KOT 323 – Organic Chemistry III

Course Objectives:

(i) To learn about nomenclature, structure and properties of amines and carboxylic acids and their derivatives as well as reactions involving these classes of compounds.

(ii) To introduce reactions involving acidic alpha hydrogen of carbonyl compounds.

(iii) To introduce chemistry of large molecules including carbohydrates and nucleic acid.

Topic	**Content**	**Number of lecture hours**	**Expected Outcome – upon completion of this course, the students should be able to:**
1. Amines	• Nomenclature, structure, properties of amines • Spectroscopy of amines • Amine salts as phase-transfer catalysts • Reactions of amines • Hofmann and Cope eliminations • Reactions of Arenediazonium salts • Syntheses of amines	5	• Name amines and draw the structures. • Interpret the IR, NMR, UV, MS spectra of amines. • Explain how the basicity of amines varies with hybridisation and aromaticity. • Predict the products of reactions of amines with various compounds and propose the mechanisms where appropriate. • Give examples of the use of arenediazonium salts in diazo coupling. • Illustrate the uses and mechanisms of Hofmann and Cope eliminations and predict the major products. • Use the knowledge of the mechanisms of amine reactions to propose mechanisms and products of similar reactions. • Show how to synthesise amines from other organic compounds. • Use retrosynthetic analysis to propose effective syntheses of compounds with amines as intermediates or products or protecting the amines if necessary.

Topic	**Content**	**Number of lecture hours**	**Expected Outcome – upon completion of this course, the students should be able to:**
2. Carboxylic acids	• Nomenclature, physical properties and acidity • Spectroscopy of carboxylic acids • Synthesis of carboxylic acids • Reaction of carboxylic acids and derivatives • Fischer esterification • Esterification using diazomethane • Reactions of carboxylic acids	5	• Name and draw the structures of carboxylic acids. • Show how the acidity of acids varies with their substitution. • Interpret the IR, NMR, UV, MS spectra of carboxylic acids. • Show how carboxylic acids are synthesized. • Show how carboxylic acids are converted to esters and amides and propose the mechanisms. • Give the mechanism of Fischer esterification and show how the equilibrium can be driven toward the products/reactants. • Predict the products of the reactions of carboxylic acids with particular reagents and give mechanisms where appropriate.
3. Carboxylic acid derivatives	• nomenclature, structure and physical properties • spectroscopy of carboxylic acid derivatives • interconversion of acid derivatives • transesterification • hydrolysis of carboxylic acid derivatives • reduction of acid derivatives • reactions of acid derivatives with organometallic reagents	6	• Name and draw the structures of carboxylic derivatives. • Compare the physical properties of acid derivatives. • Interpret the spectra of carboxylic acid derivatives. Show how the IR carbonyl stretching frequency depends on the structure of acid derivatives. • Show how acid derivatives are easily interconverted by nucleophilic acyl substitution. • Show how acid catalysis is used to synthesise acid derivatives as in Fischer esterification and transesterification and propose the mechanisms. • Show how acid derivatives hydrolyse to carboxylic acids and explain why either acid/base is a suitable catalyst. Propose the mechanisms. • Show what reagents are used to reduce acid derivatives. • Show what products result from the addition of Grignard and organolithium reagents to acid derivatives and propose the mechanisms.

