CHEM 435: Chemical Synthesis Laboratory (FALL 2014)

General Information
Instructor: Prof. Jason Shearer
e-mail: shearer@unr.edu
Office: CB 225
Office Hours: M, W 1:30 – 2:30 P.M. (or take your chances and just drop on by)

General Course Goals:
This is an advanced synthesis laboratory, and will likely be unlike any instructional laboratory you have taken. The goals of this course are to:
   a) Give you exposure to advanced synthetic techniques, including air-free manipulations
   b) Introduce you to chemical literature searches
   c) Give you experience following and expanding on literature preparations
   d) Provide you with an opportunity to improve your technical writing
In short, this course is designed to give you an idea of what working in an academic laboratory is like. As stated in goal c, you are “expanding upon literature preparations.” This is why the lab experiments given at the end of this packet are vague. They are to provide you a jumping off point so that you can explore the literature, design an experiment, and explore new reactions of your own design that have not been performed by another researcher.

Core Objectives and SLOs:

1) Core Objectives Satisfied By This Course:
Core Objective 14 (Application):
   Students be able to demonstrate their knowledge and skills developed in previous Core and major classes by completing a project or structured experience of practical significance.

2) Student Learning Outcomes:
Upon completion of this course:
SLO1) Students will be able to research a specific compound, or a family of compounds, to propose a synthetic route for isolation of this compound.
SLO2) Students will be able to perform advanced manipulations of apparatus relevant to a synthetic chemistry laboratory, use a Schlenk line to synthesize oxygen- and moisture-sensitive products.
SLO3) Students will be able to characterize chemical compounds using modern spectroscopic techniques.
SLO4) Students will be able to maintain a laboratory notebook following scientific best practices.
SLO5) Students will be able to communicate findings in a format consistent with the scholarly standards of the chemical sciences.
SLO6) Students will be able to articulate and follow ethical principles in a scientific context, including professional standards of laboratory practice, the communication of literature research without plagiarism, and the crediting of collaborators.
3) Correlation Between Core Objectives and SLOs:

- SLO1 aims to satisfy CO14 by building upon CO3 (critical analysis and use of information) and CO4 (physical and natural science)
- SLO2 aims to satisfy CO14 by building upon CO4 and CO9 (science, technology, and society)
- SLO3 aims to satisfy CO14 by building upon CO4 and CO9
- SLO4 aims to satisfy CO14 by building upon CO1 (effective composition and communication), CO2 (quantitative reasoning), CO3, CO4, and CO9
- SLO5 aims to satisfy CO14 by building upon CO1, CO2, CO3, CO4, and CO9
- SLO6 aims to satisfy CO14 by building upon CO1, CO2, CO3, CO4, CO9, and CO12 (ethics)

Required Materials:

- Laboratory goggles
- Closed toed shoes
- Long pants/skirts
- Laboratory Notebook

Grading and Requirements:

This course is graded on the A – F scale using pluses and minuses. The division of points in this laboratory will be as follows:

- 50%: Formulate laboratory experiments by searching the chemical literature and complete your laboratory experiments (500 pts total).
- 40%: Formulate well-written laboratory reports in the style of an *Inorganic Chemistry* or *Journal of the American Chemical Society* article (400 pts total)
- 10%: Be good lab citizens (this includes performing peer review!; 100 pts. total)

Grades will be assigned according to the following rubric:

A: 900 – 1000 pts.
A–: 885 – 899 pts.
B+: 875 – 884 pts.
B: 800 – 874 pts.
B–: 785 – 799 pts.
C+: 775 – 784 pts.
C: 700 – 774 pts.
C–: 685 – 699 pts.
D+: 675 – 684 pts.
D: 600 – 674 pts.
D–: 585 – 599 pts.
F: 0 – 584 pts.
Laboratory Rules:

- Never work alone in the laboratory and without an instructor/TA present.
- Always!! Wear appropriate eye protection, such as goggles, at all times.
- Appropriate clothing is also required. Lab coats are strongly encouraged. No open-toed shoes or shorts are allowed.
- Keep all working areas you are using clean. Daily cleaning and an end-of-the-semester cleaning are required.
- Prevent accidents by anticipating any undesirable events that may occur. When in doubt ask JMS or the TA. Always stay alert for actions that may lead to imploding vacuum systems, exploding reaction mixtures, rupturing water hoses, evolution of noxious gases, flying syringe plungers and needles, etc. You are responsible for researching safety hazards of each experiment. Repeated mishaps may result in a zero for lab performance.
- Clean NMR tubes, syringes, needles, cannulas, and filter sticks as soon as possible after using them to avoid clogging — residual chemicals in them decompose and solidify.
- Because the lab is located next to a lecture room with very thin walls we unfortunately cannot have a radio playing during the lab period.

Caution: Do not soak filter sticks in base bath, nor put syringes, needles spatulas, metal or rubber objects into the cleaning baths.

Safety:

We have tried to reduce the hazards associated with this laboratory; however, this course still has inherent dangers. You are responsible for understanding the following safety precautions. Failure to work in a safe manner will result in your dismissal from this course. Goggles will be worn all times by anyone in the lab. Shorts, skirts, or sandals will not be allowed. There will be no eating or drinking in the laboratory. Ipods/mp3 players cell phones are not to be used while working in the lab.

Waste:

All chemical waste must go in the appropriate waste container. There will be at approximately six waste containers, such as halogenated organic waste, non-halogenated organic waste, wash acetone, lab trash (contaminated gloves, paper towels, filter paper, etc.), solids (used MgSO₄, silica gel, etc). You are expected to know what you are working with and how to dispose of it properly. Please ask if you are not sure where to put your waste. Fill out the waste manifest with the chemical names (no abbreviations of formulas) and estimate the amount for each component immediately upon placing the items in the waste.

Attendance, Behavior, Accommodations, and Surreptitious Covert Video and/or Audio Recording:

As this is a laboratory class attendance is mandatory. Failure to attend will result in a failing grade. Plagiarism will not be tolerated and may result in a zero for an experiment, an F for the course, and/or further disciplinary action by the university. In this course you
will be working in small groups. Each member of the group must carry their weight, however all reports turned in must be done individually.

If you have a disability and will be requiring assistance please contact me or the Disability Resource Center as soon as possible to arrange for appropriate accommodations.

Surreptitious or covert video-taping of class or unauthorized audio recording of class is prohibited by law and by Board of Regents policy. This class may be videotaped or audio recorded only with the written permission of the instructor. In order to accommodate students with disabilities, some students may have been given permission to record class lectures and discussions. Therefore, students should understand that their comments during class may be recorded.

Oral Pre-laboratory Presentation:

At least two days prior to a new experiment each group must meet with Prof. Shearer (CB225) for a pre-laboratory oral presentation. The purpose of this is to assure that your group has done the necessary legwork and is prepared for the practical experimentation. The group will also be required to demonstrate appropriate understanding of the experiment and provide a written plan outlining procedures for the experiment. Everyone in the group should be prepared to discuss the chemistry associated with the corresponding experiment—especially any potential safety concerns. This will include writing chemical equations on the board. All members of the group are expected (read required) to participate and attend the pre-lab meeting together.

Laboratory Reports:

The laboratory reports are due no later than two weeks after the scheduled completion of the experiment for peer-review (i.e. your classmates). You will then have one week to revise and resubmit the manuscript to me. The final report will be due one week after the last experiment and will not be subjected to peer review.

All reports are graded out of a possible 100 points. Reports turned in late will have ten points (out of a possible 100) deducted from the final score per day of delay. The reports are to be typed on white paper with chemical equations drawn with a program such as chemdraw/chemsketch—no hand drawn structures! The reports are expected to be well written and in your own words. You will be working in groups; however, reports are to be submitted and written individually. Reports do not have to be long and are not intended to be tedious, either to write or to grade. They must however be complete, proofread, and turned in. Failure to turn in your lab reports will result in a failing grade.

