

**CHEM 251 (4 credits): Intermediate Reactions of Nucleophiles and Electrophiles**  
**(Reactivity 2)**

**Description:** An understanding of chemical reactivity, initiated in Reactivity 1, is further developed based on principles of Lewis acidity and basicity. A basic understanding of chemical kinetics is developed as a common theme through much of the course. Alternative mechanisms of ligand substitution in coordination complexes are considered in terms of steric and electronic effects. An understanding of kinetic evidence is developed in order to determine which mechanism has occurred in a particular case. Organic nucleophilic substitution pathways are studied using analogous principles. Electrophilic addition and substitution in pi systems (alkenes and aromatics) are used to extend these principles to new systems and complete an overview of polar reactions. In addition, treatment of chemical kinetics is extended to include studies of catalysts and enzymes. Applications of the material are drawn from organic, biological and inorganic chemistry. Prerequisite: CHEM 250.

**Course Goals and Objectives:**

**I. Students will become familiar with the use of kinetics in interpreting reaction mechanism. They will be able to**

1. explain the role of collisions in reactions.
  - a. Students will explain why collisions are necessary in reactions.
  - b. Students will explain how concentration affects collisions.
  - c. Students will explain how temperature affects collisions.
  - d. Students will explain the role of entropy in collisions.
2. explain reaction progress diagrams.
  - a. Students will demonstrate the relationships between elementary steps and the shape of a reaction progress diagram.
  - b. Students will demonstrate the relationship between rate determining step and reaction barriers.
  - c. Students will demonstrate the relationship between equilibrium and the shape of a reaction progress diagram.
  - d. Students will distinguish between kinetic and thermodynamic control of a reaction.

3. explain of rate laws
  - a. Students will be able to propose a rate determining step given a set of simple elementary steps.
  - b. Students will be able to propose a simple rate law based on elementary steps.
  - c. Students will be able to identify the rate determining step if given a rate law.
4. explain comparative rates
  - a. Students will demonstrate the relationship between rate constants and the relative rates of reactions.
  - b. Students will be able to propose reasons for differing rates in simple cases.
5. explain kinetics of catalysis.
  - a. Students will be able to apply limits to the Michaelis-Menten equation in order to interpret rates at low substrate concentration.
  - b. Students will be able to apply limits to the Michaelis-Menten equation in order to interpret rates at saturation.
  - c. Students will be able to apply limits to the Michaelis-Menten equation in order to graphically determine  $K_m$  and  $V_{max}$ .
  - d. Students will be able to use the Lineweaver-Burke equation in order to graphically determine  $K_m$  and  $V_{max}$ .
  - e. Students will be able to determine catalytic efficiency and biochemical turnover number (organometallic turnover frequency) from data.

**II. Students will become familiar with basic concepts of transport across cell membranes. They will be able to**

1. distinguish between passive, facilitated and active transport.
  - a. Students will be able to predict which kinds of molecules may diffuse passively.
  - b. Students will be able to predict direction of transport based on concentration gradient.
  - c. Students will show which types of transport require expenditure of energy.

**III. Students will become familiar with general concepts governing the function and regulation of enzymes. They will be able to**

1. explain binding and catalysis steps.
  - a. Students will distinguish between binding and catalysis steps.
  - b. Students will demonstrate familiarity with approaches to accelerating catalysis steps via transition state stabilization.
  - c. Students will demonstrate familiarity with approaches to accelerating catalysis steps via reactant destabilization.
  - d. Students will demonstrate familiarity with approaches to enhance binding in diffusion-controlled enzymes.
2. explain enzyme inhibition.
  - a. Students will be able to compare and contrast competitive, uncompetitive and non-competitive inhibition.
  - b. Students will be able to identify, using data, competitive, uncompetitive and non-competitive inhibition.
3. explain enzyme regulation.
  - a. Students will be able to predict some of the points along a pathway that would be subject to regulation.
  - b. Students will be able to compare and contrast allosteric inhibition and allosteric activation.

