

For Immediate Release

Twelve **College of Charleston Chemistry / Biochemistry majors** and five **faculty members** **presenting** the results of their research at the South Eastern Regional Meeting of the American Chemical Society in San Juan, Puerto Rico from October 21st, 2009 through October 24th, 2009. Each of the students conducted their research over the past academic year and summer, mentored by a faculty member and supported by grants from various agencies, including the Howard Hughes Medical Institute, the Research Corporation, the National Institutes of Health SC INBRE program, and the College of Charleston Undergraduate Research and Creative Activities program. There are over 760 presentations at the meeting, by authors from across the southeastern United States and beyond.

Effect of C- α and N-Methyl Methylation On the Conformational Structure(s) Adopted by Gas-Phase Peptides

Thursday, 22 October 2009 (Poster)

Exhibit Hall C (Puerto Rico Convention Center)

Katie P. Anderson, **Richard J. Lavrich**, Department of Chemistry and Biochemistry, College of Charleston, Charleston, SC

Much attention has been focused recently on the potential of peptidomimetics, slightly modified natural peptides, in overcoming the lack of selectivity demonstrated by peptides. Modifications are aimed at restricting the conformation adopted by the modified peptide in an effort to minimize binding to non-target receptors enhancing activity at the desired receptor.

One such modification involves replacement of protons on alpha carbons and amide nitrogens with methyl groups. The incorporation of of alkyl groups at these positions introduces a degree of steric hinderance which is postulated to prevent the formation of more compact secondary structures in favor of more extended forms.

We have recently synthesized peptidomimetics of alanine dipeptide which incorporate the above modifications.



N-Acetyl-Aib-N'-Methylamide

N-Acetyl-Aib-N'-Methyl-Methylamide

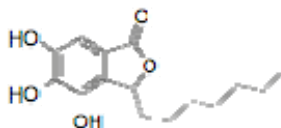
SAR Side Chain Derivatives of the Antibiotic Cytosporone E

Friday, 23 October 2009: 1:45 PM

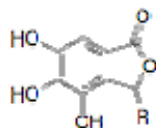
103-B (Puerto Rico Convention Center)

[Erin M. Cartwright](#), [Justin K. Wyatt](#), Department of Chemistry and Biochemistry, College of Charleston, Charleston, SC

The novel antibiotic cytosporone E, a metabolite of the endophytic fungus *Cytospora sp.*, shows weak antibacterial activity towards Gram-positive bacteria and is inactive against Gram-negative bacteria. Thus, to find a more potent antibiotic, we synthesized multiple derivatives of cytosporone E with changes in the side chain of the lactone. These derivatives were synthesized from *N,N*-diethyl-3,4,5-trimethoxybenzamide via *ortho*-alkylation of the aromatic ring with the appropriate aldehydes, followed by hydrolysis to afford the lactones. Finally, the methoxy groups were removed giving the corresponding cytosporone E derivatives. These synthetic derivatives will be assayed for a structure activity relationship (SAR) study using the Kirby-Bauer method; a few of our derivatives have been assayed. This is performed by aseptically placing filter paper disks containing each derivative onto heavily-inoculated plates of agar. The plates are then incubated overnight at 37 °C affording the antibacterial results. Future derivatives will be synthesized using the findings of this SAR study to increase potency.



Cytosporone E



R = alkyl or aryl groups

Pharmaceutical Analysis in the Quant Lab: The Potency and Degradation of Aspirin

Thursday, 22 October 2009: 11:00 AM

204 (Puerto Rico Convention Center)

[Wendy Clevenger Cory](#), Department of Chemistry and Biochemistry, College of Charleston, Charleston, SC

Pharmaceutical analysis is an important area of drug development research that appeals to undergraduate students and is well-suited to the quantitative analysis laboratory. An experiment was developed for the HPLC analysis of over-the-counter aspirin tablets, based on the assay method found in the United States Pharmacopoeia (USP) currently used in the pharmaceutical industry. Students are directed to determine the mg of aspirin in their sample after HPLC analysis and comparison to a standard. The degradation of aspirin to salicylic acid and acetic acid is investigated by comparison to a salicylic acid standard. Whether or not the tablet meets USP and FDA requirements for potency is then determined. There are a variety of aspirin tablets available at different dosage levels

(some containing other ingredients in addition to the aspirin), providing a variety of "unknown" samples. The experimental conditions and sample results will be discussed, as well as some variations on the chromatography and aspirin degradation which can be used to develop the procedure into a more advanced experiment.

