Department of Chemistry and Biochemistry

15th Annual Departmental Symposium and Poster Session in conjunction with the Petersheim Academic Exposition

April 12, 2011
5:30-9:00 PM

Science and Technology Center
Seton Hall University
South Orange, NJ 07079

5:45 PM – The Helen Lerner Amphitheater

Final Presentation of Doctoral Research

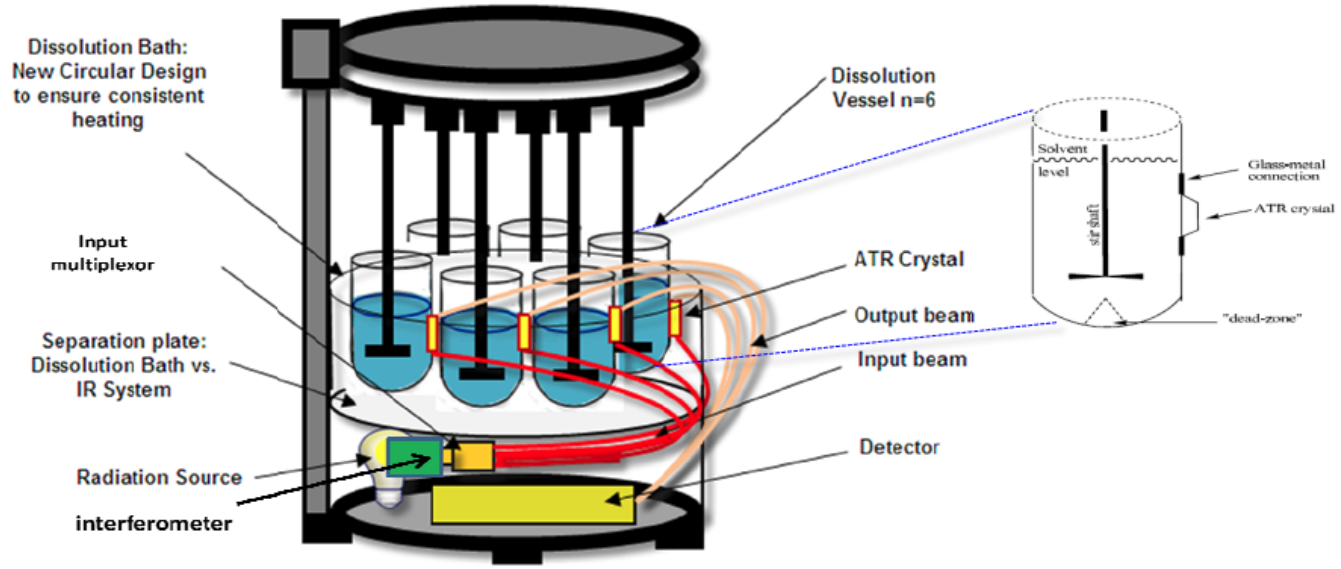
Abe Kassis

Abstract

Attenuated Total Reflection Infrared Spectroscopy (ATR-IR) as an *in-situ* Technique for Dissolution Science Studies

In this presentation I will present our studies of fundamental dissolution reactions and analysis by *in-situ* IR spectroscopy. Dissolution studies are critical tests for measuring the performance of a drug product. We have developed a novel technique using *in-situ* ATR-IR spectroscopy to monitor dissolutions of pharmaceutical drug products. The accuracy of this technique is ±3% relative to HPLC. Several OTC active drugs (i.e. acetaminophen, acetylsalicylic acid, salicylic acid, etc.) were tested during the research. This novel approach also gives the research laboratory the capability of analyzing multiple components in a single tablet. For example, individual components of Excedrin tablets were easily distinguished. Furthermore, the system has the capability of monitoring the drug transformations during dissolution. For instance, we monitored the hydrolysis of aspirin to salicylic acid using this technique. The ATR-IR system was found to have good sensitivity and can analyze samples as low as 0.03 mg/ml. This technique allows deeper insight into spectroscopy, reaction analysis, kinetics and dynamics of the dissolution studies.

A. Kassis, V. M. Bhawtankar, J. R. Sowa, Attenuated total reflection infrared spectroscopy (ATR-IR) as an in-situ technique for dissolution studies, Journal of Pharmaceutical and Biomedical Analysis (**2010**), 53, 269–273



Posters of current research of the students of Chemistry and Biochemistry

Jubilee Hall Atrium, Fourth Floor, Jubilee Hall, Seton Hall University
Tuesday April 12, 2011
7:00-9:00 PM

List of Faculty Mentors
Abstracts are organized alphabetically by the last name of the research mentor

Professor Alexander Fadeev

Preparation of silica core-shell particles with ordered mesoporous thin films.

Kyle W. Eckenroad and Alexander Y. Fadeev

In this work, we developed preparation methods for particles that consisted of a solid silica core and a mesoporous silica shell, core-shell particles. These particles are of interest for applications in adsorption, separations, and chromatography. We prepared core-shell particles using a polymer-templated sol-gel synthesis. A series of SBA-15 thin films were prepared through the condensation of tetrethoxysilane (TEOS) in the presence of Pluronic 123 and nonporous silica seed (0.5 um). The isolated materials have been characterized by nitrogen adsorption and electron microscopy. The preliminary data demonstrated the formation of core-shell particles. The effects silica seeds to TEOS ratio, the reaction temperature, and pH have been investigated. It was found that the reagent ratio had a significant effect on the thin film formation, reaching a maximum surface area at 15:85 seed:TEOS. Controlling the pH at 2 also caused a significant impact on thin film formation.

Chiral Mesoporous Silica using Pseudomorphic Synthesis

Gabriel C. Graffius and Alexander Y. Fadeev

Chiral mesoporous silicas (CMS), i.e. porous silicas with chirality present on the surface and/or in the pore morphology, form an interesting class of materials with prominent applications in enantioselective separations, catalysis, synthesis, etc. The focus of our research is to develop methods of preparation of the CMS using chiral templates and structure directing agents. Specifically, we are focused on the pseudomorphic transition method [1], a technique which involves modification of the pore morphology of the previously formed silica particles under the conditions facilitating solubility of silica (high pH and temperature) [2] and in the presence of structure directing agents.

The preliminary research has involved the synthesizing and using the chiral anionic surfactant, N-miristoyl-L-alanine [3], for pseudomorphic synthesis with the main goal of the understanding the role of the reaction conditions, such as the pH and temperature range for optimization of the synthesis. Further in the project, we will use other chiral templates such as Polylysine, Dextrose, Chitosan and Sodium Deoxytaurocholate. Nitrogen Adsorption data indicates that we have had some success in changing the pore morphology of silica particles under these conditions. These materials will be evaluated for enantioselective separations and chromatography.

1. Fajula, F. et al. Morphological Control of MCM-41 by Pseudomorphic Synthesis. Agnew. Chem. Int. Ed, 2002, 41, 2590-2592.
2. Iler, R. K. The Chemistry of Silica; John Wiley & Sons: New York, 1979.
3. Yokoi, T. et al. Synthesis of chiral mesoporous silica by using chiral anionic surfactants. Microporous and Mesoporous Materials, 2007, 103, 20-28.

Synthesis and Characterization of Fluorinated Mesoporous Silicas.

Karthik Jayaraman and Alexander Y. Fadeev

Fluorinated mesoporous silicas have attractive features for engineering of superhydrophobic and superoleophobic surfaces for wetting and adhesion control, adsorption and separations, and for several other applications in materials science and technology. In this work, we focused on the preparation of fluorinated silicas from ordered SBA-15 mesoporous silicas with well-defined uniform mesopores from the range of ~5-7 nm. The SBA-15 silicas prepared were functionalized through the covalent attachment of organosilanes with perfluorinated alkyl groups of various sizes (-CF3, -C4F9, - C6F13, -C8F17). The materials obtained were characterized using Electron Microscopy and Thermo Gravimetric Analysis. The surface area, pore size and pore volumes were determined using the Nitrogen adsorption/desorption method. The effect of the size of the fluoroalkyl chain and their grafting density on the extent of surface lyophobization and adsorption energy is discussed.

Characterization of Drug Polymorphs Encapsulated in Mesoporous Silicas

Alvin Persad and Alexander Y. Fadeev

Polymorphism has always presented an interesting phenomenon to crystallographers. Studies have been completed in the macroscopic and nanoscale realm to observe the different chemical and physical properties. Researchers have published information about polymorphism existing in the nanoscale but not in the macroscopic scale.

The nano-confinement provides stabilization for the growth of metastable polymorphs which would not be accomplished in the bulk. In the confined environment thermodynamic properties can be determined for these metastable polymorphs. This can be applied to the pharmaceutical industry, producing drugs that would be more selective, efficacious and viable at reaching its target.

In this research the following pharmaceutical drugs: Acetaminophen, Ibuprofen (IBU), carbamazepine (CBZ) were confined in the mesopores of bare and modified silicas (Pore size ~5-10 nm). The encapsulation of the drugs was achieved via saturation of pores with drug's solutions followed by evaporation of solvents. The encapsulated drugs have been characterized using thermal gravimetric analysis, differential scanning calorimetry, FTIR, and solubility tests.

The results obtained suggested formation of *new polymorphs* due to pore encapsulation. These *new polymorphs* will be investigated further to confirm its crystalline state and the physicochemical properties.

Professor James Hanson

Synthesis of meso-Tetrapyridylporphyrin Derivatives for DNA Quadraplex Binding

Mohammed R. Elshaer, Eva Morozko and James E. Hanson

Our strategy for the design of a quadruplex DNA-directed drug has been to attach a small-molecule quadruplex ligand with a polymer that possessesstrong affinity towards nucleic acids. In this work, we have synthesized and characterized water soluble *meso*-substitiuted cationic pyridyl-porphines bearing various functional groups in an effort to prepare porphyrins that can be readily conjugated to our polymers.5,10,15,20 tetra-4-pyridylpoprphine was derivatized at the nitrogen atom of the pyridyl group to formthe quaternary pyridinum salt.These derivatives possess allyl, hydroxyl, bromo, and mesylate functionality which allows for both the preparation of tentacle porphyrins as in the case of the allyl derivative that can be employed as an initiation site for polymerization or the formation of a mesh-like material where the porphyrin mayact as a cross-linking agent between adjacent polymer chains.