**IV. Students will become familiar with simple substitution reactions in organic and inorganic chemistry. They will be able to**

1. explain how substitution reactions occur in coordination complexes.
  - a. Students will distinguish between an associative and a dissociative elementary step.
  - b. Students will identify whether a reaction begins with association or dissociation based on the rate law.
  - c. Students will identify factors that make a dissociative pathway more likely.
  - d. Students will identify factors that make an associative pathway more likely.

- e. Students will identify factors that may influence the product of the reaction, such as the trans effect.
2. explain how substitution reactions occur at tetrahedral carbons.
    - a. Students will be able to identify nucleophiles, electrophiles and leaving groups in a reaction.
    - b. Students will distinguish between an  $S_N1$  and  $S_N2$  pathway.
    - c. Students will identify whether a reaction follows an  $S_N1$  or  $S_N2$  pathway based on the rate law.
    - d. Students will identify factors that favor an  $S_N1$  vs.  $S_N2$  pathway.
    - e. Students will identify factors that may lead to elimination instead of substitution.
    - f. Students will identify factors and characteristics of E1 and E2 pathways.
    - g. Students will predict regiochemical outcomes based on the mechanism.
    - h. Students will predict stereochemical outcomes based on the mechanism.
    - i. Students will be able to propose synthetic transformations employing nucleophilic substitution.

**V. Students will become familiar with organic processes catalyzed by transition metals. They will be able to**

1. explain elementary reaction steps available to organometallics.
  - a. Students will identify examples of oxidative addition reactions.
  - b. Students will identify examples of reductive elimination reactions.
  - c. Students will identify cases in which oxidative addition is likely to occur.
  - d. Students will predict whether an oxidative addition is likely to be concerted or proceed in a stepwise fashion.
2. explain some major synthetic applications of organometallics.
  - a. Students will be familiar with coupling reactions, such as Heck or Suzuki coupling.
  - b. Students will be familiar with industrial processes, such as hydroformylation or Monsanto acetic acid synthesis.

- c. Given a transition metal-catalyzed organic reaction, students will be able to propose a catalytic cycle.

**VI. Students will become familiar with how electrophiles add to carbon-carbon pi bonds. They will be able to**

1. explain representative reactions of electrophiles with alkenes and alkynes.
  - a. Students will be able to draw mechanisms for the reactions of alkenes and alkynes with proton donors.
  - b. Students will be able to draw mechanisms for the reactions of alkenes and alkynes with softer electrophiles, such as bromine and mercury.
  - c. Students will be able to draw mechanisms for the concerted addition of electrophiles to alkenes and alkyne, such as in epoxidation, cyclopropanation or hydroboration.
  - d. Students will be able to predict regiochemistry of electrophilic additions.
  - e. Students will be able to predict stereochemistry of electrophilic additions.
  - f. Students will be able to propose synthetic transformations using electrophilic additions.
2. explain representative reactions of electrophiles with aromatic systems.
  - a. Students will be able to draw mechanisms for the substitutions of aromatics with electrophiles, such as nitro cations or sulfur trioxide.
  - b. Students will be able to draw mechanisms for Lewis acid-catalyzed substitutions of aromatics with halogens, alkyl halides or acyl halides.
  - c. Students will be able to explain and predict activating effects of substituents on aromatics.
  - d. Students will be able to explain and predict directing effects of substituents on aromatics.
  - e. Students will be able to decide on the optimal order of steps in a short synthetic route involving electrophilic aromatic substitution.
3. explain general concepts of cationic olefin polymerization.
  - a. Students will be able to discuss fundamental polymer concepts such as molecular weight distribution and entanglement.
  - b. Students will be able to describe the characteristics of chain growth.

- c. Students will be able to predict mechanisms of chain termination.
- d. Students will show familiarity with methods of living cationic polymerization.

**VII. Students will become familiar with some common rearrangements in organic chemistry. They will be able to**

1. explain 1,2-hydride and -alkyl shifts.
  - a. Students will be able to predict the products of hydride and alkyl shifts.
  - b. Students will be able to predict situations in which hydride and alkyl shifts will occur.
2. explain common rearrangements involving carbonyls.
  - a. Students will be able to predict the products of pinacol rearrangement.