

SOAR Research – Faculty Proposal – Summer, 2017

Synthesis, Characterization, and DNA Binding of a Novel Rhodium Complex

Faculty: Stephen Dunham, Ph.D., Associate Professor of Chemistry

Student: Lauren Caronia

Project Start Date: May 30, 2017

Length of Project: 10 weeks

Description of the project

Synthesis, Characterization, and DNA Binding of a Novel Rhodium Complex

Cancer is a disease where cells continue to grow and divide because they lack regulatory control over cell division found in “normal” cells. An essential part of cell growth is for a cell to make a copy of its deoxyribonucleic acid (DNA) before it divides to form two new daughter cells. Drugs that bind DNA and cause a change in DNA structure and/or shape can slow down or even stop the process of DNA copying essential for cell growth. These drugs are especially useful at killing tumor cells that lack the ability to repair DNA damage. Cisplatin is a platinum metal-based drug that takes advantage of DNA-binding reactions for its chemotherapeutic activity. Platinum drugs have been used clinically for nearly 40-yrs and continue to be some of the most common drugs for cancer treatment and research development today.¹ We are interested in exploring the synthesis of another transition metal, rhodium (Rh), which also binds to DNA and could be developed into a new antitumor drug. Several dirhodium complexes have been synthesized in our laboratory, and we have studied their DNA binding reactions.² By synthesizing a variety of Rh complexes in our research, we are learning more about the fundamental chemistry of Rh compounds, and how to adjust (tune) their ability to bind to DNA, and hopefully someday kill cancers cells.

Synthesis and Characterization of a Novel Rhodium Complex

The Rh complex needed for this research project is not available for purchase from any commercial vendor. The primary goal of the project will be to carry out the syntheses, isolation, and characterization of this novel dirhodium complex.

DNA binding reactions

Once enough of the dirhodium compound has been prepared and characterized, our next goal will be to determine how quickly the Rh-compound reacts with large double

¹ T.C. Johnstone, K. Suntharalingam, and S.J. Lippard “The Next Generation of Platinum Drugs: Targeted Pt(II) Agents, Nanoparticle Delivery, and Pt(IV) Prodrugs”, *Chem. Rev.*, **2016**, *116* (5), pp 3436–3486

² S.U. Dunham, T.S. Remaley, B.S. Moore, D.L. Evans and S.U. Dunham, “Isolation, Characterization, and DNA Binding Kinetics of Three Dirhodium(II,II) Carboxyamidate Complexes: Rh₂(μ-L)(HNOCCF₃)₃ where L= [OOCCH₃]⁻, [OCCF₃]⁻, [HNOCCF₃]⁻”, *Inorganic Chemistry*, **50**, pp 3458-3463 (2011).

stranded DNA (dsDNA). We will use salmon testes dsDNA because it provides an inexpensive source of high quality dsDNA with a enough random DNA sequences to provide all possible binding sites for the new Rh-compound.

Roles and responsibilities

- The project director, Stephen Dunham, will train Lauren in the synthesis, and purification of dirhodium compounds, and the use of instrumentation, and data analysis to characterize the final molecular structure of the compound.
- Lauren will prepare and present her findings during regular research meetings (~30-60 min each day).
- Lauren will maintain a research laboratory notebook that will include regular and complete entries. Keeping a comprehensive laboratory notebook is a fundamental part of research in chemistry. The notebook will have an updated table of contents. Daily entries will be clearly written and organized with experimental details, clear references to location and organization of electronic data, and a summary of results from each experiment. Prof. Dunham will look at Lauren's notebook weekly throughout the summer and provide informal feedback. The notebook will be submitted to the Prof. Dunham upon completion of SOAR.
- Throughout the summer, Lauren will prepare summary figures that clearly illustrate the results of key experiments. These summary figures will form the basis for poster or research talks about her SOAR research.
- Lauren will prepare a final report/poster before the end of the summer. She will present her report/poster at the Annual Student Scholarship and Creative Endeavors Day in Spring of 2018.

