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Incorporating the Scientific Contributions of Research Faculty into the Chemical Education of Undergraduate Students at Emory University

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An abstract of
a thesis submitted to the Faculty of Emory College of Arts and Sciences
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Abstract

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A new method of teaching chemistry at the undergraduate level is presented. Organometallic Chemistry is used as a model to incorporate research articles relating to the subject written by Emory faculty members. Several articles are presented and it is shown how they would be beneficial to introduce to undergraduate students in this course. Using the current syllabus of the course, they are given a proposed placed in the course in which they will be most effectively introduced.

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Table of Contents

List of Figures

List of Tables

Part I

Introduction

Emory University is at the forefront of academic research in the world. With its undergraduate curriculum ranked 20th among Universities in the United States, students can expect to learn from faculty who are leaders in their research fields of expertise. [1] This gives undergraduate students the opportunity to learn directly from these faculty members by taking part in the undergraduate research opportunities that are often available at Emory. [2] The students that are able to engage in research collaborations not only use what they learn from their courses and apply it to relevant work in a field of investigation, but are also given a reason to feel proud to belong to an institution where amazing discoveries are made. Even though research opportunities for undergraduate students have increased in numbers in recent years, not every student participates in research during their undergraduate career. Reasons for this can vary from limited funding, or the availability of space in laboratories, or the lack of interest on the part of the students to participate in research, as it is not something that everyone enjoys. [2] This leaves students who are not greatly aware of the research done at their university, apart from those who independently seek that knowledge. In order to address this, a plan is proposed to introduce the contributions of research faculty into an undergraduate course to enrich the material and concepts students learn from said course.

1.1 Benefits of Introducing Research Faculty Work into the Curriculum

Even if not participating in research directly, students can still benefit from learning about the research done at their institution. By exposing students to the research published in academic journals, the student's proficiency in using the primary academic literature could be developed. [3] It could also have the same benefits as undergraduate research when it comes to increasing a student's awareness about the projects that are under investigation around them as well as being able to relate what they learn from lecture to these topics, creating a deeper understanding of their importance and relevance.

1.2 Selection of an appropriate course for proposed plan

In order to develop this new approach to the structure of undergraduate courses, a course must be selected as a pilot to incorporate faculty research. This thesis will present a plan to modify a current course being taught in the Chemistry Department of Emory University in order to properly achieve this goal. A higher-level course with a contemporary content and provocative developments in Chemistry, CHEM 327-Organometallic Chemistry, is chosen to introduce the students to the research published by faculty from the Chemistry department at Emory University. This advanced course is an elective for Chemistry majors and is taught during the fall semester. Students registering for this course would have completed two semesters of organic chemistry and two semesters of general chemistry (or equivalent AP credit). [4] With the foundation from four semesters of introductory chemistry courses students should be able to begin exposure to the chemical literature. Furthermore, even though the class is an elective for chemistry majors, the course is open to students interested in chemistry from other majors at Emory College, providing an opportunity to complement an undergraduate's education in the liberal arts.

1.3 Introduction to Organometallic Chemistry

Organometallic chemistry is the study of chemical compounds containing metal-carbon bonds. It is the combination of aspects in Inorganic chemistry and Organic chemistry.[5] The importance of the study of the subject can be understood by how both components have a tremendous role in chemistry. The Organic components come from carbon-containing compounds, where the carbon is directly bonded to the metal. Carbon is one of the most abundant elements in the universe by mass and also plays an important role in living organisms.[6,7] The second component of organometallic chemistry comes from the metal elements. Metal elements compose most of the periodic table and posses unique properties. Although all classified as metals, the presence of *d* electrons in the valance shell gives transition metals different reactive properties, which makes this group of metals the most widely used in Organometallic compounds.[5]

1.3.1 Advances in Organometallic Chemistry

There have been many advances in the field of Organometallic chemistry since the discovery of the first organometallic compound in 1760. A timeline of some of the major events in the field are given in Table 1.

Table 1 Timeline of Major Events in Organometallic Chemistry

Year	
1760	Louis Claude Cadet de Gassicourt synthesizes the first organometallic compound [8]
1827	Zeise's salt, one of the first examples of an alkene complex and the first platinum/olefin complex, is prepared [9]
1848	Edward Frankland discovers diethylzinc, the first organozinc compound discovered [10]
1863	Charles Friedel and James Craft prepare organochlorosilanes [11]
1890	Nickel carbonyl discovered by Ludwig Mond [12]
1899	Introduction of Grignard reaction by Victor Grignard [13]
1900	Paul Sabatier introduces hydrogenation in organic compounds [14]
1909	Paul Ehrlich introduces Salvarsan, an early arsenic-based organometallic compound, for the treatment of syphilis [15]
1912	Victor Grignard and Paul Sabatier win the Nobel Prize [16]
1930	Henry Gilman introduces Gilman reagent [17]
1951	Walter Hieber awarded Alfred Stock prize for work with metal carbonyl chemistry [18]
1951	Ferrocene is discovered [19]
1963	Karl Ziegler and Giulio Natta win Nobel prize for Ziegler-Natta catalyst [20]
1965	Cyclobutadieneiron tricarbonyl discovered [21]
1968	Heck reaction discovered [22]
1973	Geoffrey Wilkinson and Ernst Otto Fischer win Nobel prize for sandwich compounds [23]
1981	Roald Hoffman and Kenichi Fukui win Nobel prize for Woodward-Hoffman rules [24]
2005	Yves Chauvin, Robert Grubbs, and Richard Schrock win Nobel prize for metal-catalyzed alkene metathesis [25]
2010	Richard Heck, Ei-ichi Negishi, and Akira Suzuki win Nobel prize for their work in palladium-catalyzed coupling reactions in organic synthesis [26]

As seen in this table, the number of Nobel prizes in chemistry given to work done in Organometallic chemistry has increased in the recent years, which can be attributed to the high impact made by research in this field. The number of organometallic articles published in journals on organometallic chemistry has also continued to increase over the years.[27, 28]

The study of organometallic chemistry has provided important conceptual insights and surprising chemical structures. Organometallic compounds have served as useful catalysts for industrial processes and organic synthesis. Some of these catalysts have been useful in preferentially forming one enantiomer of a chiral product. Links have also been formed between organometallic chemistry and other fields including biochemistry, nanoscience and nanotechnology, and materials science. Organometallic compounds have also been used as catalysts in green chemistry where carbon dioxide (CO_2) and methanol (CH_3OH) are converted to acetic acid (CH_3COOH) with no significant by-products. It is also speculated that catalytic organometallic chemistry will play a large role when climate change becomes severe enough to force governmental action on the use of renewable fuels.[5]

1.3.2 Organometallic Chemistry in the Current Undergraduate Curriculum

Given the amount of advances in the field of Organometallic chemistry, it is only appropriate that the subject be introduced at the undergraduate level. Miessler and Spessard argue that Organometallic chemistry can be taught to undergraduate students who have taken a year of general chemistry and at least one semester of organic chemistry.[29] While many institutions have adopted an organometallic chemistry course into their curriculum, there has not been any universal guidelines adopted to teach an undergraduate course in the subject. The American Chemical Society does not require an Organometallic chemistry course in certified undergraduate programs and therefore does not publish guidelines for its instruction.[30] The classical division of chemistry into five subdisciplines (Organic chemistry, Inorganic chemistry, Analytical chemistry, Physical chemistry, and Biochemistry) are argued by Goedhart to dominate the undergraduate chemistry curriculum. As an interdiscipline, Organometallic chemistry coursework is limited by the lack of textbooks suitable for undergraduate students, as most are geared towards advanced graduate level courses.[31] This leads to an unknown difference in topics covered in Organometallic courses and different methods to teach the subject. These methods can range from classic lecture-style courses to courses in which undergraduates present the course material to their peers using assigned papers.[3,30] While this can present a challenge in unifying what undergraduate students are learning across the country in their Organometallic chemistry course, it also presents a unique opportunity as one can present the topics they deem important in a more provocative and stimulating style.