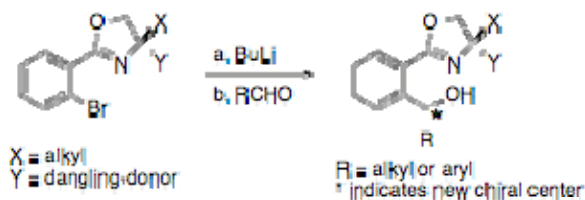
Novel Chiral Oxazolines Utilized to Control the Diastereoselectivity of the Meyers *Ortho*-Alkylation of Aromatic Oxazolines

Wednesday, 21 October 2009 (Poster)

Exhibit Hall C (Puerto Rico Convention Center)

[James A. Dean](#), [Courtney Drew](#), [Greg Goschy](#), [Justin K. Wyatt](#), Department of Chemistry and Biochemistry, College of Charleston, Charleston, SC

The Meyers *ortho*-alkylation of achiral aromatic oxazolines has been well studied and utilized. However, the use of chiral aromatic oxazolines to induce chirality in the alkylated product has not been well explored. The development of a new chiral aromatic oxazoline has been developed with the potential to control the diastereoselectivity of alkylating prochiral electrophiles (i.e. aldehydes). Control is envisioned to arise from a steric effect of an alkyl group and chelation effect of a pendant "dangling-donor" of the chiral oxazoline. The oxazoline is derived from an unnatural chiral α,α -disubstituted amino acid, which is synthesized from the naturally occurring amino acid L-phenylalanine. The synthesis and the attributes of the new chiral oxazoline will be discussed.



Results obtained for the preferred conformation(s) of the modified peptide from computational calculations will be presented. Forced Degradation Studies of Cetirizine, Loratidine and Naproxen by HPLC

Wednesday, 21 October 2009 (Poster)

Exhibit Hall C (Puerto Rico Convention Center)

[Andrea DeSantis](#), [Wendy Clevenger Cory](#), Department of Chemistry and Biochemistry, College of Charleston, Charleston, SC

In this study, over-the counter medications Zyrtec, Claritin, Aleve, and their generic counterparts were analyzed for degradation when stored at conditions other than those recommended by the manufacturer. When degradation occurs, the potency of the medication decreases while at the same time degradation products are being formed. These degradation products are variants on the drug molecule that can have a different efficacy and safety profile, as well as possible toxicity. Consumers often do not follow the storage procedures outlined on medication packaging, and therefore may be putting themselves at risk. This study investigated how storing the samples at higher temperature, in different storage containers, and with other medications impacts the stability of the drug. One part of this study involved sending samples to 10 different regions across the country and having participants store the samples in their glove compartments during the summer of 2009. Samples were returned and analyzed to determine the degradation that occurred under these conditions. HPLC was used to analyze the degraded samples and further analysis and identification of the present impurities was performed with the LC-MS.

Determination of the Secondary Structure Adopted by the Depsipeptide Analogue of Alanine Dipeptide through Torsion-Rotation Interactions in Microwave Spectra

Thursday, 22 October 2009 (Poster)

Exhibit Hall C (Puerto Rico Convention Center)

[Emily A. Devol](#), [Richard J. Lavrich](#), Department of Chemistry and Biochemistry, College of Charleston, Charleston, SC

We report progress made on the determination of the secondary structure adopted by N-Acetyl-Lactyl-N'-Methylamide, the depsipeptide analogue of alanine dipeptide by analysis of torsion-rotation interactions in microwave spectra. Depsipeptides are formed when interior amide linkages of natural peptides are replaced with esters. The parent dipeptide and the corresponding depsipeptide are shown below.



