**Dr. Mike Ruane, Associate Professor and Chemistry Department Chair**

Dr. Ruane’s group working on the development of a process to generate chiral pyranones in few steps. The generation of chiral centers from achiral starting materials is of great interest to the pharmaceutical industry in making the industrial synthesis of pharmaceuticals less expensive. Dr. Ruane’s idea is to take advantage of different synthetic techniques with known stereochemical outcomes[[1]](#endnote-1) to quickly generate biologically relevant materials.

In Scheme 1, the synthetic plan is to generate a pyranone with four chiral centers with controlled stereochemistry. Steps **1** and **2** have been shown to be generated in the literature and have been replicated by my undergraduate researchers. Currently my undergraduates have shown the formation[[2]](#endnote-2) of product **3** can be accomplished with reasonable yields (~50%) and retained stereochemistry. During the summer of 2021, my researchers and I isolated good quantities of **2** with different hydroxyl acids as starting materials so a comprehensive examination of different R1 groups can be compared for activity.

For future research, Dr. Ruane’s group would like to generate products **4-6** and determine yield and industrial feasibility of process. If proven reliable, they would then move on to showing controlled generation of all four R groups on the ring, demonstrating chiral[[3]](#endnote-3) control in few steps of a pyranone—a structure of great medicinal interest, including anti-tumor and anti-diabetes research. We have also secured a pure -lactone (**2**) from Sigma-Aldrich to specifically test the synthetic model. Our plan is to streamline the process in making **3, 4** and **5** for use with the products made in 2021, and once the process is streamlined, proceeding to analyze the stereocontrol of the process[[4]](#endnote-4).

**Scheme 1:** Overall synthetic scheme for the generation of a substituted pyranone.

Students from the Ruane Research group have, outside of the worldwide interruption of COVID, presented poster research at regional and/or national meetings on a yearly basis.

**Dr. Alison Bray, Associate Professor**

Dr. Bray's research interests include trace metal analytical techniques, environmental contaminants, and the interactions of natural waters with solid matrices, including edible plants, soils, and rocks. Dr. Bray was awarded an E. Kika De La Garza Fellowship from the U.S. Department of Agriculture (USDA) in the summer of 2014 which allowed her to develop a much deeper understanding of the USDA’s mission. As part of the fellowship, Dr. Bray spent two weeks at the USDA-ARS-CNRC in Houston, Texas working with Dr. Michael Grusak. In 2015, Dr. Bray was awarded a four-year USDA Hispanic Serving Institution grant from the National Institute of Food and Agriculture to help to support these projects and educational initiatives.

Dr. Bray has mentored many TLU undergraduate research students on projects pertaining to contaminant metals in edible plants and in consumer products such as dog food and protein powders. One area of research has focused on rice, which accumulates arsenic in its tissues and seeds as it grows in flooded and anoxic paddies. Along with her students, she has grown arsenic and cadmium contaminated rice plants in the TLU greenhouse to understand the uptake of these elements by rice. Students are utilizing both ICP-OES and ICP-MS to analyze the samples.

A second project happening in Dr. Bray’s lab is utilizing “junk” polystyrene (Styrofoam) and converting it to a hyper-crosslinked polymer (HPC). The process utilizes a Friedel‐Crafts reaction to create more cross linkages in the polymer. Based on previous experiments in the literature (Dong et al.,2020), this HCP can be utilized to adsorb contaminants including arsenic from water.

Dr. Bray currently has two students working with her during the academic year continuing the hyper-crosslinked polymer project that was started in summer of 2021. Dr. Bray and her undergraduate students regularly present their work at both local and national meetings including the American Chemical Society, Texas Academy of Science and SACNAS.

**Dr. Rachel Chupik Adams, Assistant Professor**

According to the Alzheimer’s association, 1 in 3 seniors in the U.S. dies from Alzheimer’s Disease (AD) each year. This devastating disease, for which there is no cure, is characterized by progressive neurodegeneration and the irreversible loss of memory and cognitive ability. Although the cause and progression of AD is not yet well understood, numerous studies over the past two decades have begun to elucidate certain characteristics of the disease. Playing a pivotal role in the disease pathogenesis is copper, which interacts with many of the proteins known to be involved in AD, including strongly binding to the amyloid- ( peptide, enhancing aggregation and stimulating oxidative damage[[5]](#endnote-5) [[6]](#endnote-6) [[7]](#endnote-7). Numerous studies have confirmed that addition of copper chelators dissolves the plaques formed from the aggregation.1 Furthermore, rat and mouse models have actually regained cognitive abilities when treated with the copper chelator clioquinol (5-chloro-8-hydroxy-7-iodoquinoline).[[8]](#endnote-8) In spite of these promising results, clioquinol showed severe neurotoxicity in clinical trials, while many of the other chelators either fail to effectively bind the copper or do not meet the stringent requirements for crossing the blood brain barrier.1,3 Hence, there is a need to explore copper chelating agents that are both effective and non-toxic.

Dr. Adams and her research team explore neocuproine and its derivatives as potential drug candidates. Neocuproine (2,9-dimethyl-1,10-phenanthroline) shows negligible toxicity against endothelial cells and meets the criteria for crossing the blood brain barrier.[[9]](#endnote-9) Reactions of neocuproine with various copper salts yielded a range of highly colored copper complexes, including two new five-coordinate copper complexes that were structurally analyzed using single crystal X-ray diffraction. The basic reaction scheme is shown below.

