CHEM4630 Asymmetric Organic Synthesis

Course Description:

Modern organic synthesis requires the construction of molecules in an enantiopure form (asymmetric synthesis) because the (+)- and the (-)-enantiomer display different pharmacological response. This advanced organic chemistry course focuses on protocols for diastereoselective and enantioselective carbon-carbon formation. Contemporary organocatalytic reactions involving carbon-carbon formation and carbon-heteroatom formation are also covered. Examples on the syntheses of chiral drug molecules are illustrated.

Main Course Outline (for reference only):

1. Introduction to asymmetric synthesis. Diastereoselectivity. Enantioselectivity.
2. Diastereoselective carbon-carbon bond formation. Stereoselective addition of Nu to chiral ketones and aldehydes. Cram's rule. Open chain and chelation model. Nu Additions to cyclic ketones.
3. Diastereoselective Alkylation of chiral enolates. pKa values. Kinetic deprotonation. enolate geometry. Intraannular Chirality Transfer. Exocyclic enolates. 1,2; 1,3;1,4-asymmetric induction. Five-Membered endocyclic enolate. Enolates in the Norbornyl Ring system. Six - membered endocyclic enolates. Chelate - Enforced Intrannular Chirality transfer. b-hydroxy ester enolates. asymmetric synthesis via chiral enolate synthon. Prolinol-derived enolates. Imide-derived enolates. Chiral Cyclohexanone Imine. Chiral Hydrazones. Asymmetric synthesis of chiral aldehydes and ketones.
4. The Aldol Addition reaction in stereoselective organic synthesis. Syn-anti selectivity (kinetic). Zimmerman-Traxler transition states. Diastereofacial Selectivity. Rxns of Achiral enolates with chiral aldehydes. Rxn of chiral enolate with achiral aldehydes. Rxn. of chiral aldehydes with chiral enolates. Enantioselective chiral enolate. Additions involving Allylmetal & Allylboron compounds.
5. Stereocontrol via olefinic cyclization. Halolactonizations. stereoselective epoxidation sequence for olefinic acid. asymmetric synthesis of a-hydroxycarboxylic acids. Related cyclisation: esters of olefinic acids (with loss of alkyl halide), amides, carbamates, carbonate anions, phosphate esters. Haloetherification. Iodocarbamation. Iodolactamation.
6. Asymmetric cycloaddition reactions. Diels-Alder reactions. Chirality transfer via sigmatropic rearrangements. [3,3]-Sigmatropic Rearrangements. Transfer of Chirality. Cyclic and acyclic substrates. Hetero-Clasien Rearrangement.