Up until this year we have offered a one-semester course titled Organic Synthesis (Chem 642). Over the years it became more and more obvious that we were not covering enough material during a single semester, and so the coverage of topics became less and less complete. In part this was because we were spending an ever-increasing number of lectures on introductory and remedial work, and in part because the material that one must have familiarity with has continued to grow. The issue has been addressed in the past through periodic offerings of Special Topics courses (Chem 741) that covered the important material that had been left out of Chem 642. Starting this year we will be offering a two-semester course in Organic Synthesis. Chem 642 is the first half and Chem 647 is the second half.

Chem 642 follows the organization indicated below. On average we will devote two weeks (six lectures) per topic.

1. **Introduction.** General discussion of the underlying principles of organic synthesis; exploitation of molecular symmetry; functional groups, some of the common organic reactions and how these link two (or more) functional groups.

2. **Alkene synthesis.** $E$- and $Z$-1,2-Disubstituted alkenes, tri- and tetrasubstituted alkenes. In this section of the course carboalumination reactions are discussed, as well as some organopalladium chemistry.

3. **[3,3]-Sigmatropic Rearrangements.** Claisen, Cope and oxy-Cope reactions are discussed in the context of alkene synthesis. Major points are illustrated by using examples of total syntheses in which these reactions appear as key steps.

4. **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.

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

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

There is no required text for this course. Readings will be assigned from the primary literature. Students may find the following books useful:

"Modern Organic Synthesis" by Dale Boger
"Strategic Applications of Named Reactions in Organic Synthesis" by László Kürti and Barbara Czakó
"Enantioselective Chemical Synthesis" by E. J. Corey and László Kürti
Chemistry 642 - Organic Synthesis  
Marcus A. Tius, University of Hawaii

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 reading 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 your 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. Whether you use paper or whether you use some electronic means, you should find some way to retrieve information long after you have encountered it in your reading. For what it is worth: writing structures on paper is much faster than trying to use a drawing program on your tablet or your laptop. 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.

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. (d) To become familiar with the use of SciFinder, and the primary literature in chemistry, and how to access chemical information efficiently. (Please bear in mind that information is not knowledge.) 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 13, and November 17. We have been assigned Friday, December 14, 9:45 – 11:45 a.m. for the Final Exam. We will try to schedule the Final on a day and at a time that will give the class more time.

I hope that in addition to learning some organic chemistry and developing problem solving skills this semester, you will enjoy the reading for this course, for synthesis provides both intellectual challenges and excitement.