**Scheme 1.** Reaction of neocuproine with various metal salts.

One of the problems with other copper chelators that have been studied for AD treatments is that they will indiscriminately bind either copper or zinc. Thus, Dr. Adams is also interested in the selectivity of neocuproine toward copper over other metals. Through metal displacement reactions, she found that copper will replace zinc in these neocuproine complexes, while the reverse process will not occur, leading to the conclusion that neocurpoine has a high selectivity for copper over zinc.

**Dr. Jacques Jean-Francois, Assistant Professor**

My current research interests encompass 2 axis that are not mutually exclusive.

1. **PEG-based hydrogels for therapeutic purposes**

Hydrogels are 3-D matrixes with a high-water content based on different types of polymers (natural or synthetic). Hydrogels have been used in a myriad of different applications such as enzyme immobilization, controlled release of therapeutic molecules or tissue engineering. The widespread use of those biomaterials stems among other properties from their ability to mimic environing human tissues when used as implants[[10]](#endnote-10).

Different types of strategies can be used to generate hydrogels mostly through chemical or physical methods leading to crosslinking. In our research, different types of polyethylene glycol (linear, branched) (PEG), a neutral polyether and a weakly immunogenic polymer which use have been validated in humans can be chemically crosslinked by example with bovine serum albumin (BSA) a well-characterized model protein to generate a highly hydrophilic matrix. Hydrogel’s properties (swelling, water content, mechanical properties) will depend on the characteristics of the crosslinking agents in this case PEG [[11]](#endnote-11) [[12]](#endnote-12).

The development of therapeutic biomaterials is thefocus of my research (graduate work, post-doc stint) but lack of funding has not enabled me to pursue it. The development of my research project will potentially create future collaborations with the University of Texas San Antonio and TSA Texas State University in San Marcos which have prominent scientists and more advanced resources dedicated to the field of biomaterials.

1. **Antioxidant properties of natural molecules and their analogues for potential therapeutic anti-inflammatory uses**

This second axis of my research with potential overlap with the first one is the result of a collaboration with Associate Professor Dr. Mohamed Touaibia of Moncton University (Canada) that has been ongoing from 2007 to the current time. My interest in this collaboration is to evaluate through *in vitro* tests (by example the DPPH test) the antioxidant properties of natural molecules and their analogues to identify potential leads for therapeutic purposes where there is an inflammatory component. We have focused specifically on natural molecules (flavonoids and phenolic acids) present in propolis as well as their analogues synthesized in the lab

1. Zimmerman, H. E.; Traxler, M. D. (1957). "The Stereochemistry of the Ivanov and Reformatsky Reactions. I". [*Journal of the American Chemical Society*](https://en.wikipedia.org/wiki/Journal_of_the_American_Chemical_Society). **79** (8): 1920–1923 [↑](#endnote-ref-1)
2. Dollinger, Ndakala, Hashemzadeh, Wang G.,, Wang, Y., Martinez,, Arcari, Galluzzo,, Howell, Rheingold, Figuero; *J. Org. Chem*., **1999**, *64*, 7074-7080 [↑](#endnote-ref-2)
3. Tanner, Birgersson, Gogoll, Luthmin; *Tetrahedron* **1994** 50, 9197-9824 [↑](#endnote-ref-3)
4. Wynberg; Staring *J. Am. Chem Soc.* **1982**, *104*, p166 [↑](#endnote-ref-4)
5. Baldari, S.; Rocco, G. D.; Toietta, G. *Int. J. Mol. Sci.* **2020**, *21*, 1069 [↑](#endnote-ref-5)
6. Takeda, A.; Takada, S.; Ando, M.; Itagaki, K.; Tamano, H.; Suzuki, M.; Iwaki, H.; Oku, N. *Neuroscience* **2010**, *171*, 443−450 [↑](#endnote-ref-6)
7. Giampietro, R.; Spinelli, F.; Contino, M.; Colabufo, N. A. *Mol. Pharmaceutics* **2018**, *15*, 808−820 [↑](#endnote-ref-7)
8. Cherny, R. A.; Atwood, C. S.; Xilinas, M. E.; Gray, D. N.; Jones,W. D.; McLean, C. A.; Barnham, K. J.; Volitakis, I.; Fraser, F. W.; Kim, Y.; Huang, X.; Goldstein, L. E.; Moir, R. D.; Lim, J. T.; Beyreuther, K.; Zheng, H.; Tanzi, R. E.; Masters, C. L.; Bush, A. I. *Neuron* **2001**, *30*, 665−676 [↑](#endnote-ref-8)
9. Pulukkody, R.\*; Chupik, R. B.\*; Montalvo, S.; Khan, S. K.; Bhuvanesh, N.; Lim, S.-M.; Darensbourg, M. Y. *Chem. Commun.*, **2017**, *53*, 1180-1183 [↑](#endnote-ref-9)
10. Bashir, S.; Hina, M.; Iqbal, J.; Rajpar, A. H.; Mujtaba, M. A.; Alghamdi, N. A.; Wageh, S.; Ramesh, K.; Ramesh, S. (2020) *Polymers*, 12 (11), 2702. [↑](#endnote-ref-10)
11. D’Urso, E. M.; Fortier, G. (1994) *J. Bioact. Compat. Poly.*, 9, 367 [↑](#endnote-ref-11)
12. D’Urso, E. M.; Jean-François, J.; Doillon, C. J.; Fortier, G.  (1995) *Art. Cells Blood Subs. Immob. Biotech.*, 23 (5), 587 [↑](#endnote-ref-12)