1.4 Objective of this Thesis

In order to successfully integrate the research done by faculty members into the Organometallic course, this paper will:

(1) Identify the relevant research work published by Emory faculty members done in the Organometallic field or employed to accomplish a different goal.

(2) Propose where the research contributions can be successfully integrated into the undergraduate Organometallic chemistry curriculum in order to enrich the material and concepts presented and help students see the connection between what they are learning and the research being done at this institution.

Part II

Incorporating Faculty Research

2.1 Organometallic Course at Emory University

The main goal of CHEM-327, Organometallic chemistry, is “to apply the knowledge that students have acquired from their introductory Organic chemistry and General chemistry courses in the development of an understanding of the chemical reactivity of Transition Metal Complexes.” [4] The current topics listed in the syllabus of the course are given in Table 1.2.

The content of the course follows a traditional list of topics presented in graduate level courses in Organometallic chemistry from different programs, including the graduate program in the department of chemistry at Emory University. First, the principles of structure and bonding in transition metals are reviewed, followed by an in-depth discussion of reaction mechanisms and ending with different applications in the area of Organic synthesis. In order to assess the student’s understanding of the material, the students are first challenged with three exams. Then, the fourth component of the student’s grade comes from an assignment at the end of the semester in which the student must identify a research paper published by a faculty member from the chemistry department at Emory that involves an Organometallic transformation and then use the chemical transformation to write a research proposal. While this assignment has proven to be successful in familiarizing students with a particular project of a faculty member, it also limited the exposure to other Organometallic research in the chemistry department. The development of a more effective method to expose students in the course to a greater amount research published by members of the faculty at Emory is the goal of this project.

Table 2 Topics Listed in Syllabus for CHEM 327 [32]

1) Introduction
• Organometallic Chemistry of the Transition Metals • Building Bridges Between Organic and Inorganic Chemistry
2) Fundamentals of Structure and Bonding
• Definitions of Transition Metals • Oxidation states of d-electron configuration • Formal Charges • Counting d-electrons • Coordination numbers and geometries • d-orbitals • Ligands and electron count • Hapticity and bonding nomenclature • 18 electron rule • Types of bonds in coordination compounds • Atomic and molecular orbitals • Simplified bonding descriptions
3) Reactivity of Organometallic Compounds
• Ligand Substitution • Oxidative Addition-Reductive Elimination • Migratory Insertion • β-Hydride Elimination • Four-center reactions • (2+2) Mechanisms • Activation of ligands to external attack • Reductive coupling • Transmetallation
4) Synthetic Applications:
• Hydrogenations • Hydrosilylations • Hydrozirconation • General aspects of Catalytic C-C bond forming reactions • Heck coupling reactions • Suzuki coupling reactions • Stille coupling reactions • Transition metal complexes with alkenes and alkynes • Transition metal carbene complexes • Metallacycles • Alkene (olefin) metathesis • Alkyne metathesis • Ziegler-Natta polymerization • Transition metal Allyl and Arene complexes • C-H activation

2.2 Incorporation of Faculty Research

The Chemistry department has been responsible for publishing dozens of papers every year in peer-reviewed journals in their respective divisions. Although the Emory Chemistry Department's website only lists two of its current faculty members as organometallic researchers, there are others (both past and present) that have done organometallic work that has been classified as inorganic or organic research.[33] The work published in Organometallic chemistry is analyzed for its applicability to the course material and ability to be integrated into the course. In this proposed change to the lecture, various articles are to be integrated into the course during lectures while students would be expected to read the article for background and further information. The papers will be selected to compliment the order of the material covered in the lecture.

Students must be able to gain the background knowledge of Organometallic chemistry prior to the introduction of the first article. After the lectures in fundamentals of structure and bonding an article on mechanisms (the next course topic) can be discussed in class. Subsequent articles will be paired with course topics to compliment the lecture materials.

Once the introductory topics are complete, the focus will be on incorporating the scientific contributions of Emory faculty members during the latter part of the course, the part dealing with scientific applications. Research done by Emory faculty members prior to their time at Emory is also considered, as it not only expands upon the pool of research topics to choose from, but it also allows faculty members to be recognized for their work throughout their life and not only be limited to the time they have spent at this institution.

2.3 Integration of Organometallic Research Articles

2.3.1 Introductory Topics

Although the main incorporation of scientific papers will occur with the last part of the course, it is also important to introduce some scientific work that relates to the fundamentals and reactivity of Organometallic compounds. Three research articles were chosen to illustrate the elaboration of heterocyclic systems by using transition metal ions. The first article published by professor Dennis Liotta and his collaborators entitled “Effects of Substitution on Intramolecular Alkoxypalladation Carbonylation Reactions” (Figure 1), could be introduced early in the course. Here, a Palladium catalysts is used in order to create a highly stereoselective method to build cyclic ethers. As seen below, only one of the possible stereoisomers is observed when the Palladium catalyst is used as opposed to the result by other electrophile induced reactions. [34]

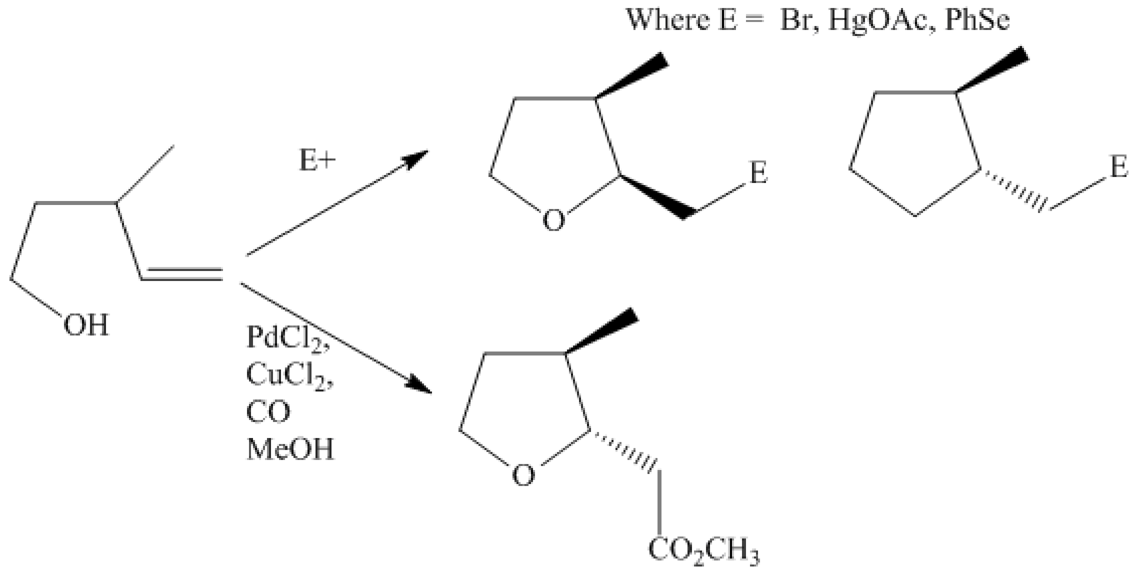


Figure 1: Electrophile-Induced Cyclization &Alkoxypalladation Carbonation Reactions

By introducing this research article students would be exposed to one of the many advantages of Organometallic reactions, selectivity. In addition, the transformation is also an opportunity to show students the correlations between what they learned in Organic chemistry and the reactivity of transition metals. For instance, the students are familiar with the Markovnikov type of addition across alkenes, and this research article is an illustration of that principle. This transformation would also allow to students to work alongside the Oxidative Addition-Reduction Elimination and Migratory Insertion, as the key steps in the construction of the ester portion of the heterocyclic system.