A change in preferred conformation was observed for the depsipeptide analogue of alanine dipeptide. The parent dipeptide was found to have only one low energy conformation, referred to as C_7 , in which a seven membered ring forms when the amide proton forms and intramolecular hydrogen bond with the carbonyl oxygen of the N-acetyl. Formation of the depsipeptide by substitution of the amide linkage with an ester

favors a C₅ arrangement in which the amide proton hydrogen bonds with the ester oxygen. The amide-to-ester modification of peptide backbone removes the H-bond donor (N-H) by replacing it with an O and weakens the H-bond acceptor (C=O) of peptides and proteins because the carbonyl of an ester group is a weaker H-bond acceptor than that of an amide group.

Development of a Stability Indicating Assay for Ibuprofen Tablets Using HPLC

Saturday, 24 October 2009

104-A (Puerto Rico Convention Center)

[Corbyn Harris](#), [Wendy Clevenger Cory](#), Department of Chemistry and Biochemistry, College of Charleston, Charleston, SC

Ibuprofen, 2-(4-isobutylphenyl)propionic acid, is a non-steroidal anti-inflammatory drug used worldwide for pain relief. In this research, a new HPLC stability indicating assay for ibuprofen tablets was developed to provide accurate detection of the potency as well as quantifying the products of ibuprofen degradation. This method was developed with ibuprofen tablets that had been subjected to forced degradation (high heat, humidity, light) in order to accurately predict the drug-related impurities that might form in a tablet during its shelf life. The method uses no acetonitrile in the mobile phase and produces a lower volume of waste than the existing United States Pharmacopoeia (USP) ibuprofen assay method. A factorial experimental design was used to optimize the HPLC conditions. The method was validated according to FDA and International Conference on Harmonization (ICH) guidance documents.

Antibiotic Cytosporone E: Analog Synthesis Via Selective Deletion of Oxygen Atoms and the Incorporation of Nitrogen

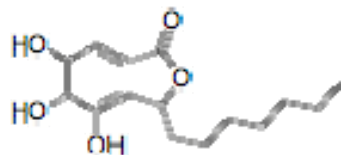
Friday, 23 October 2009: 10:15 AM

103-B (Puerto Rico Convention Center)

[Thomas L. Jenkins](#), [Justin K. Wyatt](#), Department of Chemistry and Biochemistry, College of Charleston, Charleston, SC

Cytosporone E is a biologically active, but weak, antibiotic consisting of a fused trihydroxybenzene and a 5-membered lactone (i.e., a phthalide backbone) with a seven-carbon side chain. We are using this compound as a template from which we hope to synthesize more potent derivatives by changing features of its structure. Specifically, we have focused on two alterations: the first is utilizing deletion chemistry to determine which of the oxygen atoms are needed for activity; the second is the incorporation of nitrogen into different sites on the parent antibiotic. Nitrogen will allow us to add new

substituent groups, change the overall shape and alter the functionality of the molecule. These derivatives of the parent antibiotic will be tested on both gram-positive and gram-negative bacteria in order to discern the relationship between cytosporone E's structure and its biological activity. This structure activity relationship study will provide information for developing more effective analogues of the parent antibiotic, which is needed with the ever-increasing number of antibiotic-resistant bacteria.



Cytosporone E

Effect of Dehydro Residues On the Conformational Structure Adopted by Gas-Phase Peptides

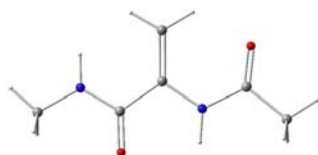
Thursday, 22 October 2009 (Poster)

Exhibit Hall C (Puerto Rico Convention Center)

[Meredith Kaywood](#), [Richard J. Lavrich](#), Department of Chemistry and Biochemistry, College of Charleston, Charleston, SC

Much attention has been focused recently on the potential of peptidomimetics, slightly modified natural peptides, in overcoming the lack of selectivity demonstrated by peptides. Modifications are aimed at restricting the conformation adopted by the modified peptide in an effort to minimize binding to non-target receptors enhancing activity at the desired receptor.

One such modification involves the incorporation of dehydro amino acids into the peptide.



