Intermediate Organic Chemistry CHEM3310/3315 (Winter 2019)

Department of Chemistry and Biochemistry, University of Windsor

Mon/Wed/Fri, 1:30 pm (DH 264)

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New announcements, outlines, suggested solutions for Tests and Assignments will be on the **Blackboard** page.

Very old assignments, tests are additionally available at **www.uwindsor.ca/chem331**

Office Hours: I'll be available after class on Wednesday most weeks, or by appointment.

Topics to be covered:

I. Reminders

Mechanisms, structure & reactivity

II. The Backbone of Organic Synthesis: The Chemistry of the Carbonyl Group

1. Carbonyl compounds as a_1 reagents

a. Reactions with main group organometallics: addition to carbonyls; synthesis of carbonyls (Weinreb amide method)
b. Reduction of carbonyls: Hydride sources (including borane)
c. The Bürgi-Dunitz angle and diastereoselective reactions: the Felkin-Anh, polar Felkin-Anh & Cram chelate models. Reactions of cyclohexanones.

2. Carbonyl compounds as d_2 reagents

a. Enols and enolates: Stability and generation; kinetic and thermodynamic enolates; silyl enol ethers.
b. The aldol condensation: the E1cB mechanism. Homo- and crossed-condensations; Knoevenagel & Stobbe condensations (example: tegoprazan)
c. The Claisen & Dieckmann condensations. Example: orsellinic acid (polyketide biosynthesis)
d. The aldol reaction: diastereoselectivity, the Ireland model and Zimmerman-Traxler transition state; the Mukaiyama aldol reaction. Examples of polyketide natural products: Erythromycin A1
e. The Mannich reaction: Eschenmoser's salt; Robinson's synthesis of tropinone
f. Alkylations: S_N2 *vs* S_N1-type alkylations. Enolate equivalents: β-keto esters, enamines, imine aza-enolates, silyl enol ethers
g. Halogenation and the haloform reaction

3. Carbonyl compounds as a_3 reagents

a. α,β-unsaturated compounds: 1,2- *versus* 1,4-addition, hard/soft nucleophiles
b. Conjugate additions: Weitz-Scheffer oxidation, Stryker's reagent; the Michael reaction – stabilised anions, Gilman reagents; the Robinson annulation.
c. Addition-elimination (& S_NAr); Example: synthesis of the antibiotic ofloxacin.

4. Umpolung reactivity of carbonyl compounds

a. Dithianes – d_1 reagents
b. Epoxides – a_2 reagents; regio- and stereo-selectivity; the Fürst-Plattner rule

5. The Wittig reaction

Stabilised and unstabilised ylids; the Horner-Wadsworth-Emmons reaction.

III. A Whole New World: Pericyclic Reactions

1. **Cycloadditions: the Diels-Alder Reaction.**
   a. The diene and dienophile
   b. Regio- and diastereoselectivity
   c. Applications in synthesis
2. **Electrocyclic reactions**
3. **Sigmatropic rearrangements:** the Cope and Claisen rearrangements
4. **The Woodward-Hoffman Rules** (time permitting)

IV. Functional Group Interconversions

1. **Reductions**
   a. Reductions of alkenes: hydrogenation
   b. Removal of functional groups: Barton-McCombie, Clemmensen, Wolf-Kishner & Mozingo reactions
   c. Dissolving metal reductions: Birch reduction of aromatic rings and α,β-unsaturated compounds; acyloin condensation
2. **Oxidations**
   a. Oxidation of alcohols: Jones, Pinnick and Swern oxidations.
   b. Oxidation of alkenes: Prilezhaev & Rubottom oxidations; OsO_4, IO_4^- & Lemieux-Johnson oxidation; ozonolysis; borohydration; the Houk Model for diastereoselective reactions.
   c. Insertion reactions: Beckmann rearrangement (example: azithromycin), Baeyer-Villiger oxidation

V. Miscellaneous reactions (*Time permitting*)

a. The Evans auxiliary
b. Prévost and Woodward-Prévost reactions
c. Evans-Saksena and Narasaka-Prasad reductions
d. Curtius Rearrangement
e. Arndt-Eistert Synthesis

Course Text

There is no specific text for this course, but the following is an excellent source of information regarding the subject material:

Organic Chemistry – Clayden, Greeves, Warren, (Wothers) 1st or 2nd Ed.

Marking Scheme

	3310	**3315**
Problem Sets	10%	10%
Term Tests[1]	30%	40%
Laboratory[2]	20%	----
Final Exam[3]	40%	50%

[1] **Midterm 1** will be 50 min in duration in class time; **Midterm 2** will be 1.5 h and **not** in class time.
[2] Laboratory sections will be held in B-76 Essex
[3] The final examination is 3 h in duration