A second interesting article that can be introduced within the reactivity portion of the course is “Palladium Catalyzed Aerobic Oxidative Amination of Alkenes: Development of Intra- and Intermolecular Aza-Wacker Reactions”, in which professor Christopher Scarborough was a collaborator. The paper describes the usefulness of Palladium-catalyst in oxidative amination reactions. The paper outlines a catalytic cycle, as shown below. [35]

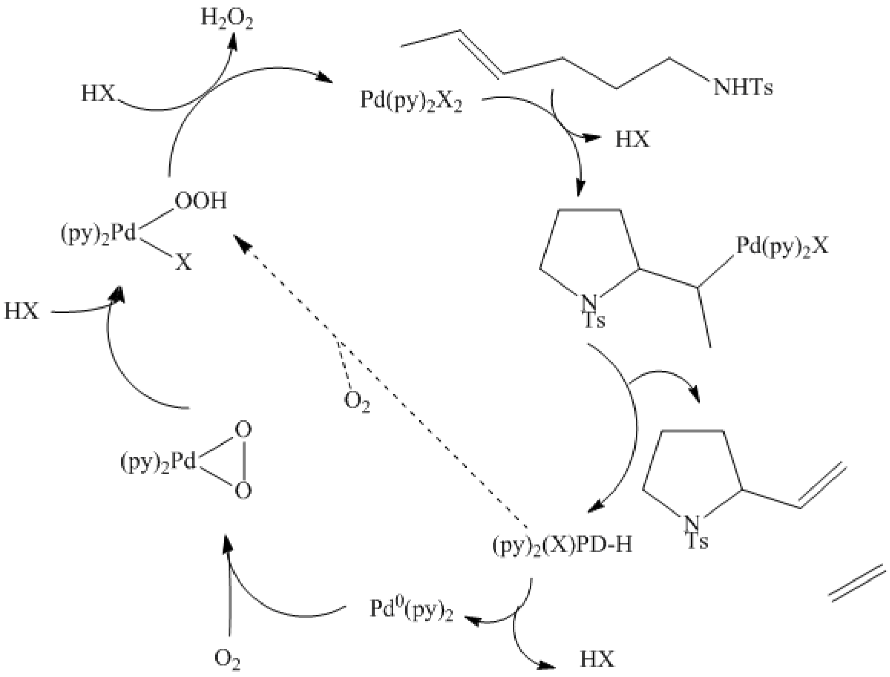


Figure 2: Mechanism of Intramolecular Oxidative Amination

This chemical transformation introduces the important concept of catalytic cycles, showing how the catalyst is able to react with the organic products without being used up. While this catalytic cycle might look difficult at first, students can fully understand each reactive step as they pertain to the elaboration of the final product and the regeneration of the metal catalyst. Students would be reminded of the Migratory Insertion and beta-Hydride Elimination reactions as they are important steps in the sequence of reaction.

A third article that is proposed to be introduced along with reactivity fundamentals is professor Padwa's "Gold-Catalyzed Cycloisomerization of N-Propargylindole-2-carboxamides: Application toward the Synthesis of Lavendamycin Analogues". This is a recent article that cites the importance of gold as a catalyst in the activation of carbon-carbon triple bonds. This Organometallic reaction is an important step for the formation of lavendamycin analogues, which could be used as antitumor antibiotics. The relevant Organometallic reaction is outlined below as well as the structure of the desired product. [36]

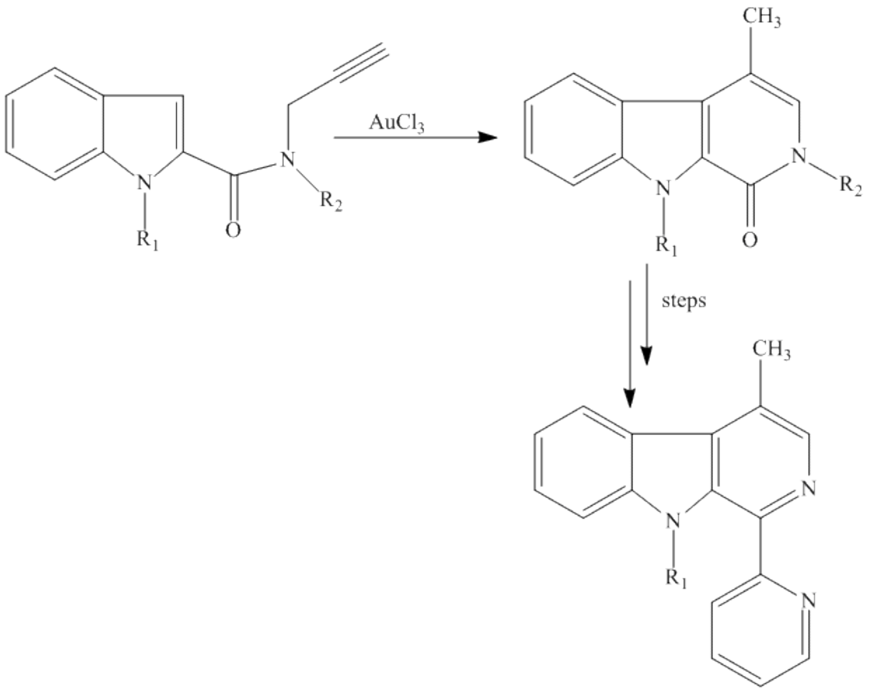


Figure 3: Gold-catalyzed cycloisomerization reaction for lavendamycin analogue intermediate

A concept that can be learned from studying this reaction is the use of metal catalysts to activate alkynes and create fused rings. This paper also highlights the importance of Organometallic chemistry in the synthesis of drugs, an important application of the science. This is the first of many papers where the students will be able to clearly see the direct correlation between the course material and real world applications. Although not difficult, this paper would be go well at the end of the reactivity, as a preview of many other synthetic applications.

2.3.2 Coupling Reactions

Coupling reactions are defined as reactions in which two hydrocarbon fragments are coupled with the aid of a metal catalyst. [37] This is a broad term and the course focuses on a couple of coupling reactions throughout the semester: Heck, Suzuki, and Stille.

