR). Quantification of bacteria cell attachment to surfaces is also important in the study of biofilm formation with numerous applications. Common to these studies is the need for an automatic method for the assessment of how bacteria cells behave when they are attached to the surface. In this study, we present a cell motion pattern classification method based on single-cell motion characterization system (SiCMoCS). When used on bright field transmitted image sequences of E. coli O157:H7 attached to a glass surface by APTES, we were able to automatically track and classify the motion of about 700 cells per image sequence individually and simultaneously with computations completed in a matter of minutes based on 10 seconds of imaging data. This is a significant improvement in throughput over the current approach, which is mostly performed manually.

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Reactions of a germylene and stannylene with water and methanol: Evidence of sigma-bond metathesis in the formation of {Sn(μ -OR)}₂

Jeremy Erickson, *jd.eric.ph@gmail.com*. Chemistry, University of California, Davis, Davis, California, United States

It has been previously assumed that the arene elimination observed during the reaction of $\text{Sn}(\text{Ar})_2$ with Bronsted acids was a result of oxidative insertion and subsequent reductive elimination of the terphenyl ligand as the arene H. However, when we reacted $\text{E}(\text{Ar})_2$ ($\text{E}=\text{Sn}, \text{Ge}$) with H_2O and MeOH to form $\{\text{Sn}(\mu\text{-OR})\}_2$ and $(\text{Ar})_2\text{Ge}(\text{H})\text{OR}$ ($\text{R}=\text{H}, \text{Me}$) and studied the mechanism of their reaction via DFT we found two reaction pathways: a hydrogen-bonded arrangement of two Bronsted acids to yield a formal oxidative insertion to yield $(\text{Ar})_2\text{E}(\text{H})\text{OR}$ and a 4-membered sigma-bond metathesis to afford $\{\text{E}(\mu\text{-OR})\}_2$ and H . The presence of an available p-orbital on the sp^2 hybridized Sn-adjacent carbon and the stability of the inert electron pair were found to facilitate the lower energy of the sigma-metathesis route leading to the formation of $\{\text{Sn}(\mu\text{-OR})\}_2$.