Laboratory reports should have the format of a scientific paper submitted for publication to Inorganic Chemistry or Journal of the American Chemical Society for example.

They should include:

• Title and author(s)
Include the names of your partner(s) in the author list. Use an asterisk by your name to indicate “to whom the correspondence should be addressed”. Lab reports are to be written individually!
• **Abstract** (in a few sentences indicate what is described in the report)—this is different from an introduction.

• **Introduction** (what is the background related to the experiment performed?)
A description of the chemistry pertinent to the experiment with a brief summary of the goals of the experiment. This should be no more than 2-3 pages. Some relevant questions listed in the description of each experiment ought to be addressed here. (Note: this is not an abstract)

• **Experimental Section** (what did you do?)
Very detailed and concise description of the laboratory procedure carried out in the lab. Including: whether the solvents and reactants were purified, and how. What means of identification and characterization were used (include models of instruments)? Yields, melting points, IR and NMR peak positions, magnetic data and other relevant data should be reported here. Look in papers published in recent journals to write this section. Simply copying the experimental procedure from literature sources is not appropriate.

• **Results and Discussion** (what happened? and so What?)
Briefly explain the reaction carried out include items like the balanced equation or equations describing the overall synthesis. Did you get what you wanted? Color and temperature changes, IR, NMR data, yield description (e.g. high/poor/moderate etc), and spectroscopic evidence of the purity of your product should be given here and interpreted. This section should contain comparisons with the literature data, such as magnetic, IR, and NMR data interpretation. If something went wrong explain what happened and why, then offer suggestions as to how to avoid those problems. Attach spectra such as IR and NMR, and also copies of relevant pages of your laboratory notebook. Compare your results with those expected or reported in the literature for a given compound. The questions listed in the description of each experiment might be helpful here. Present conclusions. (Results and Discussion can be presented together or separately)

• **Conclusion** (self explanatory)

• **References**
Your report should be well referenced back to the original literature (consult the ACS style guide and a current journal article from *Inorg. Chem.* for details on how to do this)

**Peer Review.** It has been my experience that reviewing manuscripts by other scientists makes my writing and science better. Furthermore, subjecting my manuscripts to peer review improves the quality of not only my written document, but also the science that it contains. Therefore we will be performing peer review. Think of me as your editor. I will pick two members of the class to read through your paper, who will then submit typed comments to me. Things to think about when peer reviewing:
  a) Does the data presented fully support the conclusions
  b) Is the manuscript fully referenced
  c) Does the writing make sense
  d) Are there typos, grammatical errors, etc.
  e) Do you suspect plagiarism or data fabrication
Your review should consider these. I strongly suspect that item e (plagiarism or data fabrication) will not be an issue for this class. When going through and inspecting for item d, please point out the mistakes in the manuscript. Real life reviewers do!

**Laboratory Schedule.** The following page contains a laboratory schedule. So that we do not run short on supplies the labs have been staggered. Although specific cut-off days have been listed, you will notice that some slack has been put at the end of the semester. These are not for you to have a few days off, but instead are placed in the schedule to allow for an extra day here and there in case it takes longer than four lab periods for you to do particular experiments. Please do not continue to the next experiment until you have completed the experiment you are working on.

