University of Rhode Island
Arts & Sciences, Department of Chemistry
CHM 505, Chemical Synthesis and Mechanism, Fall 2015

Thematic Areas

1. Molecular Structure and Reaction Mechanisms
2. Controlling the Reactivity of Complex Organic Molecules
3. Organometallic Complexes and Catalysis
4. Synthesis and Design of Organic Polymers
5. Synthesis and Manipulation on the Nanoscale

Course Description
The theory and design of modern synthetic schemes. Emphasis will be placed on broadly used reactions that can be applied to interdisciplinary bioorganic, organometallic and materials chemistry research such as small molecule synthesis, surface modification and transition metal coupling reactions.

Course Goals and Student Learning Objectives
The overarching goal of this course will be to prepare graduate students for research by introducing them to some of the most common modern synthetic schemes for synthesizing molecular and nanoscale structures.

Course Content Learning Outcomes
Upon successful completion of this course, students will be able to:
LO1 – design the synthesis of compounds, spanning the continuum of chemical structures studied in modern chemistry, ranging from small molecules to nanoparticles to functional materials.
LO2 – describe the molecular mechanisms incorporating the core principles of structure, bonding and reactivity by which chemical reactions occur and use these concepts to predict the reactivity of complex molecules.
LO3 – understand and critique the modern chemical literature that pertains to chemical synthesis.

Suggested Texts/Readings
Textbooks
Smith, Michael B. *March's Advanced Organic Chemistry*, vol 7, Wiley, 2013. ISBN 0470462590.
Atkins, P.; Overton, T.; Rourke, J.; Weller, M.; Armstrong, F. *Shriver and Atkins' Inorganic Chemistry*, vol 5, Oxford, 2009. ISBN 0199236178.

Other Readings
Bray, B. L. Large-scale manufacture of peptide therapeutics by chemical synthesis. *Nature Reviews Drug Discovery* **2003**, *2*, 587-59.
Halpern, J. Mechanism and Stereoselectivity of Asymmetric Hydrogenation. *Science* **1982**, *217*, 401-407.
Burda, C.; Chen, X.; Narayanan, R.; El-Sayed, M. A. The Chemistry and Properties of Nanocrystals of Different Shapes. *Chem. Rev.* **2005**, *105*, 1025-1102.
Murray, C. B.; Kagan, C. R.; Bawendi, M. G. Synthesis and Characterization of Monodisperse Nanocrystals and Close-Packed Nanocrystal Assemblies. *Annu. Rev. Mater. Sci.* **2000**, *30*, 454-610.
Hotchkiss, J. W.; Lowe, A. B.; Boyes, S. G. Surface Modification of Gold Nanorods with Polymers

Synthesized by Reversible Addition−Fragmentation Chain Transfer Polymerization. *Chem. Mater.* **2007**, *19*, 6-13.
Goddard, J. M.; Hotchkiss, J. H. Polymer Surface Modification for the Attachment of Bioactive Compounds. *Prog. Poly. Sci.* **2007**, *32*, 698-725.
Coates, G. W.; Waymouth, R. M. Oscillating stereocontrol: a strategy for the synthesis of thermoplastic elastomeric polypropylene. *Science* **1995**, *267*, 217-9.
Moses, J. E.; Moorhouse, A. D. The Growing Applications of Click Chemistry. *Chem. Soc. Rev.* **2007**, *36*. 1249-1262.
Hassan, J.; Se´vignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. Aryl-Aryl Bond Formation One Century after the Discovery of the Ullmann Reaction. *Chem. Rev.* **2002**, *102*, 1359-1469.

Assignments and Grading Policy

The grading for the course will be based on three unit exams and one final paper. The exams will be based on a paper from the current chemical literature and will be similar to the exams used for qualifying for the chemistry Ph.D. The final paper will take the form of a proposal, written in a format similar to that used for American Chemical Society Division of Organic Chemistry Fellowships, where the student will review an area of modern synthetic research and highlight opportunities for new discoveries that could significantly advance the field.

Exam 1	100 points
Exam 2	100 points
Exam 3	100 points
Research paper	100 points
Total	**400 points**

"A" grades will likely fall in the range of 400-350 points; "B" grades, 300-350 points, etc.

Course Schedule

Week	Learning Outcome	Topics, Readings, Assignments, Deadlines
1	LO2	***Theme 1: Molecular Structure and Reaction Mechanisms*** A. Structure and bonding of organic and inorganic compounds. The interdependence of orbitals and geometry.
2	LO2	A. Fundamental mechanisms of organic and inorganic reactions. B. Describing reaction mechanisms using linear free-energy relationships.
3	LO2 / LO1	A. Competing mechanisms and the nature of chemoselectivity. Kinetic isotope effects. ***Theme 2: Controlling the Reactivity of Complex Organic Molecules***

		B. Schemes for achieving chemoselectivity using protection schemes.
4	LO1 / LO3	A. Case studies in chemoselective synthesis: The synthesis of peptides and oligonucleotides. B. A case study in chemoselectivity and an introduction to stereoselectivity: The asymmetric synthesis of amino acids.
5	LO1 / LO3	A. Predicting stereocontrol via diastereomeric transition states: The Diels-Alder and other pericyclic reactions. ***Theme 3: Organometallic Complexes and Catalysis*** B. Introduction to asymmetric catalysis. Reaction energy diagrams of an asymmetric reaction: A mechanistic understanding of enantioselectivity.
6	LO1 / LO2	**A. Exam 1 – covering weeks 1-4** B. Ligand field theory. X-type, L-type ligands. The 18-electron rule.
7	LO1 / LO2	A. sigma-donating and pi-acidic ligands. Probing metal-ligand bonds by IR spectroscopy. B. Redox-active ligands. Organic and organometallic redox chemistry.
8	LO2 / LO3	A. A case study in kinetic reaction analysis: Kinetic resolution of alcohols by oxidative palladium catalysis. B. Palladium catalyzed coupling reactions, introduction and application to pharmaceutical synthesis.
9	LO1 / LO2	A. Molecular mechanisms as a function of ligand design. Systematic optimization of coupling reactions. ***Theme 4: Synthesis and Design of Organic Polymers*** B. Introduction to polymer chemistry. Polymerization mechanisms.
10	LO2 / LO3	**A. Exam 2 – covering weeks 5-8** B. Olefin metathesis: A case study in kinetic and thermodynamic control. Ring opening metathesis polymerization.
11	LO1 / LO2	A. Stereocontrolled polymerization catalysts and their mechanisms. ***Theme 5: Synthesis and Manipulation on the Nanoscale*** B. Synthesis of inorganic nanoparticles and quantum dots.
12	LO1	A. Surface modifications of inorganic nanoparticles and materials. B. Click reactions for surface modification.
13	LO1	A. Surface modification of organic materials. B. Fullerenes and other organic nanoscale structures.
14	LO1 / LO3	A. Chemical lithography by patterned surface modifications. **Research paper due.**
Final Exam		**Exam 3 – covering weeks 9-13**