Generating Water Soluble Molecularly Imprinted Nanoparticles with Affinities for Specific Nucleic Acid Sequences

Mohammed R. Elshaer, Mira Yazigi, Evelyn Brito and James E. Hanson

Molecular recognition is vital to many biochemical processes and is at the heart of promising bio-medically related technologies. Molecular imprinting has a long history as a successful method for generating molecular recognition. However, its utility has been limited since traditional molecularly imprinted polymers are insoluble. Our focus is directed towards developing a method for generating soluble, non-charged or weakly chargedimprinted polymer-small moleculeconjugated nanoparticles possessing affinities for specific nucleic acid sequences or structures. We have screened a number of polymers in an effort to identify viable candidates with nucleic acid recognition capabilities. The affinity of these polymers for nucleic acids has been evaluated by agarose and polyacrylamide gel electrophoresis, UV-vis, and circular dichroism studies. The best candidate polymers identified will be syntheticallyconjugatedwith *meso*-tetrapyridylporphine derivatives that have been prepared in our lab and also evaluated for their DNA binding properties. Development of cross-linking strategies will follow in our attempt to form water soluble, molecularly imprinted nanoparticles.

Treatment of PPS from 1,3,5-trichlorobenzene with Excess Lithium Sulfide

Kristen Kingdon and James E. Hanson

I have been working for the past few years on hyperbranched poly(phenylene sulfide) (PPS) and related polymers prepared from halogenated thiophenols or from trihaloaromatics with lithium sulfide. During our studies last year, it was discovered that adding an excess of lithium sulfide at the end of certain PPS polymerizations will cause the replacement of the remaining Cl groups with sulfides. This is important because the end product is a quite different polymer: it is softer (at times tacky), water soluble, and shows some flame resistance properties. These reactions are generally done with PPS or

Poly(phenylene sulfide-phenylene disulfide) which can react at different levels, and can cleave at various points allowing for a mixture of hyperbranched with linear polymers. In this research, I will be testing various polymers with lithium sulfide in an attempt to make them flame resistant. My first attempt is with a 1:1 ratio of 1,3,5 trichlorobenzene and lithium sulfide in NMP. The reaction is heated to 150 degrees Celsius and heated for 6-8 hours, after the 6-8 hour period an excess of lithium sulfide is added in order to replace the terminal Cl. This will be precipitated by mixing it with 6M HCl then filtered. The solubility of each product is tested in various products such as; aqueous base THF, NMP, and CH_2Cl_2. It will also be tested by infrared spectroscopy (IR), differential scanning calorimetry (DSC) and thermogravimetric analysis (TGA), and will be reduced with excess [H] to see if the product can be totally consumed. After being reduced an IR will be taken which will show the presence of any SH peaks.

Recent Advances in the Elucidation of Elasmobranch-Repelling Semiochemicals

Eric M. Stroud, James E. Hanson and Nicholas H. Snow

Recent findings in the elucidation of elasmobranch-repelling semiochemicals indicate that the repellent is a binary signal. Semiochemicals extracted from putrefied shark carcasses were fractionated into acidic, basic, and neutral components. Following pH adjustment, samples were extracted for 1 hour using a continuous diethyl ether extraction apparatus followed by hexane extraction and retained. Aqueous phases were reconstituted back to their original pHs. Basic fractions were further refined using fractional distillation at 40ºC under reduced atmosphere with a double dry-ice trap to strip and collect volatile components with 99.7% recovery. A 150mL dose of each fraction was presented to competitively feeding unconditioned *Carcharinus perezii* and *C. acronotus* using either a weighed aerosol can or a pressurized syringe. Testing was performed at the Triangle Rocks, South Bimini, under a Bahamian 2010-2011 research permit. Sharks were stimulated to feed using locally caught fish. Experimental controls were established using a water and denatured ethanol mixture.

We report that experimental controls, the neutral semiochemical fraction, volatile bases collected from fractional distillation, and a neutralized (pH 7.0) semiochemical sample did not disturb feeding activity. The complete basic fraction and the nonvolatile basic fraction both exhibited temporary repellency, with sharks initially scattering then resuming feeding after 2 minutes. Combining the complete basic and complete acidic fractions achieved the same repellent efficacy as the raw semiochemical, with all feeding behavior halted for more than 10 minutes. We conclude that a primary chemical signal is comprised of a nonvolatile base, and a second synergistic signal is acidic. Although previous tonic immobility studies with juvenile *Negaprion brevirostris* showed repellent responses to individual short chain primary amines and individual short-chain organic acids at dosages of 100uL or less to the nares, these responses were likely due to irritation of the lamellae rather than induction of a “schreckreaction” or flight signal.

Professor Yuri Kazakevich

Excess adsorption isotherm

Susanne Buntz and Yuri Kazakevich

Analyte retention process in high pressure liquid chromatography has been studied since the 1960's. Until today there have been many theories about the mechanism of analyte retention and separation in HPLC. So far it is possible to address different theories in three different categories; analyte partitioning, analyte adsorption on adsorbent surface and mobile phase adsorption on the stationary phase followed by analyte partitioning in the adsorbed layer.

The latter hypothesis will be closer investigated on reverse phase HPLC adsorbents of various commercial available C18 columns. One approach to examine this model is by applying the excess adsorption isotherms of binary aqueous/organic mobile phase on the surface of reversed phase HPLC adsorbents to examine analyte retention behavior. This experiment is an attempt to gain a better understanding of analyte retention mechanism contributed by the adsorption of different organic eluent on the bonded stationary phase.

Effects of Sampling Rate and Peak Capacity in 2 Dimensional Liquid Chromatography utilizing Conjugated Estrogens as a Model

Kurt Erz and Yuri Kazakevich

Two dimensional high performance liquid chromatography is a separation technique which utilizes two modes of separation in a comprehensive manner by means of a transfer of the first columns eluent onto the second column without any loss.
This presentation will demonstrate the characterization of the sampling rate as it pertain to a each column, their flow rates and the resulting peak capacity of each phase and for the system as a whole. The experimental work will utilize sodium salts of conjugated estrogen sulfates as a model. These estrogens derived from natural sources initially utilized an HPLC monograph for the separation of the three main components; Estrone, Equilin and 17α-dihydroequilin. Additional components such as 17α-estradiol, and 17β-dihydroequilin were found to have significant medicinal benefits and required characterization. Due to the difficulty in separation of the Equilin and 17β-dihydroequilin, the initiation of the use of a complex sample preparation and GC analysis was developed. Because of the intrinsic separation difficulties utilizing conventional RPLC, this model is ideal for the characterization of the parameters which define 2D HPLC

Experimental and Theoretical Approach to Determine the Mass of a Modified Adsorbent in a Fuse-core C18 Column

Margaret Figus and Yuri V Kazakevich

A commercially available fuse-core C18 column was characterized in terms of its modified and unmodified surface area, column pore volume, and inter-particle volume. Low temperature nitrogen adsorption (LTNA) was used to determine surface areas and pore volumes in modified and unmodified material. Column geometric parameters were determined via the minor disturbance method and retention of labeled analyte. A theoretical approach to assess the mass of modified layer of absorbent without unpacking the fuse-core column is presented. The deviation between the calculated mass of the modified adsorbent and mass determined by unpacking fuse-core column is 3.55% difference. Excess adsorption isotherm of acetonitrile and methanol from water on fuse-core C18 column were studied using minor disturbance retention data.

Professor Stephen Kelty

Molecular Modeling of Transient Receptor Potential Vanilloid Type 1 Ion Channel (TRPV1)

Kelly Raymond, Yufeng Wei and Stephen Kelty

The transient receptor potential vanilloid type 1 ion channel (TRPV1) is a member of the vanilloid type subfamily of the transient receptor potential ion channels (TRPV).[1] TRPV1 is part of the TRP family gated by vanilloids, heat and protons.[2] The putative structure of TRPV1 includes an intracellular N- and C-terminal region of variable length and six transmembrane domains with an additional short amphipathic stretch between transmembrane regions 5 and 6.[2] Currently, the only portion of the model that has been crystallized is the six ankyrin repeats that make up the N terminal region. However, a model can be generated by taking into consideration the evolutionary conservation of proteins from prokaryotes to eukaryotes. Therefore, a membrane domain was created using a eukaryotic, voltage-gated Kv1.2 K+ channel and inserting it into a lipid bilayer composed of palmitoyl-oleoyl phosphatidylcholine (POPC) for the outer membrane, and a mixture of palmitoyl-oleoyl phosphatidylethanolamine and palmitoyl-oleoyl phosphatidylserine (POPE/POPS 2:1 ratio) for the inner membrane. By creating a molecular model of TRPV1, extensive structure-function data and intra and interdomain interactions are expected to be obtained.

References:

1. Urban, L.; White, J.; Nagy, I. Molecular Structure of Transient Receptor Potential Vanilloid Type 1 Ion Channel (TRPVI). *Current Pharmaceutical Biotechnology.* **2011**, *12*, 115-121.
2. Frenandez-Ballester, G.; Ferrer-Montiel, A. Molecular Modeling of the Full-length Human TRPV1 Channel in Closed and Desenstized States. J. Membrane Biology. **2008**, *223*, 161-172.

Calculation of the Band Gap of Indium Nitride by Density Functional Theory within the Local Density Approximation Hubbard (LDA+U) Model

David Demianicz, Nicholas Abolafia and Stephen Kelty

Mixed semiconductor composites will play an important role in the design and fabrication of next generation photonic devices such as solar energy conversion materials. The properties that these mixed material devices offer include enhanced stability, tunable optical properties and robust fabrication methods. Photoabsorption results in the promotion of an electron from an occupied state to an empty state. In semiconductors, this process occurs between the highest filled state (the top of the valance band) and the lowest lying empty state (the conduction band), referred to as the band gap, E_g. By making mixed material composites, a wider range of the solar spectrum can be utilized.
A problem exists with the development of mixed nitride semiconductors ($MM'N_2$, M = Al, Ga, In) in that experimental measurements of band gap of InN are unreliable. In addition, Density Functional Theory (DFT) methods also suffer from a well recognized problem in that semiconductor band gaps are also not reliable although the reason for this is well understood. A method has been developed which mitigates these problems (DFT-LDA+U). This paper describes this method and the results of DFT calculations on the band gap of InN.

Professor Joseph Maloy

Finite-Difference Simulation of Adsorption Effects in Partition Chromatography

Nicole Charles and J.T. Maloy

Finite difference simulations [1] have been used successfully to model surface adsorption effects in partition chromatography. Later, the original software was modified to take adsorption into account [2]. Two additional input parameters were introduced: ($K_{ad}C_o$), which compares the adsorption equilibrium constant with the initial concentration of the analyte, and ($\Gamma_o A_s/C_o V_m$). $\Gamma_o A_s$ is the number of adsorption sites on the column. $C_o V_m$ is the number of analyte species contained within the mobile phase. At this point, X (n,r), a concentration dependent *variable* mobile fraction at each plate during each iteration is calculated in order to study the simulation of the chromatogram over wide ranges of the input parameters.

The computational details of this simulation are being studied to evaluate how its results may be used in the interpretation of experimental chromatography when it exhibits the effects of adsorption.

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1. see J.T. Maloy, "Digital Simulation of Electrochemical Problems," *Laboratory Techniques in Electroanalytical Chemistry*, Marcel Dekker, New York, 1996, pp. 583-620.