The Heck reaction is the Palladium catalyzed reaction of an unsaturated halide (or triflate) with an alkene and a base to form a substituted alkene. [38]

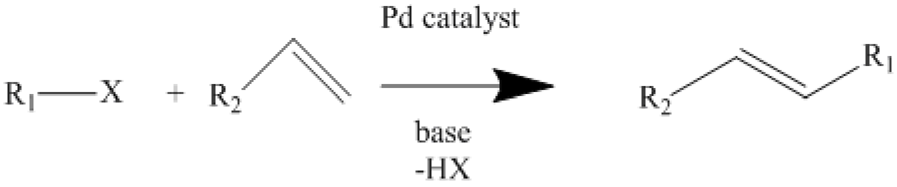


Figure 4: General Scheme of the Heck Reaction

The Suzuki reaction is the Palladium catalyzed reaction of an aryl- or vinyl-boronic acid with an aryl-or vinyl-halide to form a couple product. [39]

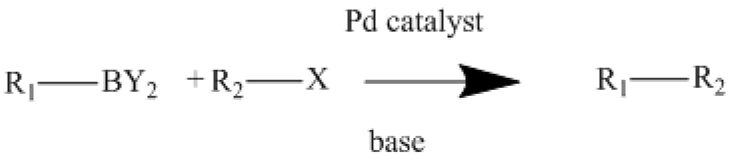


Figure 5: General Scheme of the Suzuki Reaction

The Stille reaction is the Palladium catalyzed reaction of an organotin compound with an organic halide to form a coupled product.[40]

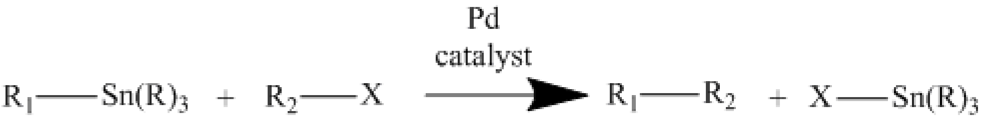


Figure 6: General Scheme of The Stille Reaction

There are four articles that primarily involve coupling reactions that are proposed to be incorporated into the course.

First, Dr. Simon Blakey's collaborative work, "The First Suzuki Cross-Couplings of Aryltrimethylammonium Salts", gives a great example of innovative work using coupling reactions. Their work led to the creation of a novel catalyst system capable of activating aryl – ammonium bonds for Suzuki cross coupling reactions, benefiting the scientific community as arylamines are readily available and have lots of applications as pi-nucleophiles. [41] The reaction that the course would focus on is below.

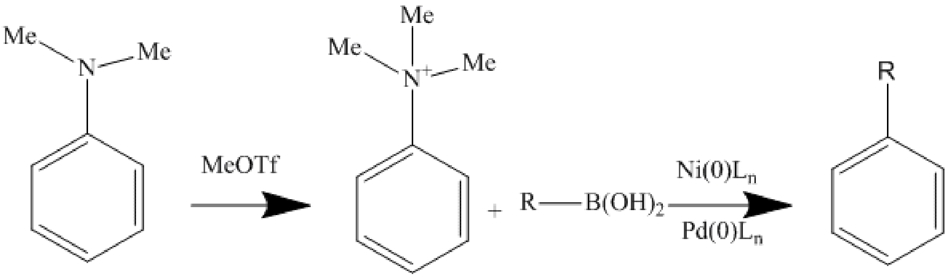


Figure 7: Cross Coupling of Aryltrimethylammonium Salts

As seen above this reaction resembles the Suzuki reaction, where the triamethylammonium takes the place of the halide. This article is of great relevance to the organometallic course as it shows the usefulness of the Suzuki reaction when it comes to synthesis of organic products. It also addresses the wide range of coupling reactions that can be used to achieve certain organic products.

An interesting article in which organometallic chemistry is used to synthesize an anti-cancer agent is Professor Liotta's work "Synthesis, Antiviral Activity, Cytotoxicity, and Cellular Pharmacology of 5-Carboranyl-Pyrimidine Nucleosides". They worked together in order to synthesize new boron containing nucleosides that would stop cancer cells in humans utilizing boron neutron capture therapy (BNTC) . In order to synthesize compounds with a high boron content, a criteria for ideal compounds used for BNTC, they create an intermediate using organometallic chemistry. [42]

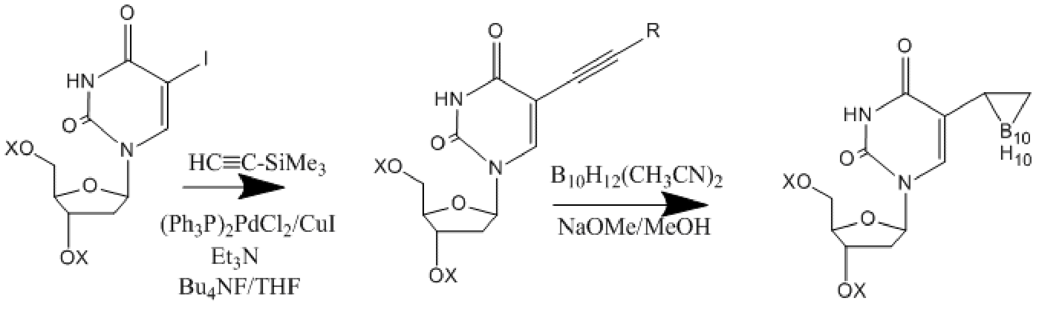


Figure 8: Synthesis of Boron Containing Nucleosides

Here, a palladium catalyzed coupling reaction is used to add the alkyne to the ring, a step needed to create a high boron-containing compound. Although a deviation from the three reactions being studied, one can see the resemblance to other coupling reactions. Students will be able to learn of a more practical application of organometallic chemistry, one relating to fighting cancer.

Lastly, another article that relates coupling reactions to health is Dr. Goldsmith "An Efficient Synthesis of 2-Aryl and 2-Alkenyl-3-Alkoxy-Cyclohexenones by a Modified Stille Reaction". Dr. Goldsmith worked on analogs for the angiogenesis inhibitor, fumagillin, which is also used in the treatment of cancer. His team was able to use a modified Stille coupling reaction to synthesize 2-alkeynyl-3-alkoxy-cyclohexones, which could be used as fumagillin analogs, in a milder and more direct way.[43]

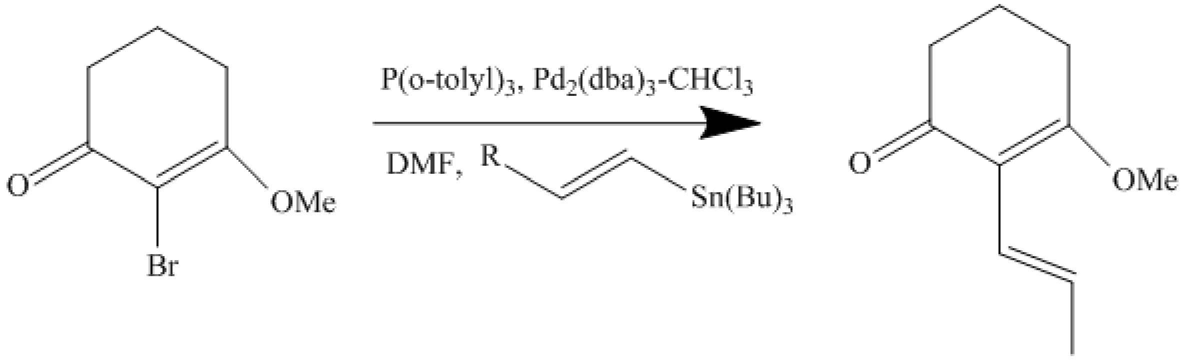


Figure 9: Modified Stille Reaction to Synthesize 2-Aryl and 2-Alkenyl-3-Alkoxy-Cyclohexenones

This is another research paper by an Emory faculty member that uses organometallic reactions to find a way to fight cancer. It emphasizes the Stille reaction, which is a topic that is directly covered in this course. The reaction above shows the palladium catalyst and organotin reactant, typical of a Stille-like reaction. Not only is this reaction beneficial for a student to become familiar with, but it's also an interesting application of organometallics.