Project Timetable

- Weeks 1-4: Setup dirhodium synthesis reactions and training on the operation of various instruments including HPLC for characterization of synthesis reactions, and compound isolation.
- Weeks 5-7: Optimize synthesis and scale up reaction size to purify enough compound to characterize the structure of the Rh-complex by NMR spectroscopy.
- Weeks 8-10: Study reactions of Rh-complex with dsDNA to determine the speed of the DNA binding reaction and if time allows determine the type(s) of DNA bases that bind to the Rh-complex.

Summary of benefits

Student engagement in discipline-appropriate scholarly research. Lauren will be engaged in bioinorganic chemistry research that includes reading and summarizing primary literature, planning and performing experiments that require the use of several different instruments, and collecting/analyzing/organizing significant amounts of data. In addition, she will prepare and receive feedback on various visual representations of experimental results (i.e. preparing figures in a format appropriate for publication in a Chemistry journal). Prof. Dunham will work with Lauren to prepare a scientific poster

for presentation of her research at the 2017 Landmark Summer Research Conference, and for the 2018 Spring Annual Student Scholarship and Creative Endeavors Day.

Impact on faculty, campus community, and discipline. Lauren's work on this project will contribute to the discipline of bioinorganic chemistry by synthesizing a new Rh-complex and studying its reactions with DNA. This project will benefit Prof. Dunham by building upon work of several former research students (Donchez & Kuperavage Summer 2011, Donchez Honors '12-'13, Bartulovich Summer 2014, Honors 14-'15, and Mates Summer 2016). Lauren's results will help us better understand the types of complexes formed between dirhodium compounds and DNA. It is anticipated that her research will be part of a future publication about these compounds in a peer reviewed Chemistry journal. By presenting her research during the summer to the SOAR group, and as a poster at both the 2017 Landmark Conference and at the Moravian Scholarship and Performance Day in April 2018, Lauren's work will impact the campus community at Moravian by exposing others to interesting and complex nature of bioinorganic chemistry research.

Budget Items

- \$500.00 to offset the costs for reagents required for synthesis and characterization of a new dirhodium compound.
 - dirhodium trifluoroacetate, 2 g \$ 518
- Remaining equipment and reagent expenses will be covered by the Department of Chemistry at Moravian College.

Dirhodium trifluoroacetate is a commercial starting material required for the synthesis of many dirhodium complexes. It is a consumable reagent so there are no standard supplies of this compound available at Moravian.

Project Title: Synthesis, Characterization, and DNA Binding of a Novel Rhodium Complex

Student: Lauren Caronia, Undeclared major with intent to major in Neuroscience, expected date of graduation in 2020

Faculty Mentor: Stephen Dunham, Ph.D., Associate Professor of Chemistry
On-campus housing not requested

I am very excited to have the chance to participate in a SOAR project. I wish to participate in this project because I think it will provide useful information. The creation of a new Rhodium compound could help others in the future in developing new drugs that more efficiently kill tumors in cancer patients. Thus, creation of this new compound would be a very valuable and important step forward in helping to treat cancer. I am also very interested in chemistry and it would be a fun learning experience for me to be able to expand my knowledge of chemistry in a way that classroom learning cannot. During this project, I would have the opportunity to spend many hours in the laboratory on the research which will allow me to be more advanced in class laboratories that I will be taking in the future. Chemistry is also an important component of my intended major of Neuroscience so this project will also help me to become more comfortable in using the chemistry skills that I will need in the future. I also hope to work on research for Neuroscience for some part of my career after graduation so this experience will help me to see what it is like to carry out a science-based research project. Overall, this project will be a great learning experience and the outcome will help others in the future.

One of my expected outcomes for this project is to gain experience working in a laboratory. This includes learning procedures that are not covered in other science classes. This also includes taking my previous laboratory knowledge and using it to complete new and more challenging tasks. I also expect to be able to create a new Rhodium compound. This is a procedure that will require me to quickly learn new skills and use them in conjunction with the knowledge I already have which is a task that I am prepared and excited for. I can then help to determine how quickly this new compound will react with large pieces of DNA. I expect this project to not only help me further my own knowledge and experience but to also provide important and useful information that will help others. I expect to be challenged during this research project but I am excited and ready to take on those challenges.