2. Kevra, S.A.; Bergman, D.L.: Maloy, J.T. *J. Chem. Ed.,* **71**, 1994, 1023-1028

Developing a Dynamic Process Simulation in Partition Chromatography Model

Fei Hao, Antonio Macaluso and Joseph T. Maloy

Chromatography is used as a critical separation method in both industry and academic researches, and it has also been fully studies since nineties with regard to the mechanism of separation. One of the earliest models for chromatography is partition chromatography which came from dephlegmation tower in chemical engineering. Molecules equilibrate between mobile phase and station phase, assuming that a fixed fraction of solute for each specific analyte is contained within mobile phase at each theoretical plate. Along with the RP chromatography and other types of chromatography development and investigation, adsorption model which based on Gibbs excess adsorption theory became more favorable among scientists. However, no matter which models focused before, all of them are established with a fundamental assumption that every process in separation achieves equilibrium ideally within columns. In this report, I developed software which focused on algorithms for the finite-difference digital simulation of dynamic process partition chromatography.

References:

1. Hao, F.; Macaluso, A.; Maloy, J. T. Pittcon®'11, March 15, 2011 – Paper No. 860-6
2. Kevra, S.A; Bergman, D.L; Maloy, J.T. *J. Chem. Educ.* 1994. 71.1023-8
3. Zeng, W.; Steiginga, J. R.; Maloy, J. T. EAS 2000 # 408

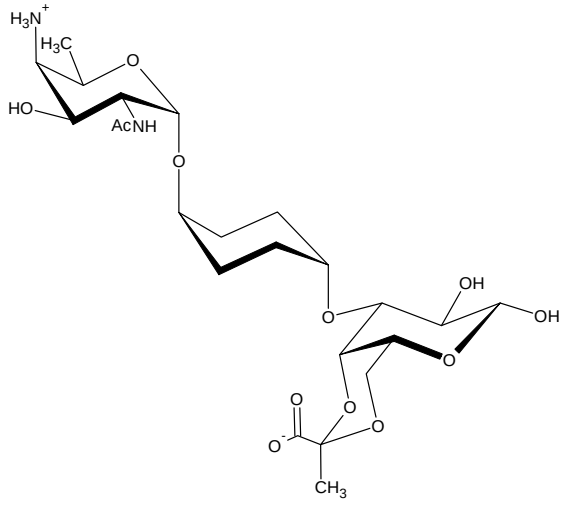
Professor Cecilia Marzabadi

Synthesis of an Immunomodulatory Zwitterionic Polysaccharide

Vikram Basava and Cecilia Marzabadi

Zwitterionic polysaccharide A1 (PSA1), isolated from the capsule of the anaerobic bacterium *Bacteroides fragilis*, has been shown to stimulate both innate and adaptive immune responses in mammals and is believed to be important in establishing a balanced immune system which is mediated by T-lymphocytes. The immunologic property is because of its zwitterionic character and any attempts in neutralizing either of the charges results in a strongly reduced biological activity of the polysaccharide.

In order to better understand the mechanism of immunological activity, attempts are being made to synthesize the charged sugar moieties and attach them together by PEG resins or cycloalkane diol chains. Evaluation of the polysaccharide's ability to produce cytokines and chemokines in antigen presenting cells and T-cells using sandwich ELISA assay tests will be carried out on the molecules synthesized. The results obtained will aid in the development of agonists and antagonists for the treatment of asthma and allergies, as well as, other immunological disorders.



References:

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2. Tzianabos, A.; Wang, J. Y.; Kasper, D. L.; *Carbohydrate Research*, **2003**, *338*, 2531-2538

The Synthesis of Carbohydrate Fused Benzopyrans

Sumiea Eltayeb and Cecilia H. Marzabadi

Carbohydrates comprise the most abundant natural product molecules. The general empirical formula for the carbohydrates is $C_n(H_2O)_n$. Carbohydrate chemistry has been a topic of interest and is attractive for drug design because of these molecules' unique structures and biological activities such as recognition, fertilization and signal transduction. Glycals are unsaturated sugars that contain a double bond between C_1 and C_2. Manipulations of this double bond have been the focal point of many syntheses that use glycals. The goal of this research is to synthesize carbohydrate-fused chromanes as potential anticancer drugs by using [4, 2] Diels-Alder reactions (Cycloaddition reactions). Much of this research will focus on reacting tri -O- substituted D-glucal with O- hydroxybenzaldimine in the presence of an acid catalyst. Different catalysts will be tested to find the most efficient mechanism and good yields of product.

Synthesis and Analysis of Novel Copolymers of Alkyl Ring-Substituted 2-Phenyl-1,1-dicyanoethylenes with 4-Fluorostyrene

Emi Hanawa and Gregory Kharas, Department of Chemistry, DePaul University, 1110 West Belden Avenue, McGowan South, Chicago, Illinois 60614

Trisubstituted ethylene (TSE) monomers, alkyl ring substituted 2-phenyl-1,1-dicyanoethylenes, $RC_6H_4CH=C(CN)_2$ (where R is 2-methyl, 3-methyl, 4-methyl, 4-ethyl, 4-isopropyl, 4-butyl, 4-isobutyl, and 4-*tert*-butyl) were synthesized by Knoevenagel condensation of ring substituted benzaldehyde with malononitrile, catalyzed by piperidine. TSE monomers were copolymerized with 4-fluorostyrene by radical chain polymerization with ABCN. Structural analyses (IR, ^{1}H- and ^{13}C-NMR) and compositional analysis (nitrogen analysis) showed the resulting polymers were copolymers. Thermal properties were analyzed by TGA and DSC. The average molecular weights were determined by GPC. The relative reactivities of 4-fluorostyrene addition to each TSE monomers were determined. All copolymers had a higher T_g than that of poly(4-fluorostyrene), indicating a substantial decrease in chain mobility of the copolymers due to the high dipolar character of the TSE monomer unit. The copolymers decomposed rapidly in one stage followed by a slower decomposition of the residue.

A Novel Synthetic Method for Septanoses and Septanose C-Glycosides from Hexose Sugars.

Nada Khan and Cecilia Marzabadi

A new methodology to synthesize septanoses and septanose glycosides (C- and N-) is described using different divergent routes. These syntheses will be accomplished by ring opening of hexose/pentose sugars; stereoselective introduction of a carbon atom; and recyclization to the septanose sugar or glycoside. The starting material for these sequences is 2,3,4,6-tetra-O-benzyl-D-glucopyranose.

In one scheme, the cyclic sugar will be subjected to homologation of a carbon by a Wittig reaction, oxidation of the resulting secondary alcohol, hydroboration/oxidation, and cyclization to yield a septanose C-glycoside. Similarly, epoxidation of sugar aldehyde will be followed by concurrent intramolecular ring opening of the epoxide in basic conditions, to yield a septanose. Likewise, in a third route we will first reduce the starting sugar with $NaBH_4$ to give the acyclic diol. Both alcohol groups of the diol will be converted into halo groups and this dihalo intermediate will be then treated with compounds like urea or thiourea to yield a septanose having N atom in the ring system.

Synthesis of Potential Anti-Cancer/ Antibiotic Drugs

Alexandra Kolodziejski, Dr. Cecilia Marzabadi

Cancer has become one of the most threatening diseases present in society today. Although drug solutions exist, they provide only temporary aid; the patient continues to face prolonged agony of the disease. Research utilizing new materials and methods is necessary to find a cure.
Ortho-hydroxy-benzaniline and 3,4,6, tri-O-benzyl-D-glucal were reacted with various catalysts in an effort to produce a sugar-based benzopyran. Synthesized products were purified using extraction with ethyl acetate and by preparatory thin layer chromatography. They were analyzed using Nuclear Magnetic Resonance spectroscopy.
Research has thus far yielded promising results in product formation: the appearance of a distinguished spot in the TLC suggested a complete reaction; NMR results illustrating new peaks, further supported this claim. TLC plates were prepared to purify the potential product. If experiments yield the expected products, we anticipate these compounds will act as intercalators, stopping the production of cancer cells in the body.

Professor Wyatt R. Murphy, Jr.

Synthesis and Characterization of Ru(tpy)(AA)(Cl) Compounds,

John F. Boczany and Wyatt R. Murphy, Jr.

Ruthenium polypyridyl complexes containing the dipyrido[3,2-a:2',3'-c]phenazine (dppz) ligand have been of intense interest due to the "molecular light switch" effect upon partial intercalation to DNA. Only a few reports of the $[Ru(tpy)(dppz)X]^+$ (tpy = 2,2,';6',2''-terpyridine) system have been made, with no significant derivatives. The synthesis of a series of tpy-based complexes was achieved by reacting $Ru(tpy)Cl_3$ with one of the four ligands of interest. The ligands being studied are dppz; 9,10,20,22[3,2-a:2',3'-c:3",2"-h:2'",3'"-j]tetrapyrido-pentacene (tatpp); 11,11'-bidipyrido[3,2-a:2',3'-c]phenazine (bdppz); and benzo[i]dipyrido[3,2-a:2',3'-c]phenazine. Both the bdppz and the tatpp were studied with one and two metals bound. The compounds were characterized though UV-Vis, CV, NMR, and elemental analysis.

Synthesis and Study of Tetrametallic Complexes of Ruthenium

Brian Cook* and Wyatt R. Murphy, Jr.

The previously synthesized tetrametallic ruthenium complexes involving the bridging ligands dpp and bpm were investigated further using size exclusion chromatography and NMR techniques. The general formula for these complexes are $\{Ru[(BL)Ru(bpy)_2]_3\}(PF_6)_8$ In this paper, dpp = 2,3-bis(2-pyridyl)pyrazine and bpm = 2,2'bipyrimidine. They were used as standards for the complexes involving the bridging ligands containing tatpp and bdppz. In this paper, tatpp = 9,11,20,22-Tetraazatetrapyrido[3,2-a:2'3'-c:3",2"-1:2"',3"'-n]pentacene and bddpz = 1,1'-Dipyrido[3,2-a:2',3'-c]phenazin-1,1'-yldipyrido[3,2-a:2',3'-c]-phenazine.
A new complex has been targeted for synthesis, a mixed metal complex system involving a Ru^{II} center (optically active with the optical isomers resolved) with three Re^{I} complexes surrounding it, or $\{Ru[(dppz)Re(bpy)(CO)_2]_3\}^{5+}$. The bridging ligand used for this tetrametallic species was dppz (synthesized by combining 1,10-phenanthroline-5,6-dione with 1,10-phenanthrolin-5,6-diamine via condensation). This complex will be fully characterized with spectroscopic, electrochemical and structural analysis, as well as an analysis of the two optical isomers.