2.3.3 Carbenes

Carbenes are an important element of organometallic chemistry. They are defined as molecules containing a neutral carbon with two unshared valance electrons.

Figure 10: General Structure of a Carbene

They are important in chemistry as they are able to act as electrophiles or neuclophiles in cyclopropanation reactions, such as the one give below. [44]

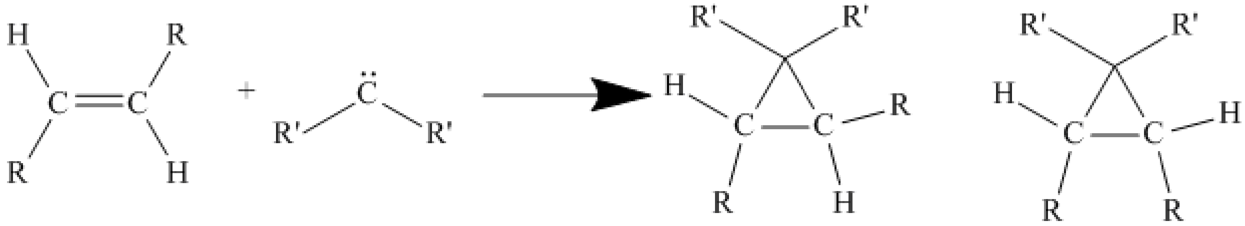


Figure 11: General Cyclopropanation Reaction

Dr. Davies summarizes his work with a carbene precursor in "Methyl (E)-4-Phenyl-2-diazo-3-butenoate". This compound is important in cyclopropanation reactions catalyzed by a metal. This cyclopropanation can be applied to the synthesis of pharmaceutical targets. The compound also reacts to synthesize highly functionalized seven-membered rings as well as bridged bicyclic systems. [45] These reactions are given below:

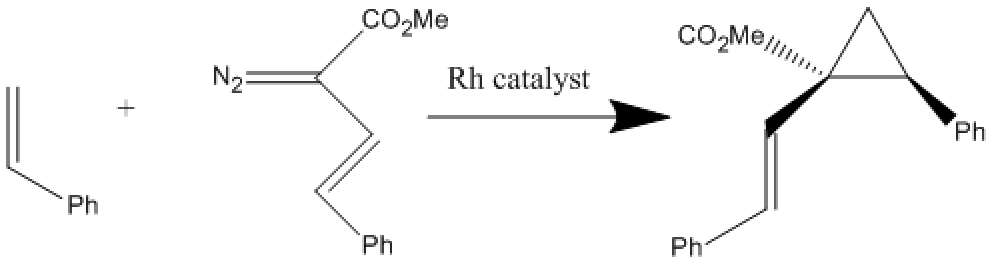


Figure 12: Cyclopropanation reaction between the butenoate complex and styrene

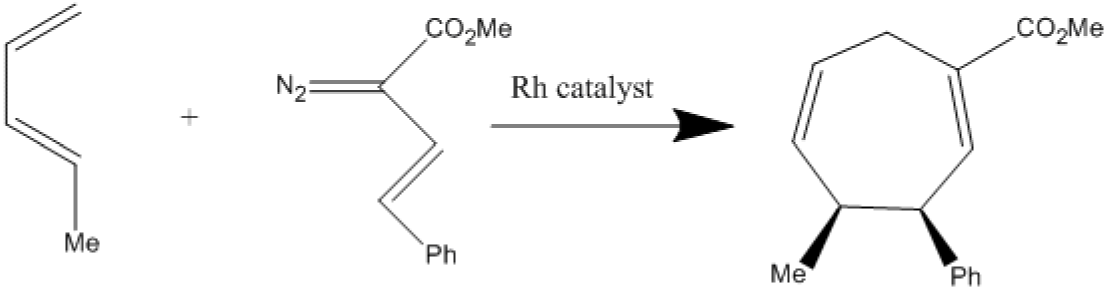


Figure 13: Reaction for Synthesis of Seven-Membered Ring using the Butenoate complex

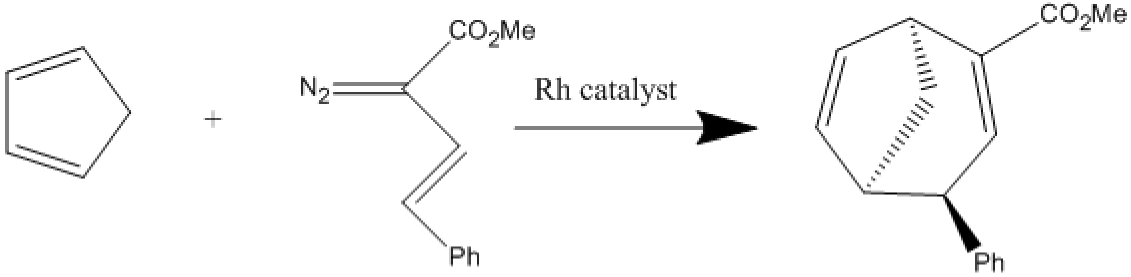


Figure 14: Reaction for Synthesis of Bicyclic System using Butenoate Complex

This is a very informative paper that could be used in the organometallic class as it addresses the different applications for carbenes in organometallic chemistry. It not only addresses the different chemical reactions it can participate in, but it also delves into their usefulness in pharmacology.

“Sequential Rhodium-, Silver-, and Gold-Catalyzed Synthesis of Fused Dihydrofurans” by Dr. Davies deals with not only carbene cyclopropanation reactions but also a novel concept, a triple cascade sequence involving three different metal catalysts. His team not only discovers a sequential way to synthesize the fused dihydrofuran product, but also create a one-pot procedure to do so. [46] The synthesis reaction is given below in both a condensed and detailed version:

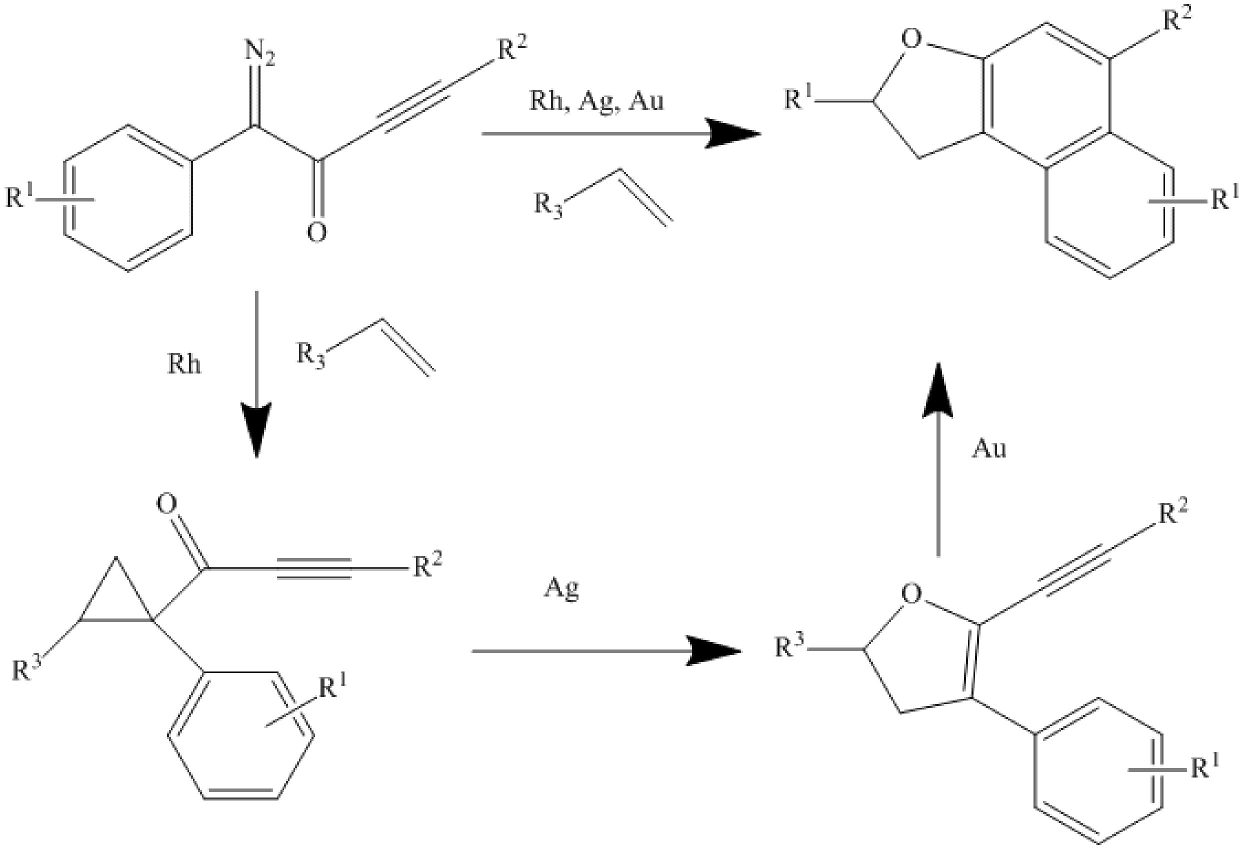


Figure 15: Triple Cascade Sequence for the Synthesis of Bezo-fused Dihydrofuran

Although only the first reaction in the multi-step sequence deals with the cyclopropanation of a carbene, the paper as a whole serves to enhance the carbene section in the course. The paper not only describes an interesting and novel concept in synthetic chemistry, but it also highlights the diversity in the type and use of metal catalysts. As seen in the reaction above, three different catalysts are used and each catalyst has a different effect in the process of the reaction. A student can gain a lot by familiarizing themselves with the work published on carbene and cyclopropanation reactions.

2.3.4 Metallacycles

A metallacycle is a compound similar to a cabocyclic compound, except that a metal has replaced a metal carbon center. They are important reactive intermediates in catalysis. [47]

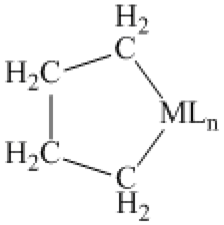


Figure 16: A standard metallacycle

Dr. Liebeskind took advantage of the reactivity of metallacycles in his paper "Regiospecific Total Synthesis of (±)-Nanomycin A Using Phthaloylcobalth Complexes. He demonstrated that a cobalt metallacycle could be used to synthesize complex naphthoquinone natural products. This was an important discovery as many naphthoquinone-derived natural products contained antibiotic and antitumor properties. [48] An important intermediate reaction for this synthesis consists of forming carbon-carbon bonds using an insertion-reductive elimination reaction such as the one given below.

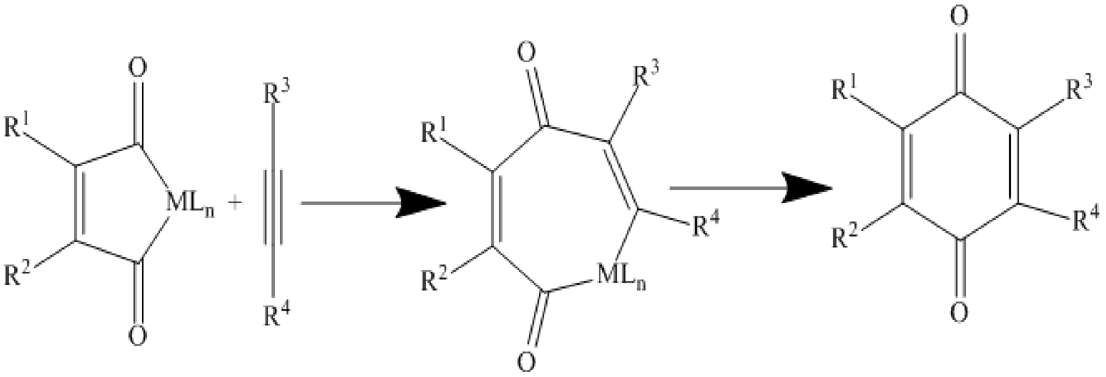


Figure 17: Insertion-Reductive Elimination Reaction with Metallacycle

Here we find another reaction that not only has applications in organometallic synthesis, but also in creating antitumor and antibiotic agents.

2.3.5 Metathesis

Metathesis refers to the redistribution of chemical bonds. There are two general types of metathesis covered in this course, Olefin (or alkene) and alkyne metathesis. Both types of reactions are generally driven by a metal catalyst. [49.50]