**What if my experiment does not work?** In the event that you absolutely cannot successfully complete an experiment talk to Prof. Shearer. Failure to complete an experiment, as long as an honest effort to perform it, will not affect your grade. However, a lab report on a failed experiment will still be required.
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Dec 11 10:15 am (T)  Check-out/Exam  Check-out/Exam  Check-out/Exam  Check-out/Exam
**Metal-Metal bonding**

Synthesis and characterization of [Mo(OAc)$_2$]$_2$, K$_4$Mo$_2$Cl$_8$$\cdot$2H$_2$O, Mo$_2$Cl$_4$(PR$_3$)$_4$

Introduction

Metal-metal multiple bonds have been known now for about 40 years. Re$_2$Cl$_8^{2-}$ was the first such complex characterized. One of the most famous compounds with a quadruple bond is tetraacetatodimolybenum(II). This molybdenum compound is unusual as it is diamagnetic; mononuclear Mo(II) compounds are usually strongly paramagnetic. These anomalies can be explained by invoking M-M bonding in the dimmer, and this Mo(II) acetate dimmer is recognized as having a M-M quadruple bond. The Mo(II) acetate dimmer must be converted into the octahalide. From the halide the phosphine complex may be synthesized. We will use 1,3,5-triaza-7-phosphaadamantane (PTA) as the phosphine in this laboratory.

Since most Mo(II) compounds, including the acetate dimmer, are readily oxidized by atmospheric oxygen, they must be prepared under an inert atmosphere. This may be done using either a dry box or Schlenk techniques; the latter will be used in this laboratory.

**Tools at your disposal:**

IR, NMR, X-Ray, UV-Vis, mass spectrometry

**Questions to be addressed:**

1. Explain why [Mo(H$_2$O)$_6$]Cl$_2$ is paramagnetic and [Mo(OAc)$_2$]$_2$$\cdot$(H$_2$O)$_2$ is diamagnetic.
2. Show using an MO diagram which orbitals are used for the $\sigma$, $\pi$, and $\delta$ M-M bonds. Consider the Z axis to be the M-M bond axis.
3. Re$_2$Cl$_8^{2-}$ was the first M-M quadruple bond discovered. What is the symmetry of this molecule? Using the information in question 2 how can you show that this must be the symmetry?
4. What is the balanced reaction for the synthesis of [Mo$_2$(OAc)$_4$]? 

**References:**

NiDach Experiment

N,N’-bis(mercaptoethyl)-1,5-diazacycloheptane, H₂bme-dach, and its nickel complex.

(bme-dach)Ni is an N₂S₂Ni complex that is used in bioinorganic chemistry to model certain Ni-enzyme active sites. Options for studying the reactivity of (bme-dach)Ni: (1) Alkylation with dibromo alkanes; (2) Metallation reactions of (bme-dach)Ni with Ni, Cu, or Zn; or, (3) you may design your own new experiment with instructor approval far in advance. A possibility is to try a reaction that has been done with (bme-dac)Ni and to compare it to that of (bme-dach)Ni. Remember you must have a well-stated hypothesis and a way to test it.

NiN₂S₂ compounds can also be used as ligands for other metal-centers. The lone-pairs on the coordinated thiolate sulfur atoms can bridge to form multi-metallic complexes. M(CO)₄ complexes are common. It would be interesting if you made one of these compounds as well.

You will need to isolate and characterize all products. Tools at your disposal will be IR, UV-vis, cyclic voltammetry, NMR, and X-ray crystallography. You will be given the reference for the synthesis of (bme-dach)Ni; the rest are up to you to find in the (bme-daco)Ni literature.

_Inorganic Chemistry, 2001, 40, 3601-3605._

_Inorganic Chemistry, 2008, 47, 2056-2063._

**Tools at your disposal:**

IR, NMR, X-Ray, UV-Vis, mass spectrometry

**Problems to be addressed.**

1. What kind of reaction is required for the synthesis of H₂bmedach?
2. Why not use NiCl₂ instead of Ni(acac)₂? Are Nickel Salts poisonous?
3. Does order of reagent addition matter (metal and ligand)?
4. Describe the Ni-S bond orbital overlap.
5. How does S-modification by electrophiles affect the electronic character of Ni in (bme-dach)Ni?
6. How do charge transfer and d to d transitions differ?
7. What factors influence the geometry of N₂S₂Ni?
8. What is the effect of sulfur-metallation on (bme-dach)Ni (i.e. formation of bridging M(CO)₄ compounds)?
9. What bioinorganic systems can N₂S₂Ni complexes model?
Complexes of the tris-pyrazoleborate (Tp) are used extensively throughout inorganic chemistry. In this laboratory you will attempt to prepare Tp* (the methyl derivative of Tp) and two of its nickel complexes:

A main focus of this lab is to have you search the literature using SciFinder Scholar to develop your synthesis. Therefore I strongly recommend starting your literature searching at least a week before your meeting with me.