STOP-FLOW KINETIC STUDIES, HPLC STUDIES, AND PREPARATION OF Δ AND Λ ISOMERS OF RUTHENIUM COMPLEXES

Samantha Gribben and Wyatt R. Murphy, Jr.

Optically active ruthenium complexes containing the dipyrido[3,2-a:2',3'-c]phenazine (dppz) ligand have been observed to bind to DNA with high yield via a partial intercalation mechanism. The chiral DNA shows a thermodynamic preference for different isomers, depending on the metal ion. This observation is the rationale for the present study.

Ruthenium complexes were synthesized in order to study stop-flow kinetics of the interaction with DNA. $[Ru(bpy)_2(phen\text{-}dione)]^{2+}$ was successfully reacted in two separate reactions with the ligands 1,2-

diaminobenzene and 2,3-diaminonaphthalene using literature methods. Using sodium arsenyl-(L)-(+)-tartrate and sodium arsenyl-(D)-(-)-tartrate, the complexes $[Ru(bpy)_2(phen\text{-}dione)]^{2+}$ were prepared and isolated as Δ and Λ isomers by literature methods. Stop-flow fluorescence will be used to investigate the interaction of Δ and Λ enantiomers binding with calf thymus. The racemic mixtures of the ruthenium complexes will be separated and studied in the future to achieve the previously synthesized Δ and Λ isomers using high performance liquid chromatography.

Investigation of the degree of coordination of tridentate ligands to $Re(CO)_5Cl$ and $RuCl_3 \cdot 3H_2O$ via NMR,

Samona Hall and Wyatt R. Murphy

Conflicting reports of tridentate coordination to rhenium(I) tricarbonyl chloride have been made In order to resolve these conflicts, ruthenium and rhenium complexes tris-(2-pyrazoyl)-methane (tpm) were synthesized from appropriate metal starting materials. 1D and 2D H-1 NMR spectroscopy will be used to determine the degree of coordination of the ligand to the metal. Observation of the pyrazoyl and bridgehead protons and distance measurements will confirm the nature of the bonding. Further, the $Ru(tpm)Cl_3$ precursor will be used to prepare bimetallic complexes with polypyridyl bridging ligands and fully characterized. Electronic and infrared spectroscopy, and cyclic voltammetry will be used to characterize the complexes. Results to date will be reported.

Investigation of the degree of coordination of tridentate ligands to $Re(CO)_5Cl$ and $RuCl_3 \cdot 3H_2O$ via NMR,

Tisha Hutchinson and Wyatt R. Murphy

We are currently investigating new bidentate bridging ligands based on the coupling of 1, 10-phenanthroline 5-6 dione with aromatic tetraamines. These ligands will be coordinated to the $Re(CO)_3Cl$ and analyzed via IR, UV-Vis, NMR and HPLC to determine the excited state and electron transfer properties. Research to date will be reported.

Synthesis and Characterization of [Ru(tpy)(dppz)(NO2)]+

Carly Winton and Wyatt R. Murphy

Dppz complexes have been known to bind easily to DNA. When coordinated to metal complexes, nitro groups can be readily converted to the nitroxide radical under hypoxic conditions observed in cancer cells. The precursor [Ru(tpy)(Phen-dione)Cl]+ has been prepared and the conversion to the dppz and nitro derivatives is currently under investigation. Preliminary results including spectral and electrochemical data will be reported.

Synthesis and characterization of [Ru((dpp)Re(CO)3Cl)3]2+

Victoria Lonnay and Wyatt R. Murphy

Over the past thirty years, there has been a growing interest in the properties of polymetallic dendric cluster of four or more metals to polypyridyl bridging ligands. More efficient syntheses of larger systems have been difficult due to the preparations involving the coupling of racemic mixtures of starting materials.
The complex $[Ru((dpp)Re(CO)_3Cl_3]^{2+}$ will be synthesized from enantiomerically resolved starting materials using Divergent and Convergent syntheses. $Re(dpp)(CO)_3Cl$ and $[Ru(dpp)_3](PF_6)_2{\cdot}H_2O$ have been prepared using methods described by Brewer, Murphy, Spurlin, Petersen, Baiano, et.al.

These complexes will be characterized and purified using High-performance liquid chromatography (HPLC), Nuclear magnetic resonance **(**NMR**),** Ultraviolet-Visible spectroscopy (UV-Vis), Infrared spectroscopy (IR), and electrochemistry. Our products will be sent out for elemental analysis.

Professor David Sabatino

How Do We Make Peptides in The Lab?

Stesha C. Joseph, Lathamol A. Kurian, Leah R. Poland, Tammy A. Silva and David Sabatino

Peptides are one of the essential biological molecules of life that function to stimulate cell growth, differentiation, structure and activity. In nature, peptides are made by specifically linking amino acids with the guidance of biological molecules such as messenger RNA (mRNA), transfer RNA (tRNA) and the ribosome. Bruce Merrifield (Nobel Prize, 1984) inspired by nature, developed solid-phase peptide synthesis (SPPS) for making peptides in the laboratory. SPPS allows for the chemical synthesis of peptides by the incorporation of Fmoc amino acid building blocks. This method provides potential for incorporating un-natural or modified amino acids (such as the D-amino acids) for investigating the basis of structure and function of peptides.[1] To help illustrate this concept, this presentation will highlight the synthesis and characterization of biologically relevant poly-(D-Arg) and DIYET sequences.[2,3] With peptides in hand, opportunity now exists for exploring the structural and biophysical properties that underscore peptide biology inside the cell.

References:

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DNA synthesis Then, Now and at Seton Hall University

Anthony Maina, Maria E. Bender and David Sabatino

Inside the living cell, DNA functions as nature's vital biological molecule by delegating its genetic information into the synthesis of proteins. In nature, DNA is replicated in a semi-conservative process by using a template strand to guide the enzymatic assembly of nucleotides into full length oligonucleotides. In the 1950's, coinciding with the discovery of the double helix structure of DNA by Watson and Crick (Nobel Prize 1962) Michelson and Todd first reported the chemical synthesis of a dithymidine in solution. Over the next two decades, the use of a solid-support facilitated DNA synthesis, until the process was automated by Ogilvie and co-workers (McGill University, Montreal Canada) in the early 1980s with use of the first gene instrument for making DNA. In this presentation, we'll be describing the automated solid-phase phosphoramidite approach for making DNA in the lab, its post-synthesis work-up and purification procedures for analysis and characterization of synthetic DNA.

Making RNA the Solid-Phase Synthesis Way

Pradeepkumar Patel, Cory LaRochelle, Vincent Mondello and David Sabatino

RNA has been known as nature's intermediary molecule in transmitting information encoded in DNA into proteins. Compositionally and chemically similar to DNA (ribose instead of a deoxyribose and uracil for thymine base), RNA adopts a variety of structures to provide functional diversity. For example, RNA functions in gene regulation (RNAi), catalytic activity (RNAzymes) and protein translation, stimulating interest to explore the basis of RNA function. Key to this endeavor is an efficient synthesis method. Nature uses a DNA template to guide assembly of ribonucleotides into RNA. Alternatively, we can make RNA in the laboratory by solution phase preparation of the prerequisite RNA phosphoramidite building blocks and their incorporation into RNA by solid phase synthesis. In this presentation, the use of a gene machine will be highlighted to facilitate RNA synthesis followed by post-synthesis work-up and purification. With purified material, opportunity now exists for evaluating structural and functional properties in RNA.

Professor M. Alper Sahiner (Department of Physics)

Preparation of Copper Indium Selenium Photovoltaic Cells by Dip-Coating

Andrew Klump, Shaneil Samuels and M. Alper Sahiner

While the efficiency of the best photovoltaic cells to date is around 20% conversion of sunlight to electricity, the high price tag to create these devices makes them far from cost efficient. Instead of relying on the expensive conventional vacuum-based processes to create Copper Indium Selenium (CIS) photovoltaic cells, a two step process of first dip-coating and then pulse laser deposition is substituted. $Cu(NO_3)_2 \cdot H_2O$ and $InCl_3$ are dissolved in methanol to form the precursor solution, the viscosity of which is adjusted by adding ethyl cellulose. The ITO coated glass is then dipped into the solution and retracted at various rates to form the first layer. Next, solid Se formed into a pellet that is vaporized using a pulse laser deposition (PLD) system. Subsequently, the evaporated Se deposits onto the surface on the already coated glass. The crystalline structure of cell prior to depositing Se and after deposition Se will be characterized by x-ray diffraction (XRD). Finally, the electrical characteristics of the completed cell will be analyzed by the Keithley 2602 SYSTEM SourceMeter.

Colossal Magneto-resistive LCMO Thin Film Resistivity Testing Using PPMS

Daniel Guerreo and M. Alper Sahiner

The electrical characterization of the pulsed laser deposited (PLD) thin films of colossal magneto-resistive (CMR) materials are presented. Specifically, in PLD prepared $La_{1-x}Ca_xMnO_3$ epitaxial thin films are studied using a 4-point dynamic measurement system using our Physical Property Measurement System (PPMS). PPMS (by Quantum Design) will allow us to measure the resistivity under increased magnetic fields, up to 7 Tesla, and maintain the entire system under 4 degrees Kelvin. The colossal magneto-resistive (CMR) films will change their resistivity based on the magnitude of the magnetic field allowing us to examine the maximum and minimum resistance of the $LaCaMn0_3$ sample. Non-linear *V–I* measurements will be obtained below CMR critical temperature. The films are mounted onto PPMS sample stages by using indium solder material for good electrical contacts. . Our electrical characterization results will determine the optimum Ca proportion where the CMR effect is maximum.

Synthesis and Electrical Characterization of $CuIn_xGa_{1-x}Se$ (CIGS) Photovoltaic Thin Films

Jimmy Barrientos, Christopher Reehil and M. Alper Sahiner

The ability to convert a wider range of the solar spectra into electricity required for the next generation of solar cells. Presently, the correlation between the composition and the photovoltaic (solar energy conversion) properties of these CIGS (CuInGaSe) thins films is not well determined. The objective of this project is to search specific compositions of CuInGaSe based thin films that will be able to tune into broader wavelength ranges of the solar spectrum. The name thin film solar cells is derived from the films exhibiting direct band gaps producing a photovoltaic effect allowing the cells to be a couple of micrometers thin. CIGS thins films are mainly utilized in photovoltaic cells in the form of polycrystalline thin films. In order to explore this next generation solar cell CIGS thin film will be fabricated by the Pulse Laser Deposition technique and electrical properties will be investigated to determine their photovoltaic efficiency.