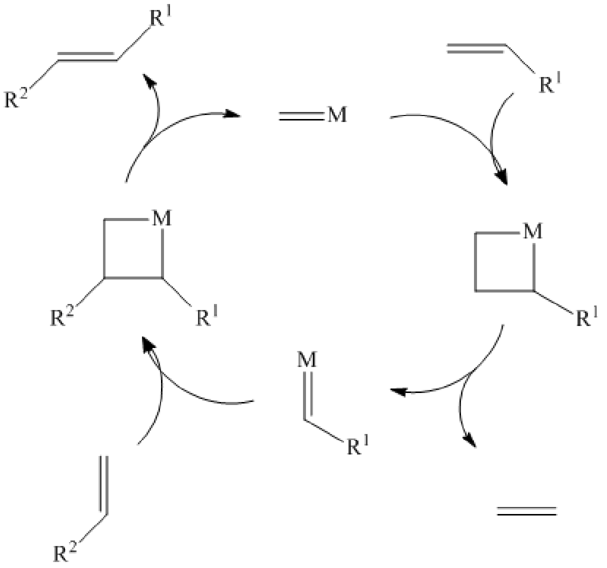


Figure 18: General Olefin Metathesis Reaction Catalyzed by Metal M

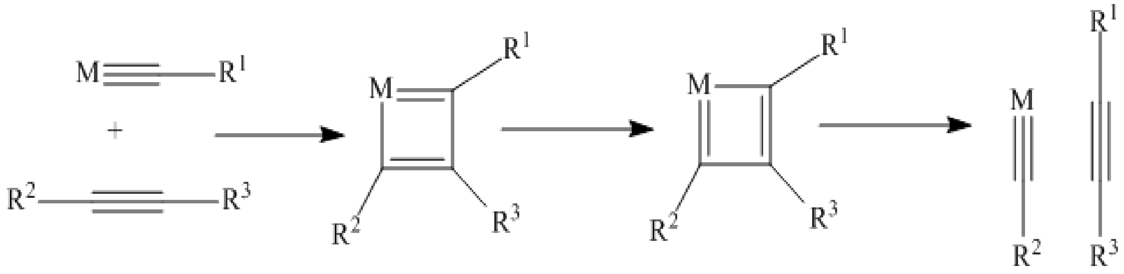


Figure 19: General Alkyne Metathesis Reaction Catalyzed by Metal M

There are two articles by Dr. Crowe that can be incorporated into the study and teaching of carbenes in the organometallics class. In “Highly Selective Cross Metathesis of Terminal Olefins” He describes the importance and advantages of metathesis for the olefin synthesis while providing a pathway for these reactions. The metathesis reactions are concluded to simpler, especially coupled with the Molybdenum catalysts, which are readily available. An important reactivity fact of styrene is also discussed, as it inhibits self-metathesis of terminal alkyl olefins and only slowly self-metasize themselves, also improving reaction outcomes. [51]

Figure 20: Metathesis reaction with Styrene

Dr. Crowe also explains the importance of metatheses reactions in the synthesis of Allylsilanes, which are important neuclophiles in organic synthesis. His team also develops a more efficient synthesis for these compounds and explains the mechanism in “Preparation of Alkylsilanes via Cross-Metathesis”. This organometallic reactions uses readily available organic reagents in order to achieve the results, also making it a more favorable method. [52]

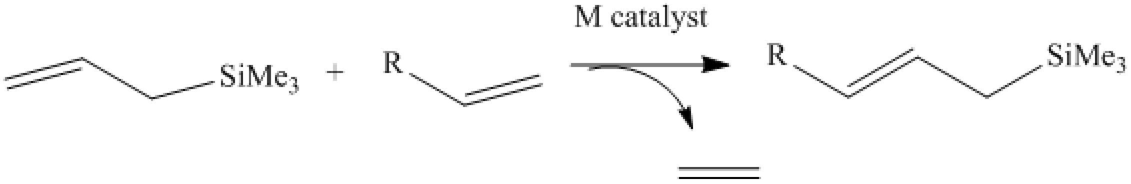


Figure 21: Synthesis of Alllylsilane by Metathesis Reaction

Both of these papers by Dr. Crowe's team show the usefulness of organometallic reactions in the synthesis of organic products. Students will be able to how this organometallic topic is directly used in research, and should therefore be studied at the same time metathesis is introduced.

2.3.6 Further Advanced Applications

The following papers are proposed to be covered at the end of the course, after all the topics outlined in the syllabus have been discussed. They delve into more advanced topics that would help the course come to a good conclusion. The students would be able to utilize everything they have learned throughout the semester when learning about these articles and the science behind them.

The first of these papers is Dr. Blakey's "Enantioselective C-H Amination Using Cationic Ruthenium (II) – pybox Catalysts". Here Dr. Blakey describes his work to design a proper Ruthenium catalyst for an asymmetric amination reaction. He uses this catalyst in order to create an enantioselective pathway for this amination reaction, the reaction of which is given below. [53]

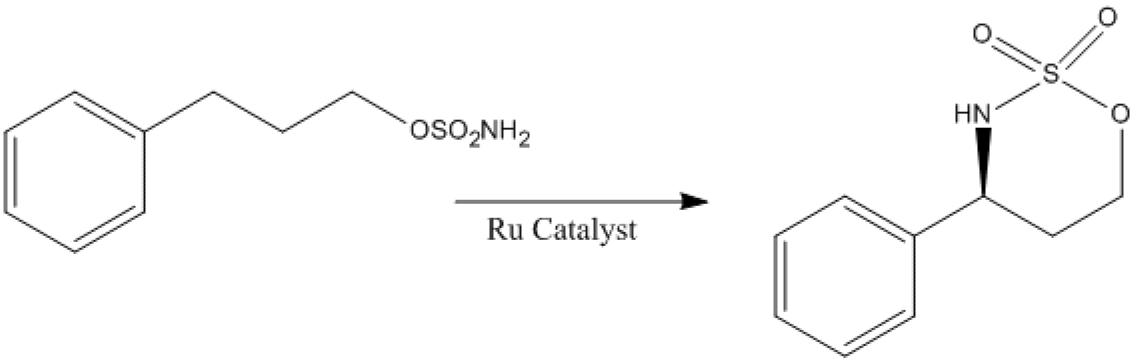


Figure 22: Enantioselective C-H Animation by Ruthenium Catalyst

The focus of this work is different from the papers studied before as the emphasis is heavily placed on the design of the catalyst. This is something that is applicable to every topic that is covered in the course, as the selection of the proper catalyst will improve the reaction one works with. The paper also deals with the activation of carbon-hydrogen bonds, a topic covered late in the semester, making it a great selection for it to be covered at the end of the course.

The next article that is proposed to be introduced at the end of the course is Dr. Liebeskind's "Ambient Temperature Synthesis of High-Enantiopurity N-Protected Peptidyl Ketones by Peptidyl Thiol Ester-Boronic Acid Cross-Copling". Here they introduce a cross-coupling reactions of thiol esters and boronic acid compounds in order to synthesize enantiopure N-protected peptidyl ketoenes. Palladium was used as a catalyst and carboxybenzyl (Cbz) was used in order to protect the amine group during the cross coupling reactions. [54]

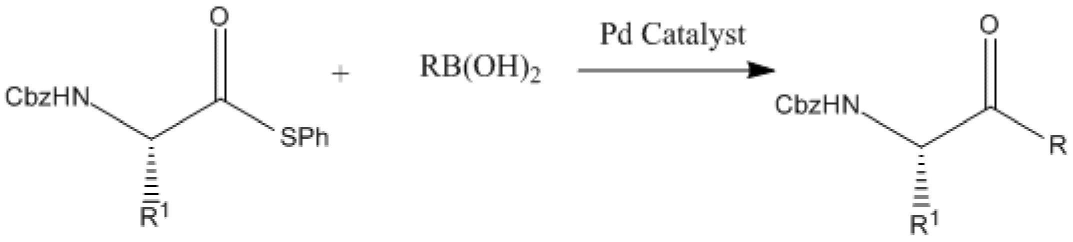


Figure 23: Highly Enantioselective Synthesis of N-Protected α-Amino Ketones Reaction

The chemistry from this paper brings together a lot of topics covered in the class as well as topics covered in organic chemistry, making the study of this paper useful in building bridges between different areas of chemistry. First, the main organometallic reaction used by this process is a cross coupling reaction, a topic that is covered thoroughly in the class. Next, the concept of protecting groups is also used here in order to reduce the reactivity of the amine. This is a concept typically covered in organic chemistry which a student can use to understand the process used by the researchers. Lastly, the concept of reactions in which only one enantiomer is desired is also studied here. This is another research paper where the organometallic chemistry is used to more efficiently synthesize a product.