Topic	**Content**	**Number of lecture hours**	**Expected Outcome – upon completion of this course, the students should be able to:**
4. Condensations and alpha substitution of carbonyl compounds	• enols and enolate ions • α-halogenation of ketones • α-bromination of acids • Alkylation of enolate ions and enamines • Aldol condensation of ketones and aldehydes, dehydration of aldol products and crossed aldol condensations • Aldol cyclisation and planning syntheses using aldol condensation • Claisen and crossed Claisen condensations • Syntheses using □-dicarbonyl compounds • Malonic ester synthesis • Acetoacetic ester synthesis • Michael reaction • Robinson annulation	6	• Show how enols and enolate ions act as nucleophiles. Give mechanisms for acid-catalysed and base-catalysed keto-enol tautomerisms. • Give mechanisms for acid-catalysed and base-promoted alpha halogenation of ketones and acid-catalysed hydrogenation of acids. Explain why multiple halogenation is common with basic catalysis and give mechanism for the haloform reaction. • Show how alkylation and acylation of enamines and lithium enolates are used synthetically. Give mechanisms for the reaction. • Predict the products of aldol and crossed aldol reactions before and after dehydration of the aldol products. Give mechanisms for the acid- and base-catalysed reactions. Show how aldols are used to make β-hydroxy carbonyl compounds and α, β-unsaturated carbonyl compounds. • Predict the products of Claisen and crossed Claisen condensations and propose mechanisms. Show how Claisen condensation constructs the carbon skeleton of a target compound. • Show how the malonic ester synthesis and the acetoacetic ester synthesis are used to make substituted acetic acids and substitute acetones. Give mechanisms of the reactions. • Predict the product of Michael additions and show how to use these reactions in syntheses. Show the general mechanism of Robinson annulation and use it to form cyclohexenone ring.

Topic	**Content**	**Number of lecture hours**	**Expected Outcome – upon completion of this course, the students should be able to:**
5. Carbohydrates and nucleic acids	• Classification of carbohydrates • Monosaccharides • Erythro and threo diastereomers • Epimers • Cyclic structures of monosaccharides • Anomers of monosaccharides • Reactions, reduction and oxidation of monosaccharides • Ether and ester formation • Chain lengthening and shortening • Fischer's proof of the configuration of glucose • Periodic acid cleavage of sugars • Disaccharides and polysaccharides • Introduction to nucleic acids • Ribonucleosides and ribonucleotides • Structure of ribonucleic acid • Deoxyribose and structure of deoxyribonucleic acid	7	• Draw the Fischer projection of glucose and the chair conformation of the □ anomer of glucose. • Recognise the structures of other anomers and epimers of glucose drawn as either Fischer projections of chair structures. • Name monosaccharides and disaccharides and draw their structures. • Predict which carbohydrates mutarotate, which reduce Tollens reagent and which undergo epimerisation and isomerisation under basic conditions. • Predict the products of the reactions of selected reagents with carbohydrates. • Use the information gained from the above reactions to determine the structure of an unknown carbohydrate. Use the information gained from methylation and from periodic acid cleavage to determine the ring size. • Draw the common types of glycosidic linkages and recognise these linkages in disaccharides and polysaccharides. • Recognise the structures of DNA and RNA and draw the structures of a ribonucleotide and a deoxyribonucleotide.

Topic	Content	Number of lecture hours	Expected Outcome – upon completion of this course, the students should be able to:
6. Amino acids, peptides and proteins	• Structure and stereochemistry of α-amino acids • Acid-base properties of amino acids • Isoelectric points and electrophoresis • Synthesis of amino acids • Resolution of amino acids • Reactions of amino acids • Structure and nomenclature of peptides and proteins • Peptide structure determination • Solution-phase peptide synthesis • Solid-phase peptide synthesis • Classification of proteins • Levels of protein structures • Protein denaturation	7	• Correctly name amino acids and peptides and draw the structures. • Use perspective drawings and Fischer projections to show the stereochemistry of D- and L-amino acids. • Explain which amino acids are acidic, basic and neutral. Use the isoelectric point to predict whether a given amino acid will be positively or negatively charged or neutral at a given pH. • Show how HVZ/NH_3, Gabriel-malonic ester and Strecker syntheses might be used to make a given amino acid. • Predict products of the esterification, acylation reaction and reaction with ninhydrin. • Use information from terminal residue analysis and partial hydrolysis to determine the structure of an unknown peptide. • Show how solution-phase peptide synthesis or solid-phase synthesis would be used to make a given peptide. Use appropriate protecting groups to prevent unwanted couplings. • Discuss and identify the four levels of protein structure. Explain how the structure of a protein affects its properties and how denaturation changes the structure.
TOTAL		**36**	