Professor Nicholas H. Snow

Thermodynamic Performances of Ionic Liquid Capillary GC Columns

Kenneth W. Banks and Nicholas H. Snow

Over the past decade, there has been an increased interest of using ionic liquids as a stationary phase for GC capillary columns in gas chromatography. The reasons for this interest are due to the ionic liquid properties such as low volatility and high thermal stability. The characteristic of having Ionic molten salt (organic cation and inorganic anion combination) along with column polarity and low temperature makes it an ideal stationary phase. Supelco is the maker of several ionic liquid GC capillary columns: IL59, IL69, IL76, IL82, IL100 and IL111. The numbers represent polarity. Higher numbers represent higher polarity. Thermodynamic performances such as resolution, theoretical plates, separation factor, tailing factor, enthalpy, entropy, Vant Hoff plot, and Gibbs free energy are to be investigated. Starting with the IL59 capillary GC column, the Vant Hoff plot was initially investigated. A sample solvent mix consisting of six solvents was chromatographed. Isothermal conditions were set with oven temperatures ranging from 40ºC to 120ºC using a 5890 FID Hewlett Packard Gas Chromatograph. Symmetrical peaks were obtained using the IL59 column with good peak resolution. The Vant Hoff plot showed good linearity for the six solvents under these isothermal conditions.

Trace Analysis of Cocaine and Salvinorin A in Urine Using SPME coupled with GCxGC-ToFMS

Brian B. Barnes and Nicholas H. Snow

Cocaine is a well-known drug of abuse that has been popular in the US since the 1980s. Studies of this drug using GC-MS and LC-MS have been well-documented in the literature. These techniques have been of great benefit, but they do have some limitations. One limitation is their ability to perform trace analysis. Salvinorin A is a hallucinogenic drug found in the Salvia divinorum sage plant. The biochemical action of this drug has been well-documented in the literature, but analysis using chromatographic techniques is limited. Forensic scientists are constantly looking for faster and more sensitive analytical methods to analyze drugs of abuse at trace levels. SPME coupled with GCxGC-ToFMS meets these criteria. Applications of both techniques in the fields of environmental, forensic, and flavor analysis have been discussed in the literature. SPME reduces sample preparation time, produces LODs and LOQs in the low picogram range, and minimizes matrix effects. This increases the sensitivity of the technique and improves extraction precision. GCxGC-ToFMS uses orthogonal separation to produce a higher peak capacity than standard GC-MS. ToFMS further increases sensitivity with rapid full spectrum acquisition, allowing identification of all peaks produced from a single run. Cocaine and Salvnorin A were extracted from spiked samples of urine using SPME-GCxGC-ToFMS. The limits of detection and quantitation determined for cocaine were 41 ppb and 410 ppb, respectively. The limits of detection and quantitation for Salvinorin A in urine using SPME were 33 ppb and 110 ppb, respectively. The values for cocaine in urine and Salvinorin A were lower than values reported in the literature. The linear range and recovery of Salvinorin A and cocaine in water and urine were also determined and will be discussed. Thus, use of SPME-GCxGC-ToFMS demonstrates an effective method for trace analysis of drugs of abuse below the required limits for toxicology.

GCMS Solid Phase Micro Extraction of Fragrances using PDMS and Ionic Liquid Fibers

Erin Hartman, Brian B. Barnes and Nicholas H. Snow

Ionic liquids are salts that are liquids are room temperature. Examples include ammonium and sulfonium. Ionic liquids are subdivided into two categories: room temperature IL (melting point lower than 25°C) and regular IL (melting point lower than 100°C). The chemical properties of ionic liquids are what make them unique and versatile. They have negligible vapor pressure, high thermal stability, variable viscosity, hydrophobic and hydrophilic capabilities, and IL can undergo multiple solvent interactions. Ionic liquids have a dual nature separation capability because they can be used for both polar and non polar substances. Due to their useful properties, ionic liquids can be used in the lab as a solvent, the stationary phase in gas chromatography, and a new and interesting use is as a coating on an SPME fiber. The polymeric ionic liquid fibers will be tested to determine the capabilities and boundaries. Various separations will be analyzed to determine if the IL fiber is more efficient than the traditional fibers. Eight fragrance samples will be tested using the traditional 100micron PDMS fiber to obtain a standard GCMS spectrum. Then, the same samples will be tested under identical conditions using the ionic liquid fiber.

Screening of Polycyclic Aromatic Hydrocarbons in Fish Oil Using Headspace Solid-phase Microextraction- Gas Chromatography- Mass Spectrometry (HS-SPME-GC-MS)

Joseph Ravino and Nicholas H. Snow

An extraction technique has been developed for the analysis of fish oil using Headspace Solid-phase Microextraction-Gas chromatography-Mass spectrometry (HS-SPME-GC-MS) in the screening for Polycyclic Aromatic Hydrocarbons (PAHs). PAHs are Environmental Protection Agency (EPA) controlled compounds which are high in toxicity and are carcinogenic. Due to the 2010 Gulf of Mexico oil spill, it is suspected that PAH containing crude oil has contaminated Menhaden, a species of fish which is located in the area. In this project, HS-SPME-GC-MS has been used to analyze capsule oil and menhaden oil samples in the process of determining if PAHs are present, and to determine the abundance of these compounds when applicable. This was done in conjunction with the EPA Method 610 for the determination of PAHs. Initial experiments have indicated that PAHs are not likely present in the capsule fish oil, while the presence of PAHs in Menhaden oil samples is still being investigated.

Static Headspace Extraction - Gas Chromatography (SHE-GC) – Investigation of variable parameters using organic solvents as analytes

Michael Sithersingh and Nicholas H. Snow

Using Static Headspace Extraction – Gas Chromatography (SHE-GC) technique with pressure balanced headspace sampling system, peak responses obtained by varying the solvents and headspace sampler parameters were compared and investigated. The following organic solvents were used as analytes: Methanol, ethanol, acetone, acetonitrile, methylene chloride, tetrahydrofuran and pyridine. Peak responses obtained for the following solvents & solvent mixtures as diluents were compared: Water, 1 : 1 mixture of water & dimethyl sulfoxide and dimethyl sulfoxide. Also, peak responses from the above

diluents with and with out the electrolytes (salting out) were compared. Peak responses obtained by varying the following individual headspace sampler parameters were investigated: Oven thermostatting time, sample volume in the headspace vial and injection time. The resulting peak area responses for the varied headspace sampler parameters with different solvents and solvent mixtures were plotted for comparison and investigation.

Analysis of YABA in Water and Urine Using SPME-GC x GC- ToFMS

Peter Malychev, Brian Barnes and Nicholas Snow

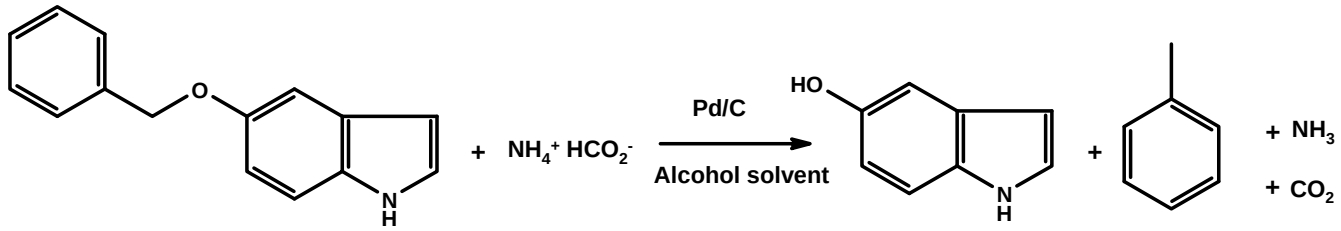
SPME and GC x GC-ToFMS is a relatively new and powerful technique. The benefits of SPME include the high sensitivity, low limit of detection (LOD), low limit of quantitation (LOQ), and minimized sample preparation time. Samples were analyzed using GC x GC-ToFMS, which contains two columns for separation, the first based on vapor pressure, the second based on polarity. This allows for a more complete separation of the sample. The mass spectrometer (MS) provides high sensitivity rapid scans and identification of all the components of the substance. The samples analyzed were designer drugs. These compounds are synthetic and often more powerful versions of conventional street drugs, which are often not subject to legal restriction, and can even be easily made from household products. The drug analyzed was Yaba, a mixture of methamphetamine, ecstasy, ketamine, and caffeine. The goal was to determine linear range, LOD, LOQ, and recovery from urine. The LOD for caffeine and methamphetamine was 26ppb and 15ppb, respectively. The final goal is to determine a single extraction and separation method for Yaba, using SPME and GC x GC-ToFMS.

Professor John R. Sowa, Jr.

A Study of the Kinetics of Catalytic Hydrogen Transfer in Selected Deprotection Reactions Using Ammonium Formate

Andrew Bach and John R. Sowa, Jr.

In this poster we present our proposed study of the kinetics of selected catalytic hydrogen transfer deprotection reactions using ammonium formate as the hydrogen transfer agent, palladium on carbon as the catalyst, and an alcoholic solvent. The use of ammonium formate as a hydrogen transfer agent is known but its kinetics has not been studied thoroughly. The deprotection reactions to be studied will use CBZ and benzyl protected substrates (such as 5-benzyloxyindole). The use of ammonium formate as a hydrogen transfer agent offers a viable alternative to traditional catalytic hydrogenation, which uses hydrogen gas in a closed, pressurized system that requires special equipment and handling.

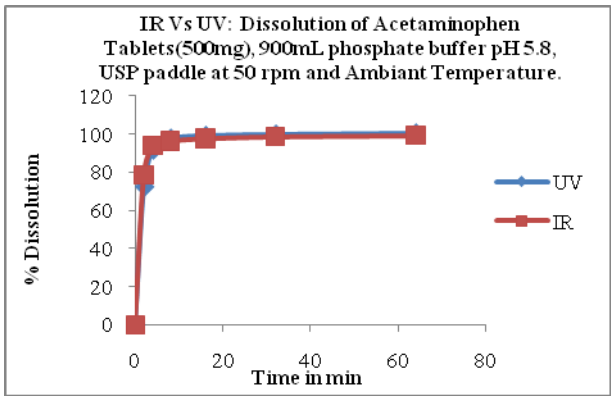


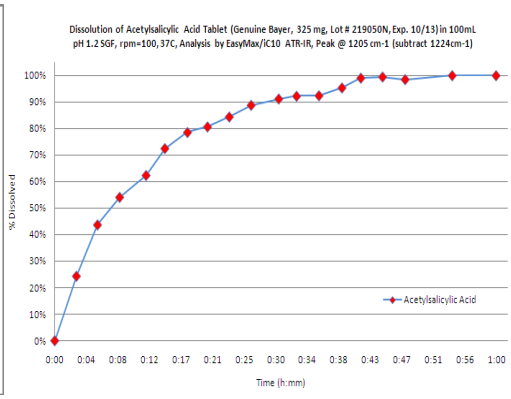
5-Benzyloxyindole **5-Hydroxyindole**

In-Situ Dissolution Monitoring of Pharmaceutical Tablets using ATR/FTIR

Vrushali Bhawatankar and John R. Sowa, Jr.