The conformational flexibility of peptidomimetics containing dehydro residues is expected to be restricted due to the double bond between the C^a and C^β atoms. The presence of the sp² hybridized carbon atom, the extended conjugation of the pi system,

and the restriction of the side chain due to the double bond are special features which make the system an attractive target for conformational study.

We have recently synthesized the dehydro analogue of alanine didpeptide. Results obtained for the preferred conformation(s) of the modified peptide from computational calculations will be presented.

EDXRF Analysis of Old Roman Coins: A Radiogenic Connection

Thursday, 22 October 2009: 10:40 AM
204 (Puerto Rico Convention Center)

W. Frank Kinard, Department of Chemistry and Biochemistry, College of Charleston, Charleston, SC

We have analyzed a random set of old Roman coins by energy dispersive x-ray fluorescence spectrometry. The copper content of the coins ranged from 98% to 30% while the other major constituent was lead, ranging from almost 60% to less than 1%. Many of the impurities measured in the coins are elements such as arsenic, antimony, zinc, and silver that are associated with sulfur based minerals. The production of bronze coins also introduces some of these elements in the minting process. One interesting result of the analysis is that we found trace amounts of thorium (<10 parts per thousand) and uranium (<250 parts per million) which had concentrations that scaled with the lead content of the coins. This emphasizes the fact that the lead comes from the end product of the natural radioactive decay series of thorium and uranium. This data is used in a senior analytical course to ask students to look for bivariate relationships in analytical data. It is also an important topic in introducing students to non-destructive methods of analysis.

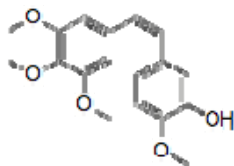
Development of a Novel Anticancer Agent Modeling Combretastatin A-4 Using QSAR

Saturday, 24 October 2009 (Poster)
104-A (Puerto Rico Convention Center)

Jillian Kyzer, **Taylor McAneney**, **Justin K. Wyatt**, Department of Chemistry and Biochemistry, College of Charleston, Charleston, SC

The anticancer drug combretastatin A-4 (CA-4) binds specifically to the colchicine-binding site in the formation of microtubulin. This binding restricts the flexibility of the protein, which prevents cell division at the end of mitosis. Because CA-4 stops cell division, it is most effective against cells that divide rapidly, like cancer cells; however, it does stop normal cells from dividing as well. We are designing and synthesizing CA-4 analogs that are potent against tumors but have a lower level of cytotoxicity. To

determine which derivatives were to be synthesized docking experiments of the colchicine-binding site were conducted compared to colchicine. This was not an effective tool. Currently a quantitative structure-activity relationship (QSAR) study is being conducted. This is where other derivatives of CA-4 that have already been synthesized have numerical values for their binding capability and potency. These numbers will be entered into the QSAR equation to find the "hot spots" necessary for activity. This will afford a 3D-image based on these "hot spots" from other compounds. We will then see if our structures we are currently synthesizing fit into the model based on the QSAR, and also design others based on the results.



Combretastatin A-4

Secondary Structure of Peptidomimetics Thru Torsion-Rotation Interactions in Rotational Spectra

Thursday, 22 October 2009: 4:35 PM

208-A (Puerto Rico Convention Center)

Richard Lavrich, Department of Chemistry and Biochemistry, College of Charleston, Charleston, SC

A systematic investigation on the effect that targeted modifications made to the side chains and/or backbones of natural peptides have on the three dimensional shapes they can adopt will be presented. These modified peptides, know collectively as peptidomimetics, have attracted great interest as potential candidates to overcome the limitations of natural peptides as beneficial drugs, the most significant of which is the ability of natural peptides to adopt multiple conformations. The large number of conformations of natural peptides greatly reduces their selectivity in biochemical processes as they have the ability to react with multiple receptors. It is believed that the targeted modifications made in the formation of the peptidomimetics serve to restrict the ability to form particular conformations potentially allowing greater control of its biochemical function.