**Tools at your disposal:**

IR, NMR, X-Ray, UV-Vis, mass spectrometry

**Questions to be addressed:**

1. How does the synthesis of Tp* differ from other syntheses you have performed?
2. How does the UV-Vis spectrum of the 4-coordinate chloro adduct differ from the 6-coordinate complex? What is accounting for the differences? For those wishing to model these compounds computationally you can perform TD-DFT studies (ask me about them!).
3. The NMR spectra of the complexes should look different than “normal” ones. Why?
4. If you can obtain a crystal structure of these complexes, describe how the structure differs from ideal geometry.
Meso-tetraphenylporphyrin and Fe and Zn Complexes

Porphyrs are important biological cofactors, and have a long history in synthetic, physical and biological chemistry. In this lab you will be attempting to prepare an Fe(II), Fe(III), and Zn(II) complex of a prototypical porphyrin: meso-tetraphenylporphyrin. You will be using a newly developed efficient procedure to prepared the Fe(III)-Cl and Zn(II) derivatives (found in Molecules, 2011, 16, 2960). To make the Fe(II) derivative you will need to reduce the Fe(III) porphyrin. Please do a literature search to identify appropriate synthetic procedure for this complex.

Tools at your disposal:

IR, NMR, X-Ray, UV-Vis, mass spectrometry

Questions to be addressed:

1. The Zn complex should be highly colored. What is the origin of the intense color? Is this unusual? Why or why not?
2. Identify the bands in the UV-vis spectrum?
3. Heme is a porphyrin complex of Fe(II) and is an O₂ transporter. What is the product upon exposing your Fe(II) complex to O₂? How might you modify the porphyrin structure to generate the O₂ adduct to mimic the reversible reaction of reduced heme with O₂?
4. The Zn(II) complex should produce a “normal” NMR spectrum while the Fe(III) will not. Why?
5. In this experiment you made a symmetric porphyrin. Asymmetric porphyrins have many uses in materials and biological chemistry. How could you modify your synthesis to make an asymmetric porphyrin? What would be the disadvantage of such a modification?
**Jacobson’s Catalyst**

Epoxides are an important class of organic molecules frequently used in chemical synthesis and found in nature. A number of methods are available to synthesize epoxides, one of which involves the oxidation of an olefin. Until relatively recently no effective methods were available to prepare highly enantioomerically enriched epoxides from unfunctionalized olefins. This was solved by Eric Jacobson, who developed a salen derived Mn complex capable of performing olefin epoxidation with high entantimetric yields. In this lab you will prepare Jacobson’s catalyst and oxidize two styrenes (styrene and alpha-methylstyrene) forming the corresponding styrene-oxides. Bleach will be used as your oxidant in a dichloromethane solution of olefin.

Lead article: Larrow and Jacobsen *Organic Syntheses* **1998**, 75, 1. (DOI: 10.15227/orgsyn.075.0001)

**Tools at your disposal:**

- IR, NMR, chiral GC, mass spectrometry

**Questions to be addressed:**

1. What is the role of formation of the tartrate salt of diamminocyclohexane? What would happen if you did not perform this step?
2. Was your synthesis of the 3,5-di-tert-butylsalicylaldehyde successful? What problems did you encounter?
3. What is catalyst load and what was your catalyst load?
4. What is e/e and what is yours? Which enantiomer predominated?
5. How does the size of the olefin influence the e/e? Why is this trend observed? What do you predict would happen to your e/e is you oxidized 1,2-dihydronaphthalene?