Dissolution studies are critical tests for measuring the performance of a drug product. In the past few years, the importance of the dissolution test has increased. Using in-situ ATR/FTIR spectroscopy we developed a methodology of analyzing and monitoring dissolutions of pharmaceutical APIs. The accuracy of this technique was found to be ± 3% relative to HPLC and UV using salicylic acid calibrator tablets and acetaminophen tablets. Additionally, research was conducted on multi-component drugs such as Excedrin and Extended Release Acetaminophen tablets. We are still working on multicomponent tablet. In fact, we also performed the Hydrolysis of Aspirin and will study the chemistry behind the dissolution by React IR. With all these experiments we further plan to study such kind of compounds which don't have chromophore. With improved sensitivity, this is a promising method for monitoring dissolution of pharmaceutical tablets with an excellent automated capability for distinguishing individual components.

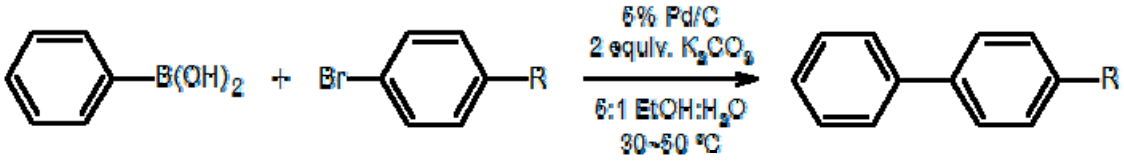




Kinetic Studies of Suzuki Cross-Coupling Reaction by HPLC and ReactIR™

Jiangnan Cao and John R. Sowa, Jr.

The Hammett Plots have been used to determine how reaction mechanisms vary as a function of the electronic changes induced by subtituents. The Suzuki cross-coupling reaction is the organic reaction of an aryl- or vinyl-boronic acid with an aryl- or vinyl-halide catalyzed by a palladium(0) complex. In this study, an aryl-bromide with different *para*-substituents on it was employed to react with phenyboronic acid.



The reaction was catalyzed by heterogeneous catalyst and carried in air and in oxygen-free conditions. The reverse phase HPLC has been used to investigate the substituent electronic effects on the Suzuki coupling reaction and the relative mechanism. Recently the Suzuki Coupling reaction has been found that it could be monitored and analyzed by *in-situ* IR spectroscopy. This new method brings potential benefit and provides deeper understanding on the mechanism of the Suzuki reaction.

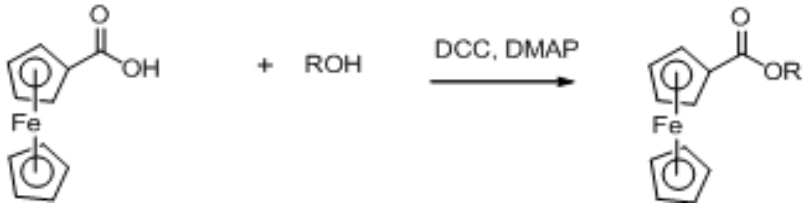
Using Ferrocene For Improved LC-MS Detection of Arteriosclerotic Chlorinated Fatty Alcohols

Charles M. Defendorf and John R. Sowa, Jr.

John Bowden,and David A. Ford, Department of Biochemistry and Molecular Biology, Saint Louis University, St Louis, MO

Molecular targets for arteriosclerosis such as chlorinated alcohols in the blood eluted by Liquid Chromatography (LC) and detected by Mass Spectrometry (MS) may be detectable before arteriosclerotic plaques.[1] Build-up of plaque leads to artery wall stiffening interfering with artery elastic recoil function.[1,2] Researchers are interested to develop innovative methods to detect, track, and analyze molecular targets linked to atherosclerotic plaques to improve diagnostic speed enabling early detection and disease prevention while observing the biological mechanisms involved in atherosclerotic plaque formation.

Research shows chlorinated fatty alcohols in the bloodstream as one molecular target that may be key to understanding the development of arteriosclerosis.[3] Reports show the detection of the 2-chlorohexadecanal (2-ClHDA) molecule in atherosclerotic tissues at concentrations 1400 fold greater than found in normal artery walls.[4] 2-ClHDA is a long chain chlorinated fatty aldehyde that is reduced in living systems to a chlorinated fatty alcohol (α-ClFOH).[5] We improve detection of the chlorinated alcohols using NN-Dicyclohexylcarbodiimide (DCC) as a reagent to convert ferrocene-carboxylic acid into a reactive acylating agent for coupling to an alcohol functional group of long chain fatty alcohols like α-ClFOH.[6,8] Overall mass is increased with a four part isotopic ratio while imparting an electro-active functional substituent creating a strong and predictable LC-MS fragmentation pattern for improved detection.[7,8] Initial results indicate that the ferrocene derivatives of fatty alcohols are 10,000 times more sensitive when detected by LC-MS than the free alcohol alone. Our work now focuses on using this method for detection of ppm alcohol concentrations.



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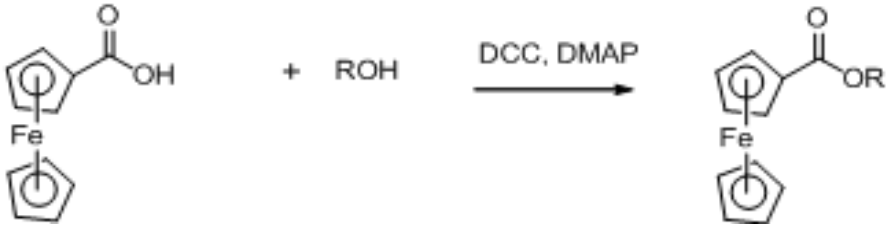
Charles M. Defendorf and John R. Sowa, Jr.

John Bowden and David A. Ford, Department of Biochemistry and Molecular Biology, Saint Louis University, St Louis, MO

Molecular targets for arteriosclerosis such as chlorinated alcohols in the blood eluted by Liquid Chromatography (LC) and detected by Mass Spectrometry (MS) may be detectable before arteriosclerotic plaques. Build-up of plaque leads to artery wall stiffening interfering with artery elastic recoil function. Researchers are interested to develop innovative methods to detect, track, and analyze molecular targets linked to atherosclerotic plaques to improve diagnostic speed enabling early detection and disease prevention while observing the biological mechanisms involved in atherosclerotic plaque formation. Research shows chlorinated fatty alcohols in the bloodstream as one molecular target that may be key to understanding the development of arteriosclerosis. Reports show the detection of the 2-chlorohexadecanal (2-ClHDA) molecule in atherosclerotic tissues at concentrations 1400 fold greater than found in normal artery walls. 2-ClHDA is a long chain chlorinated fatty aldehyde that is reduced in living systems to a chlorinated fatty alcohol (α-ClFOH). We improve detection of the chlorinated alcohols using NN-Dicyclohexylcarbodiimide (DCC) as a reagent to convert ferrocene-carboxylic acid into a reactive acylating agent for coupling to an alcohol functional group of long chain fatty alcohols like α-ClFOH. Overall mass is increased with a four part isotopic ratio while imparting an electro-active functional substituent creating a strong and predictable LC-MS fragmentation pattern for improved detection. Initial results indicate that the ferrocene derivatives of fatty alcohols are 10,000 times more sensitive when detected by LC-MS than the free alcohol alone. Our work now focuses on using this method for detection of ppm alcohol concentrations.



SEPARATION OF ACETONITRILE AND WATER MIXTURE USING NOVEL SEPARATION TECHNIQUES AND ITS ANALYSIS USING REAL TIME IR SPECTROSCOPY AND KARL FISCHER.

Mithilesh.Deshpande and John R. Sowa, Jr.

Worldwide shortage of Acetonitrile, commonly used HPLC solvent has forced us to implement a strategy for conserving our existing stocks . Number of methods have been tried to successfully separate this solvent mixture. Methods ranging from distillation, salting out, sugaring out, pervaporation, freezing them below freezing temperature etc.

Ionic liquids (ILs) are playing an increasingly important role in separation science and received significant attention in recent years by the academic and industrial chemical community as green and potential environmentally friendly compounds. More specifically, ILs demonstrated to possess the ability to act as

extraction solvents to separate azeotropic mixtures. In our present research we propose use of Ionic liquids to separate Acetonitrile and water mixture and its analysis by React IR and Karl Fischer.

Fig 1

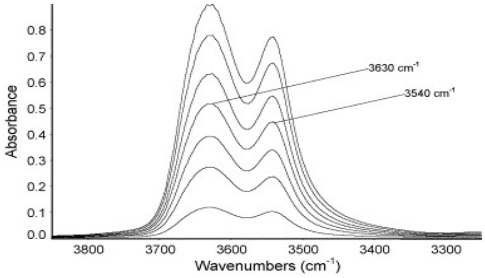


Fig 2

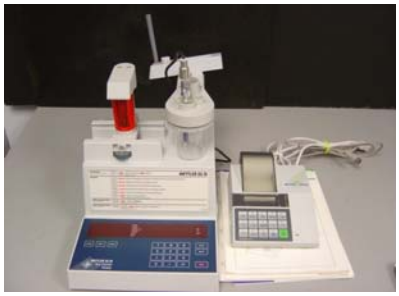


Fig 1. Differential spectra of water in acetonitrile illustrating the two main water absorption bands , the symmetric and asymmetric OH stretching bands at 3630 and 3540 cm^{-1}, respectively.

Fig 2. Karl Fischer DL-18

Development of a Procedure to Extract Oils from *Brevoortia Tyrannus* and *Brevoortia Patronus*

Dustin Hanos and John R. Sowa, Jr.