High-resolution microwave spectroscopy has been used to probe the stable secondary structures adopted by small gas-phase peptides and their corresponding peptidomimetics. The current study utilizes the recently developed rotor-axis angle formulism which exploits torsion-rotation interactions in microwave spectra. Analysis of the spectral splitting caused by the coupling of torsional motions of low barrier methyl tops with overall rotation of the peptide allows a highly precise determination of the angles these

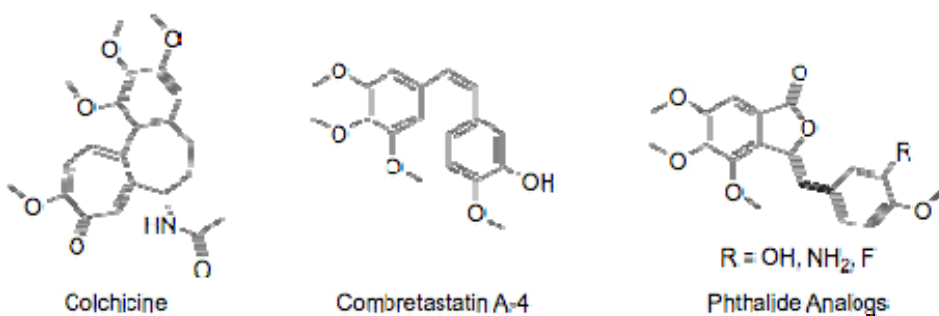
rotating methyl groups make with the principle axis frame of the peptide. These angles have been shown to be extremely sensitive to small changes in torsional angles along the peptide backbone. As a result, they can be used as sensitive probes of conformation and provide an unambiguous determination of the preferred secondary structure adopted by the peptide.

Development of a Novel Anticancer Agent Modeling Combretastatin A-4

Thursday, 22 October 2009: 3:45 PM
207 (Puerto Rico Convention Center)

[Taylor McAnaney](#), [Jillian Kyzer](#), Matthew D. Brooker, **Justin K. Wyatt**, Department of Chemistry and Biochemistry, College of Charleston, Charleston, SC

Combretastatin A-4 is a naturally occurring anti-tumor agent that binds specifically to the colchicine-binding site on tubulin, a key protein in the process of cell division. Both molecules (colchicine and combretastatin A-4) cause a decrease in elasticity, therefore preventing cell division. Although combretastatin A-4 is an effective anti-tumor agent, it is very cytotoxic, making it a less than ideal drug choice. The goal of this research project is to synthesize analogs of combretastatin A-4 that are less cytotoxic, while still maintaining potency against cancer. The synthesized analogs will differ from the structure of combretastatin A-4 by the addition of a lactone ring, which is attached to the double bond (making a phthalide derivative). This lactone ring is significant because, as a five-membered ring, it introduces ring-strain into the system as well straining the double bond, which alters the conformation of the molecule. Starting with a series of substituted 4-anisaldehydes, a sequence of reactions will be performed in order to obtain the derivatives.



Computation Study of Ansa-Beryllocenes

Wednesday, 21 October 2009: 4:00 PM

104-A (Puerto Rico Convention Center)

Jason S. Overby, Department of Chemistry and Biochemistry, College of Charleston, Charleston, SC

Bis(cyclopentadienyl)beryllium and its various substituted derivatives constitute an interesting class of metallocenes due to unusual patterns in bonding and reactivity. The unknown ansa-metallocenes of beryllium constitute an intriguing class of molecules due to the dramatic effects a bridging unit may have on the structure. This study will provide some theoretical insight into the bonding and electronic structure of ansa-beryllocenes.

Structural Characterization of Copper-Selenium Complexes Relevant to the Antioxidant Activity of Selenium

Saturday, 24 October 2009 (Poster)

104-A (Puerto Rico Convention Center)

Pamela Riggs-Gelasco, Department of Chemistry and Biochemistry, College of Charleston, Charleston, SC

Craig A. Bayse, Department of Chemistry and Biochemistry, Old Dominion University, Norfolk, VA

Julia Brumaghim, Department of Chemistry, Clemson University, Clemson, SC

Oxidative stress resulting from reactive oxygen species (ROS) has been implicated in a wide array of ailments, including heart disease, cancer, neurodegenerative diseases and diabetes. While the antioxidant properties of selenium complexes are well celebrated, less is known about the molecular mechanism of the protective effect. One possibility is that selenium compounds such as selenomethionine and selenomethylcysteine coordinate copper and iron ions and prevent the formation of ROS from the Fenton-type chemistry that can occur in the presence of these metal ions. Indeed, metal complexation of these selenium-substituted amino acids was observed to reduce hydroxyl radical mediated damage of plasmid DNA. We have used Cu and Se x-ray absorption spectroscopy to ascertain the solution structure of copper complexed to selenomethionine and selenomethylcysteine. The metrical details of the three coordinate Cu(I) complexes will be reported here. The experimental results will also be compared to computational models.