Another interesting and relevant article to be included here is “Dual Mechanisms of DNA Damage by MoCH$_3$(η^3-allyl)(CO)$_2$(phen) Complexes” by Dr. Mohler. This is a very different kind of article from the ones introduced before. Dr. Mohler explains the two general mechanisms by which this Molybdenum compound damages DNA. While not explicitly outlining the specific mechanism by which this metal compound cleaves bond in DNA molecules, Dr. Mohler writes about the experimental steps taken in order to deduce the mechanisms by which this degradation happens. Dr. Mohler concludes that the two general mechanisms are backbone cleavage and base modification. [55]

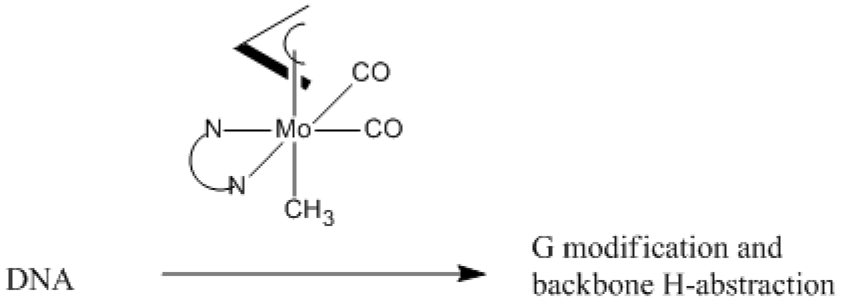
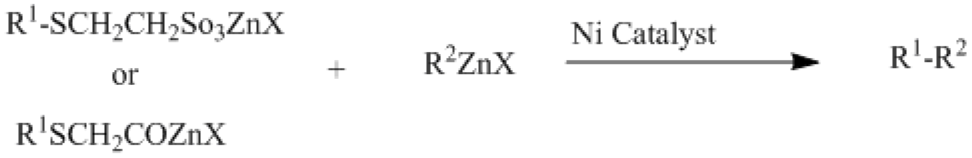


Figure 24: Damage to DNA caused by MoCH$_3$(η^3-allyl)(CO)$_2$(phen) Complexes

This article requires a good comprehension of organometallic chemistry and scientific approaches to different problems to understand. Since this article will be introduced later in the semester, a student will be expected to possess both from the material thought and the experience studying other research articles. The application of organometallic chemistry is used here in order to understand a process that happens *in vivo.* An interesting concept is applied here where experiments are done in a lab in order to understand what happens in organisms. This is another article that allows students to expand their understanding of the potential of organometallic chemistry research.

The last article to be introduced in this section is “Bioinspired Organometallic Chemistry” by Dr. Liebeskind. His team works on mimicking nature’s ability to achieve highly efficient metal-mediated catalysis of thiorganics at an ambient temperature. Four metalloenzymatic processes are studied in order to better understand their natural occurrence: the organozinc cross-coupling of thioethylsulfonates and thioglycolates, the thiol ester cross coupling using alkylative activation, the thiol ester-boronic acid cross coupling mediated by CuTC, and the selective Zn(II)-mediated alcoholysis of S-benzoylglycolic acid. [56]



$$\begin{matrix} R^1\text{-}SCH_2CH_2So_3ZnX \\ \text{or} \\ R^1SCH_2COZnX \end{matrix} + R^2ZnX \xrightarrow{\text{Ni Catalyst}} R^1\text{-}R^2$$

Figure 25: Organozinc Cross-Coupling of Thioethylsufonates and Thioglycolates

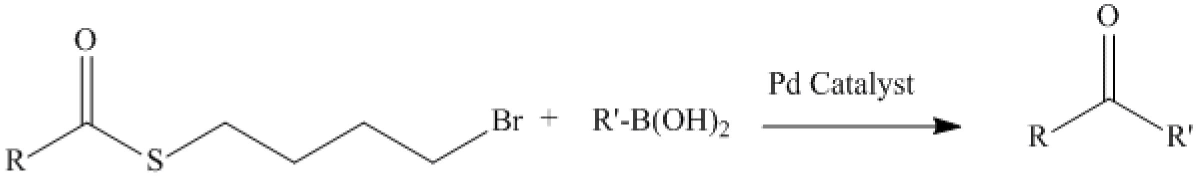


Figure 26: Thiol Ester Cross Coupling Using Alkylative Activation

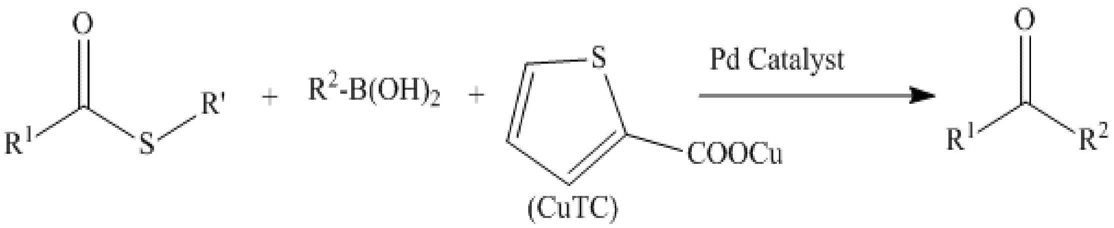


Figure 27: Thiol Ester-Boronic Acid Cross Coupling Mediated by CuTC

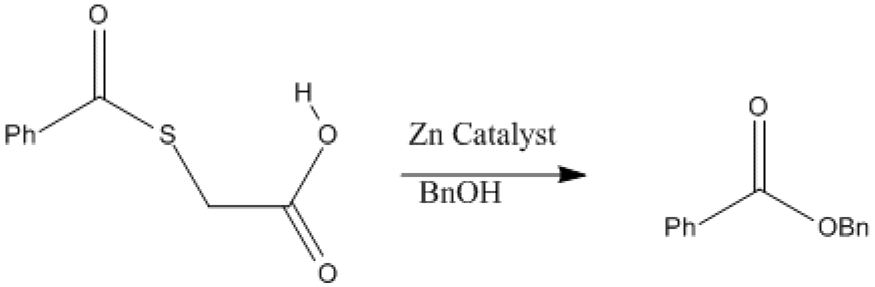


Figure 28: Selective Zn(II)-Mediated Alcoholysis of S-Benzoylglycolic Acid

This is another great article that brings together two different science areas: organometallic chemistry and biology. It is also a great article to introduce at this part of the course as it includes several different organometallic reactions and is a great example of the applications of the material students have learned so far. The complexity of these reactions would also require a good comprehension of organometallic chemistry, making it a proper article to study at the end of the chapter.

Part III

Conclusion

This paper presents a strategy to integrate scientific research articles by members of the faculty from the chemistry department at Emory University into the undergraduate Organometallic chemistry course, CHEM-327. The incorporation of research discoveries published in scientific journals to support the teaching of the fundamentals and applications of Organometallic chemistry has the potential to be immensely beneficial to the pedagogy of this course. The incorporation of research discoveries would allow students to: see direct applications of the concepts learned in the course, improve their scientific paper reading proficiency, and increase their knowledge of the impactful research that has taken place at this institution. The implementation of a method to asses the outcome of this teaching strategy would result in a conclusion of how effective the incorporating faculty research will have on an undergraduate's education. If proven effective with this course, the method could be expanded to other science courses at Emory University.

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