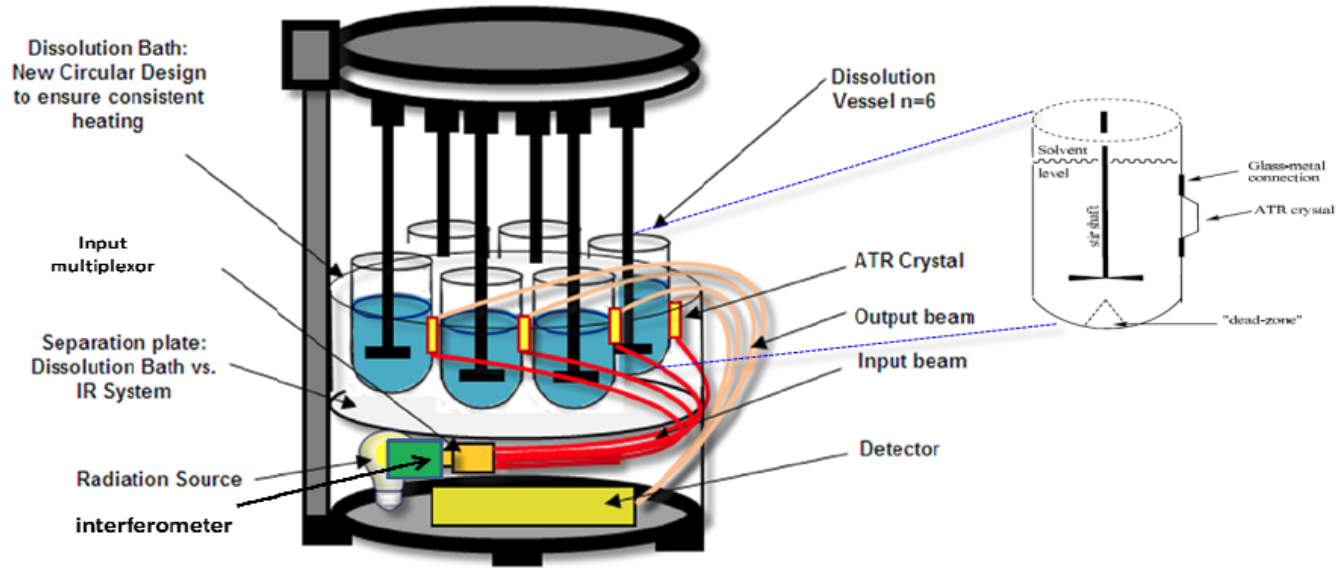
The recent Deepwater Horizon Oil spill that occurred in the Gulf of Mexico was an environmental disaster and its impact on the local aquatic environment is massive, and difficult to comprehend. The basis of this research involves two species of fish *B. Patronus* and *B. Tyrannus*, both also known as Menhaden, and their possible ability to consume and retain polyaromatic hydrocarbons that are present in the water from the oil spill. These polyaromatic hydrocarbons would most likely be present in the algae, which the Menhaden consume, or would be taken in through the gills of the fish, and would then be present within the fish's metabolites, or stored within the fishes' oil.

The development of a proper procedure for oil extraction was crucial to the entire Menhaden Research Project, and this presentation aims at conveying the development of the oil extraction procedure and the difficulties that were faced while trying to find oil in the actual fish. The development began with simple homogenization and centrifugation, which yielded no oil in initial trials, and later advanced to using dichloromethane extractions, oil to oil extractions, and hexane extractions to determine a relative amount of oil that are present within the fish. The experiments proved that the fish being used for the experiment were too young, and had yet to develop sufficient oil stores within their bodies to be properly extracted by centrifugation.

Attenuated Total Reflection Infrared Spectroscopy (ATR-IR) as an *in-situ* Technique for Dissolution Science Studies

Abe Kassis, Vrushali Bhawtankar and John R. Sowa, Jr.

In this presentation we will present our studies of fundamental dissolution reactions and analysis by *in-situ* IR spectroscopy. Dissolution studies are critical tests for measuring the performance of a drug product. We have developed a novel technique using *in-situ* ATR-IR spectroscopy to monitor dissolutions of pharmaceutical drug products. The accuracy of this technique is ±3% relative to HPLC. Several OTC active drugs (i.e. acetaminophen, acetylsalicylic acid, salicylic acid, etc.) were tested during the research. This novel approach also gives the research laboratory the capability of analyzing multiple components in a single tablet. For example, individual components of Excedrin tablets were easily distinguished. Furthermore, the system has the capability of monitoring the drug transformations during dissolution. For instance, we monitored the hydrolysis of aspirin to salicylic acid using this technique. The ATR-IR system was found to have good sensitivity and can analyze samples as low as 0.03 mg/ml. This technique allows deeper insight into spectroscopy, reaction analysis, kinetics and dynamics of the dissolution studies.



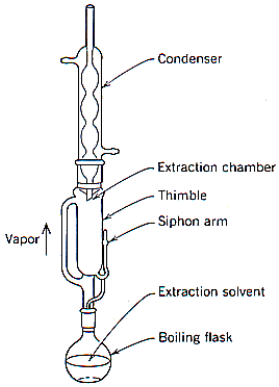
A. Kassis, V. M. Bhawtankar, J. R. Sowa, Attenuated total reflection infrared spectroscopy (ATR-IR) as an in-situ technique for dissolution studies, Journal of Pharmaceutical and Biomedical Analysis (**2010**), 53, 269–273

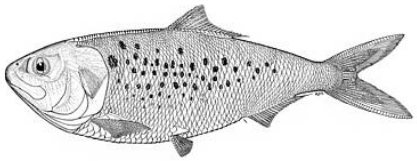
Methanoloic KOH Soxhlet Extraction of PAH's in Menhaden Fish Oil

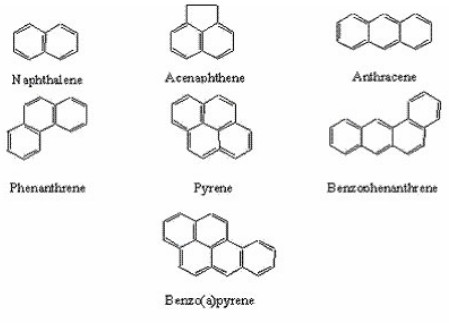
Vanessa R. Pinheiro and John R. Sowa, Jr.

In this presentation I will present my part in the Menhaden project. The Oil Spill of April 2010 sent millions of barrels of crude oil into the Gulf, a place where many fish migrate toward and reside in the summer. Because the Menhaden is an oily fish, it was chosen to be studied for polycyclic aromatic hydrocarbons, or PAH's, which are found in crude oil. My job in this project is to extract any possible

PAH's present in the skin and muscle of the Menhaden fish through the Soxhlet method so that it may be sent for further analysis.



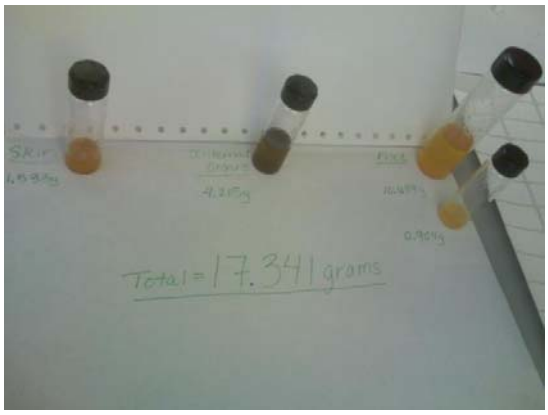


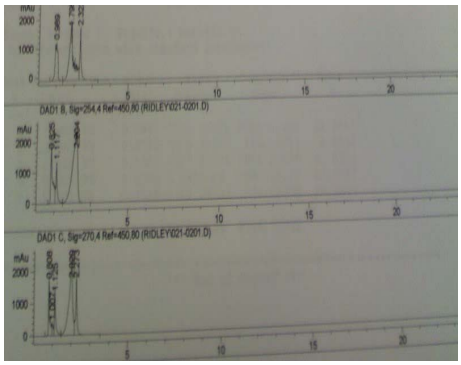


Fish Oil Extraction and PAH Detection using HPLC

Lauren Ridley, Jonathan Adessa and John R. Sowa, Jr.

On April 20, 2010 the Deep Water Horizon of the Mississippi Canyon exploded. The resulting oil spill had a huge impact on the Gulf of Mexico's wildlife and human livelihood. The animals that live in this region are used for consumption and when the spill occurred, this consumption was halted and it was unclear the extent that the spill would have on wildlife. This project is meant to show how the oil spill not only affects those in the Gulf but how the oil may potentially be a risk for the food consumption in New Jersey. The first part of this study was aimed at the extraction of oil from a fish called Menhaden, a common aspect of both Gulf and New Jersey waterways. The extraction of this oil proved to be difficult by standard blending and centrifugation. It was determined that the best method for extraction needed to be done on fish that were older than a year and dissection of parts including removal of the internal organs and removal of muscle from the skin. This presentation will not only show how this extraction took place but will also show how the analysis of the oil was done using HPLC. The HPLC was used to show the major components of the Gulf oil and to also see if these components were apparent in the oil of the Menhaden. Thus far the study has given us some of the common PAH's present in the Gulf oil including Naphthalene. Standard curves have been made of vary concentrations to compare to components found in the fish oil.

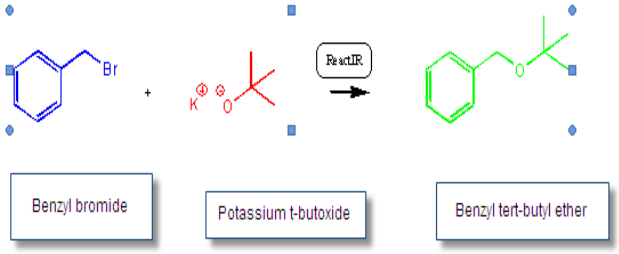


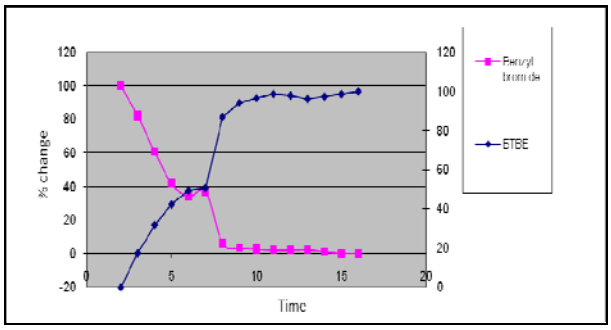


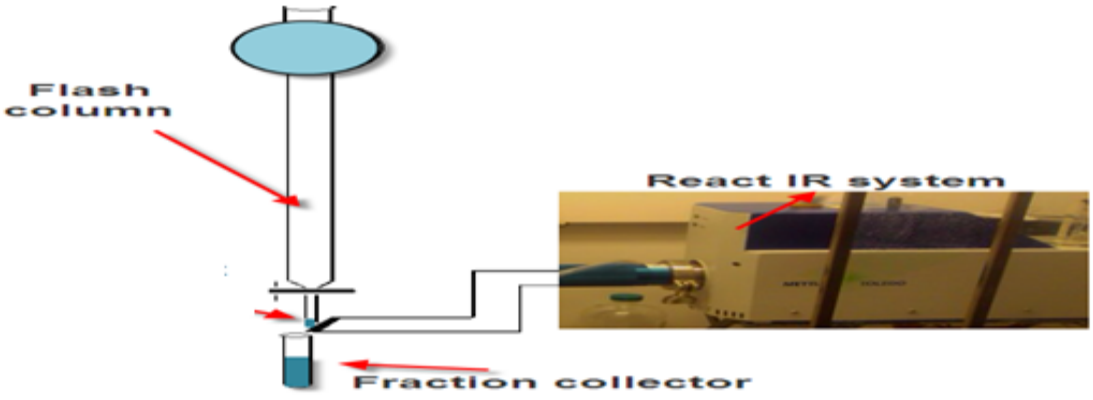
Design of Flash-IR System A Process Analytical Technology Tool Integrated with Reaction Monitoring

Gopalakrishnan Venkatasami and John R. Sowa, Jr.