Effect of Solvent On Molecular Conformation: Microwave Spectra and Structures of 2-Aminoethanol and 3-Aminopropanol Water Complexes

Thursday, 22 October 2009 (Poster)

Exhibit Hall C (Puerto Rico Convention Center)

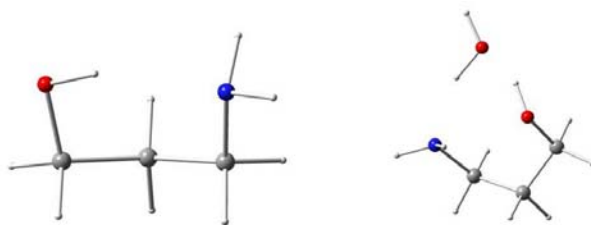
[Daniel G. Smith](#), [Richard J. Lavrich](#), Department of Chemistry and Biochemistry, College of Charleston, Charleston, SC

When present, the formation of intramolecular hydrogen bonds serves to stabilize the molecular conformation(s) adopted by gas phase monomers. Complexation with water introduces the potential formation of intermolecular hydrogen bonds as well. In general, the intramolecular hydrogen bonding network established in the monomer is preserved as the formation of intermolecular hydrogen bonds with water are established.

Few examples exist of the disruption of a monomers intramolecular hydrogen bonding network upon complexation. Recently, we reported one such case, the 1:1 complex of 2-aminoethanol (2AE) and water. Conformation of the 2AE monomer is stabilized by the formation of a five membered ring that results from the intramolecular hydrogen bond that forms between the alcohol proton and the amino nitrogen.

Based on structural analysis from high resolution microwave spectra, an increase in the O-C-C-N dihedral angle of the 2AE monomer was observed upon complexation with water. During formation of the 1:1 complex, the monomer's intramolecular hydrogen bond was sacrificed in order to accomodate insertion of the water molecule and the formation of intermolecular hydrogen bonds.

The current study investigates the 1:1 complex of 3-aminopropanol (3AP) and water.



Intramolecular hydrogen bonding in the 3AP monomer forms a six-membered ring which has been shown both computationally and experimentally to be stronger than the five-membered ring formed in 2AE. We seek to determine whether the increased strength of the intramolecular hydrogen bonding network in 3AP will be sufficient to resist the changes observed during complexation of 2AE with water.

The Analysis of Glucosinolates Using HILIC-ESI-MS

Wednesday, 21 October 2009 (Poster)

Exhibit Hall C (Puerto Rico Convention Center)

[Maggie Thomasson](#), [Wendy Clevenger Cory](#), Department of Chemistry and Biochemistry, College of Charleston, Charleston, SC

In this research, a method for the measurement of glucosinolates in plants of the *Brassicaceae* family was developed using HILIC-ESI-MS. Glucosinolates are compounds found in a variety of plants which offer them some protection against herbivorous predators. A glucosinolate found in broccoli, glucoraphanin, has been observed to have potentially therapeutic properties for humans when eaten, including protection against stomach cancer. The separation of glucosinolates - particularly glucoraphanin - by traditional reversed phase (RP) HPLC is difficult due to their polar nature. Our research involves the use of Hydrophilic Interaction Liquid Chromatography (HILIC), which is well-suited for the analysis of glucosinolates. Additionally, it requires a highly organic mobile phase for the retention of these polar analytes, which makes it compatible with ESI-MS. This presentation will include preliminary results on the development of this method as well as data on a variety of brassicaceous seeds, which are rich in glucosinolates.