Name of the Programme: M. Sc -I (Organic Chemistry)

Course Code: CHO-503 **Title of the course:** Synthetic Methodologies in Organic Chemistry

Number of Credits: 04

Effective from AY: 2022-23

Prerequisites for the course:	Students should have studied organic chemistry courses at M.Sc. Chemistry in semester I	
Course Objective:	1. To study various concepts related to carbon-carbon bond formation. 2. To understand designing of organic synthesis to make molecules of interest. 3. To plan total synthesis based on protection-deprotection strategy.	
Content	**1. Chemistry of enols and enolates** a. Keto-enol tautomerism; Introduction, acidity, basicity concepts & pKa scale, neutral nitrogen and oxygen bases. Formation of enols by proton transfer, mechanism of enolization by acids & bases, types of enols & enolates, kinetically & thermodynamically stable enols, consequences of enolization, stable enolate equivalents, preparation and reactions of enol ethers. b. Formation of Enolates; Introduction, preparation & properties, non-nucleophilic bases, E / Z geometry in enolate formation, kinetic vs. thermodynamic control, other methods for the generation of enolates, issue of enolate ambidoselectivity. c. Alkylation of enolates; diverse reactivity of carbonyl groups, alkylation involving nitriles and nitroalkanes, choice of electrophile for alkylation, lithium enolates of carbonyl compounds and alkylation, specific enol equivalents to alkylate aldehydes and ketones, alkylation of β-dicarbonyl compounds, problem of regioselectivity during ketone alkylation and the remedy provided by enones. d. Reaction of enolates with aldehydes and ketones; Introduction, aldol reaction including cross & intramolecular version, enolisable substrates which are not electrophilic in nature, controlling aldol reactions with specific enol equivalents, specific enol equivalents for carboxylic acids, aldehydes and ketones. e. Acylation at carbon; Introduction, the Claisen ester condensation (intramolecular and inter / crossed), acylation of enolates by esters, preparation of keto-esters by the Claisen reaction, directed C-acylation of enols and enolates & acylation of enamines.	No of hours 22

	f. Conjugate addition of enolates; Introduction, thermodynamic control vs. conjugate addition, utility of various electrophilic alkenes in conjugate addition, formation of six-membered rings via conjugate addition and nitroalkanes as versatile synthons. g. Examples pertaining to the application of following condensation reactions in organic synthesis; Mukaiyama reaction, Perkin reaction, Dieckmann condensation, Michael addition, Robinson annulation, Sakurai reaction, Knoevenagel Reaction, Darzen, Stobbe, Benzoin, Pechmann condensation.	
	2. Synthetic utility of important name reactions / methodology a. Mannich Reaction, Nef Reaction, Mitsunobu and Appel Reaction, Baylis Hillman reaction, Mc. Murry coupling, vicarious nucleophilic substitution, Steglich and Yamaguchi esterification. b. Ring closing and cross metathesis; Grubb's various generation, Grubbs-Hoveyda, Schrock catalysts.	8
	3. The Ylides in Organic Synthesis a. Phosphorus Ylides; Nomenclature and Preparation. Wittig olefination: mechanism, stereoselectivity, cis- and trans selective reactions, Wittig reagents derived from α-halo carbonyl compounds. b. Modified Wittig, Horner – Wadsworth – Emmons, Stille-Gennari modification with achiral and chiral substrates, Peterson reaction, Julia Olefination. c. Sulfur Ylides; Sulfonium & sulfoxonium ylides in synthesis, diphenylcyclopropyl sulfonium ylides & their reactions with carbonyl compounds / Michael acceptors	8
	4. Protecting Groups in Organic Synthesis a. Introduction and effective use of protecting groups, umpolung of reactivity. b. Common protective groups namely acetals & ketals, dithio acetal/ketals, trialkylsilyl, TBDMS, THP, MOM, MEM, SEM & benzyl ether, methyl ether, benzyl amine, Cbz, *t*-Boc, Fmoc, *t*-butyl ester and methods for deprotection. Some examples of multistep synthesis using protection-deprotection procedures.	6
	5. Asymmetric Synthesis a. Chiral pool (chiron approach). b. Chiral auxiliary approach; Oxazolidinone & norephedrine-derived chiral auxiliary controlled Diels-Alder reaction and alkylation of chiral enolates and aldol reaction, Alkylation using SAMP and RAMP.	12

	c. Chiral Reagents - Use of (-)-sparteine. d. Asymmetric catalysis; CBS catalyst, Ruthenium catalyzed chiral reductions of ketones, Catalytic asymmetric hydrogenation of alkenes, Asymmetric epoxidation (Sharpless and Jacobson), Sharpless asymmetric dihydroxylation reaction, Organocatalyzed aldol reaction (Use of proline).	
	6. Halogenation and esterification reactions a. Formation of Carbon Halogen bonds; Substitution in saturated compounds, alcohols, carbonyl compounds, substitution at allylic and benzylic compounds, bromodecarboxylation (Hunsdiecker reaction), Finkelstein reaction, iodolactonisation. b. Acid and base catalyzed esterification and hydrolysis.	4
Pedagogy	Mainly lectures and tutorials. Seminars / term papers /assignments / presentations / self-study or a combination of some of these can also be used. ICT mode should be preferred. Sessions should be interactive in nature to enable peer group learning.	
References / Readings	1. W. Caruthers, I. Coldham, Modern Methods of Organic Synthesis, Cambridge University Press, 4th Ed, 2016. 2. M. B. Smith, Organic Synthesis, McGraw–HILL, New York, International Edition, 1994. 3. J. Clayden, N. Greeves, S. Warren, P. Wothers, Organic Chemistry, Oxford University Press, 2nd edition, 2012. 4. R. Bruckner, Advanced Organic Chemistry – Reaction Mechanisms, San Diego, CA: Harcourt /Academic Press, San Diego, 2002. 5. J. Fuhrhop, G. Penxlin, Organic Synthesis – Concepts, Methods, Starting Materials, VCH Publishers Inc., New York, 1994. 6. H. O. House, Modern Synthetic Reactions, W. A. Benjamin, 1965, 2nd Ed. (revised with corrections). 7. M. Nogradi, Stereoselective Synthesis, VCH Publishers, Inc., Revised and Enlarged Edition, 1994. 8. F. A. Carey, R. J. Sundberg, Advanced Organic Chemistry, Springer India Private Limited, 5th Ed, 2007. 9. T. Laue, A. Plagens, Named Organic Reactions, John Wiley and Sons, Inc., 2005.	
Course outcomes:	1. Students will be in a position to explain how a carbon-carbon bond can be constructed along with the selectivity in bond formations. 2. Students will be able to apply knowledge of various reactions in constructions of simple to complex organic molecules. 3. Students will be in a position to design protecting group strategies for synthesis of organic molecules. 4. Students will understand use of protecting groups in organic synthesis.	