The objective of the study is to develop a single real time reaction monitoring PAT tool integrated with flash chromatographic purification system using ATR-IR detection for the purpose of obtaining a product in highest possible purity. We have monitored Williamson ether reactions. We have also developed a flash chromatography procedure monitored by ReactIR for the separation of reaction products.





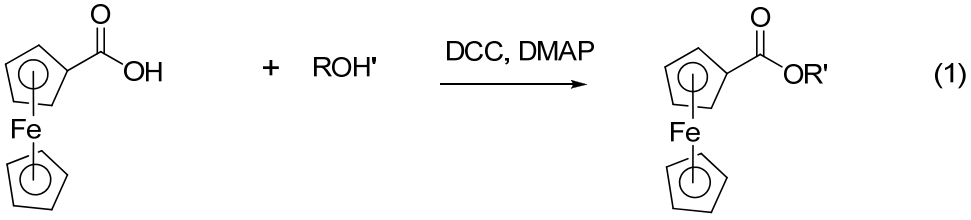


Modification of Long-chain Fatty Alcohols with Organometallic Chromaphores to Enhance Sensitivity in LC/MS

Faith Njoku,[a] Maria Claros,[a] Agatha Koni,[a] Charles Defendorf,[a] John R. Sowa, Jr.,[a] John Bowden,[b] David A. Ford[b]

[a]Department of Chemistry and Biochemistry, Seton Hall University, 400 South Orange Avenue, South Orange, NJ 07079; [b]Department of Biochemistry and Molecular Biology, St. Louis University Health Sciences Center, St. Louis, Missouri 63104

The focus of this research is the completion of an esterification reaction between ferrocene carboxylic acid and fatty alcohols that have physiological relevance. An esterification is the chemical process of the formation of esters from carboxylic acids. Esters, which are compounds of the chemical structure R-COOR', where R and R' are either alkyl or aryl groups. A method for preparing esters involves carbodiimides reagents EDCI and DCC which facilitate the reaction of carboxylic acids (R-COOH) with alcohols (R'OH) (eq 1).



(1)

For this research, we are interested in developing the reaction of ferrocene carboxylic acid with alcohols 1-octadecanol and cholesterol. The alcohols 1-octadecanol and cholesterol are metabolites found in human blood and it is important to be able to detect these molecules. However, these alcohols are considered to be weak chromaphores, i.e., they respond weakly to various spectroscopic and spectrometric methods of detection. Derivatization of these alcohols with ferrocene carboxylic acid should improve the ability of these molecules to be detected as the ferrocene moiety is a strong chromaphores. In particular, we are interested in the response of this chromaphores in mass spectrometry. The improved signal enhancement will enable us to identify the chemical composition of the alcohol metabolites, in order to gain better understanding of where they come from and their impact on human health.

Possible Polycyclic Aromatic Hydrocarbons CH_4, CH_3CH_3, $CH_5CH_2CH_3$, CO_2 absorbed by Subsurface Plume

Shannon Dugan, Nicole Lahanas and John R. Sowa, Jr.

The purpose of this research is to detect polycyclic aromatic hydrocarbons (PAHs) that may be absorbed in air, soils, and water as a result of both direct and indirect emissions. PAHs released into the environment by the break-down of fossil fuels generally associated with transportation and the generation of electricity. The deepwater Horizon oil spill in the Gulf of Mexico, which lasted about 83 days, and estimated leaking 25,000 barrels of oil per day into the water is the reason why this research is being performed at this time. With this in mind, there is reason to believe the BP Oil Spill is the cause of PAHs in the gas state absorbed by the sub-surface oil plume. Further, these organic compounds have been identified as Mutagens in bacterial cells, which if are the case, is passed along the ecosystem by bacteria found in the water via the food chain.

Professor Yufeng Wei

Identifying the Structure and Function of the Transmembrane Domain of Transient Receptor Potential (TRP) Channel Proteins Through NMR Studies

Dana F. Cordasco and Yufeng Wei.

The transient receptor potential (TRP) channel proteins are a family of cation channels present in the cell membranes of many eukaryotic organisms. The TRP channels are involved in many different biological activites, including temperature sensing. It has been postulated that the transmembrane S1-S4 domain of the protein controls responses to agonist binding and voltage gating. Specifically, the TRPV1 and TRPM8 proteins will be studied. Both the TRPV1 and TRPM8 proteins are thermosensitive, and are representative of the TRP family. The TRPV1 and TRPM8 proteins will be produced via standard molecular biology methods. Once the protein samples have been produced, solution state NMR experiments, with the S1-S4 domain in liposomes simulating cell membrane structure, will be conducted to determine the membrane-bound structure and function of this domain. Mutagenesis experiments will also be performed. The structure and dynamics of the mutants will also be studied via NMR to determine the key residues for agonist binding and voltage gating. The elucidated structure of both the TRPV1 and TRPM8 channel proteins will be deposited in the Protein Data Bank, to aid other scientists in future research into this important family of proteins.

Quantitative measurement of PIP_2 binding to lipid vesicles using SPR

Elizabeth T. Giampiccolo and Yufeng Wei

TRPV1's polymodal sensitivity to stimuli makes it a point of interest for study; however, hampering progress is the lack of structural information. Experimentation shows that derived lipids are capable of regulatory function of the TRPV1. Binding of phosphatidylinositol (4, 5)-biphosphate, (PIP_2), inhibits TPV1, and this inhibition is released when PIP_2 is hydrolyzed to diacyglycerol and inositol (1,4,5) triposphate.

Using concentration jump experiments to investigate ligand gated ion channels, provides information about activation and inactivation rates. In this experiment, ligands are applied in a sudden movement across lipid membranes, accomplished by use of small unilamellar vesicles. POPC simulate the outer membrane, and formation of POPE/POPS unilamellar vesicles will simulate the inner membrane.

The protein-protein interaction is evaluated in real time using surface plasmon resonance (SPR) spectroscopy. SPR provides both the kinetic and equilibrium properties of the interaction obtained.

Mutagenesis Experiments in the C-terminal domains of TRPV1 AND TRPM8 Protein Channels

Raffi M. Manjikian and Yufeng Wei

This research involves mutagenesis experiments in the C-terminal domains of the TRPV1 and TRPM8 protein channels. These experiments provide an opportunity to study the effects of PIP_2 interactions. Point mutations in these regions reduce activation or desensitization of the channels, as well as alter the heat/cold sensitization. Structural and dynamic studies will be performed on these mutant proteins to

examine the effects of mutations on the structural integrity and dynamic properties of these channels. Dynamic studies on these mutants could reveal more insight into the activation mechanism, as different mutations only modify part of the protein channel function. The dynamic profiles corresponding to different mutations can also distinguish the mode of activation of these channels. Mutation sites are R786Q/K789Q and K789Q/R798Q for TRPV1, and K995Q, R998Q, R1008Q, Y1005F, and L1009R for TRPM8. These mutations demolish the channel thermo sensitivity or PIP2 binding.

Insights into the Regulation of TRPV1 and TRPM8 through C-terminal Domain Structural Analyses

Edward C. Twomey and Yufeng Wei

This research aims at characterizing the structures and dynamics of the C-terminal domains (CTD) of two Transient Receptor Potential (TRP) protein channels, TRPV1 and TRPM8. TRPV1 and TRPM8 are temperature-sensing TRP channels, and channel C-terminal domains are thought to be responsible for the regulation of channel functions by a range of extracellular stimuli, including temperature, phosphatidylinositol 4,5-biophosphate ($PI(4,5)P_2$), and Ca^{2+}/Calmodulin. The TRPV1 and TRPM8 CTDs are being produced to prepare for novel NMR spectroscopic studies. The entire CTD DNA sequences of both TRPV1 and TRPM8 have been successfully cloned into pET28b expression vectors, and numerous conditions have been tested for protein production. Thus far, protein expression has been limited. The DNA sequences are currently being optimized for improved bacterial expression. In a related study, the coiled-coil protein domains are being removed from the CTD sequences to facilitate TRPV1 CTD and TRPM8 CTD expression, and provide additional information on channel oligomerization.

NMR Dynamics of PED/PEA-15 protein Reveals Novel Binding Patterns with ERK2

Dana F. Cordasco, Edward C. Twomey, Raffi M. Manjikian and Yufeng Wei

Mitogen-Activated Protein Kinase (MAPK) signaling pathways are involved in the regulation of many cellular functions, including cell proliferation, differentiation, apoptosis and survival. The MAPK pathway is tightly regulated by protein-protein interactions, making it an ideal therapeutic target. Loss of MAPK pathway regulation leads to a variety of diseases, including diabetes and cancer. Extracellular-signal Regulated Kinase 1 and 2 (ERK 1/2) pathways, part of the MAPK family, are activated by a variety of external stimuli, including growth factors, hormones and neurotransmitters. Inactivated ERK2 is primarily found in the cytosol. Once the ERK/MAPK cascade is initiated, ERK2 is phosphorylated on its Thr-183 and Tyr-185 residues. This phosphorylation results in ERK2 stimulation, allowing it to redistribute in the cell nucleus and act as a transcription factor. Previous studies have shown that PED/PEA-15 (phosphoprotein enriched in diabetes/phosphoprotein enriched in astrocytes), a 15 kDa noncatalytic protein with a death-effector domain (DED), complexes with ERK2 in the cytoplasm and prevents redistribution into the nucleus. NMR studies detailing the fast backbone dynamics in the ps – ns timescale of PED/PEA-15, in its free-state and in the complex with ERK2, characterize the key motions involved in ERK2 recognition and binding, revealing striking binding patterns that orchestrate the reorganization of DED and immobilization of the C-terminal tail.

Professor Heping Zhou (Department of Biological Sciences)

Use of Microarray Technology to Monitor the Expression of Inflammatory Mediators

Hader Elashal, Patrick Fedick and Heping Zhou

The innate immune system encompasses many cellular and molecular mediators that play a vital role in the host's defense against invading pathogens. Cytokines and chemokines are small protein mediators that play key roles in regulating the host's inflammatory response during bacterial infections. Instead of traditional techniques, microarray technology allows multiplexed measurements of inflammatory mediators, which enables researchers to measure the expression of many inflammatory genes simultaneously with a minimum requirement of biological samples. This study involved optimizing the parameters for microarray printing such as the printing solution, spot spacing, and washing regimen. The DNA spots printed on the microarray substrate were processed and visualized by ethidium bromide staining and scanning on a microarray scanner. The experimental results indicated that the DNA spots could be successfully printed on the microarray slides, which is an initial step leading to successful printing of oligonucleotide arrays. This is important for measuring the expression of inflammatory genes following bacterial expression.