Preparation and Studying for this Course. During the first two or three weeks of the semester you should review your undergraduate organic chemistry, focusing your attention on stereochemistry, mechanism and reactions. Most undergraduate textbooks have a section on synthesis; review this section too. Chem 642 will require a lot of reading. You should make every effort to keep up with the reading and not allow yourselves to get behind. Letting your assignments accumulate for a week with the intention of getting caught up over the weekend is unwise. Reading the chemical literature is unlike reading a novel or the Sunday paper: you must learn to read critically. You must look for the important ideas, try to understand them, and try to waste as little time as possible with the insignificant details. For example, in reading a research paper, for the purposes of this course it is unlikely that much of the experimental section will be of interest. (If, on the other hand, we were interested in duplicating the work in our lab, the experimental section would be very useful.) You should take notes on your reading, and to keep such notes organized in such a way that you can retrieve the information. This is a practice that you should follow for the entirety of your professional career. To a large degree, your success as professionals in chemistry will depend upon your ability to retrieve, assimilate, and use the flood of new information coming from the literature. This is true regardless of your area of specialization. The more effort you put into this course, the more you will get out of it.

There is no textbook required. Students may wish to purchase a copy of “Modern Organic Synthesis” by Dale Boger. This can be purchased from TSRI Press on the web.

Goals for the Course. There are several related goals for Chemistry 642. (a) To become familiar with common chemical reactions which are used in synthesis. (b) To have an appreciation of the fundamentals of mechanism, so we can understand the limitations, the stereochemical consequences and the proper way to apply individual reactions to a problem in organic synthesis. (c) To learn how to apply retrosynthetic strategy, so that we can design total syntheses systematically, should inspiration or insight fail us. (d) To become familiar with the library, SciFinder, and the primary literature in chemistry, and how to access chemical information efficiently. The order in which these goals have been listed is not a reflection of their relative importance.

Assignments and Grading. There will be assigned homework problem sets. You will have several days to work on these, and they will be collected, corrected, and returned to you. These will not be graded, therefore you may ask for help in completing these assignments. You are urged to work on these problems independently, rather than in a study group. You will benefit much more from struggling unsuccessfully with a challenging problem, than from solving it quickly with help. There will be two mid-semester examinations and a final examination. In order to give you sufficient time, I have scheduled the mid-semester examinations on two Saturday mornings, October 4, and November 8. We have been assigned Friday, December 19, 9:45 – 11:45 a.m. for the Final Exam. We will probably schedule the Final for the afternoon of that day in order to give the class more time.

I hope that in addition to learning some organic chemistry this semester, you will enjoy the reading for this course, for synthesis provides both intellectual challenges and excitement.
This course follows the organization indicated below. It is probably not possible to cover all the topics 1 through 12 in the course of a single semester.

1. **Introduction.** General discussion of the underlying principles of organic synthesis; exploitation of molecular symmetry; functional group transforms and functional group interchanges. This section also serves to refresh students' memory of common organic reactions, and how these link two (or more) functional groups.

2. **Alkene synthesis.** 1,2-Disubstituted alkenes, tri- and tetrasubstituted alkenes. In this section of the course carbometallation reactions are discussed, as well as some organopalladium chemistry. Claisen, Cope and oxy-Cope reactions are discussed in the context of alkene synthesis. Throughout this section the major points are illustrated by using examples of total syntheses in which these reactions appear.

3. **The Diels-Alder reaction.** A general discussion covers the Alder rule, the endo rule and the orientational preferences in the diene. Intramolecular Diels-Alder reactions are discussed, as are retro-Diels-Alders and hetero-Diels-Alders. Examples from total synthesis.

4. **Cation-olefin cyclizations** are discussed as another method for the synthesis of six-membered rings. The synthesis of the alkene starting materials is covered briefly, with greater emphasis on the choices of initiating and terminating functional groups.

5. **The Alder ene reaction** is covered in the context of the synthesis of five-membered rings. The Conia variant.

6. **The Nazarov cyclization;** contemporary variants as methods of synthesis of five-membered rings.

7. **The Pauson-Khand cyclization** and variants.

8. **Organometallic versions of the ene reaction** are discussed, and this is used as an introduction to other methods for forming C-C bonds that utilize palladium catalysis.

9. **The vinylcyclopropane rearrangement** is briefly discussed as a method for the synthesis of five-membered rings. This serves as an introduction to **The divinylcyclopropane rearrangement** for the synthesis of seven-membered rings.

10. The Simmons-Smith reaction, and the enantioselective variants are discussed as methods for the **synthesis of three-membered rings.** Carbenoid reactions are covered. Photochemical and other methods for the synthesis of four-membered rings are covered.


    There is no required text for this course. Readings are assigned to the class from the primary literature. This has the added advantage of teaching students how to use the library, how to use SciFinder, and how to extract useful information from a scientific paper.