PAPER-II: SUBSTITUTION REACTIONS AND STEREOCHEMISTRY

Semester	Subject Code	Category	Instruction Hours						Credits
			Lecture		Theory		Practical		
			Per Week	Per Semester	Per Week	Per Semester	Per Week	Per Semester	
I	21CPCH1B	Core	4	60	4	60	0	0	4

COURSE OBJECTIVES:

- Understanding the fundamental mechanism involved in electrophilic reactions, nucleophilic reactions and reactions that involve transient species.
- Understanding the basic aspects of stereochemistry such as chirality, nomenclature, stereoselectivity Vs stereospecificity, asymmetric synthesis and the conformational analysis of six membered ring systems.

COURSE OUTCOMES:

- On the successful completion of course, students will be able to achieve excellency in education as follows

CO Number	CO statement	Knowledge level
CO1	Gain knowledge about aromaticity, isotopic labeling techniques, kinetic isotope effect and the ambident nucleophiles	**K2 & K4**
CO2	Get clear idea about the nucleophilic attack on saturated carbon atoms leading to substitution reactions, different mechanisms of nucleophilic substitution, effect of solvent on the rate of reaction, neighboring group participation and the alkylation of active methylene compounds.	**K2 & K3**
CO3	Use various reagents in a logical manner in organic synthesis, understand various types of aromatic electrophilic substitution, nucleophilic substitution reaction and their mechanism	**K3 & K4**
CO4	Gain knowledge about basic principles of stereochemistry, to apply various concepts such as stereochemistry and fundamental principles of stereoselectivity in organic chemistry and also to identify and differentiate prochirality and chirality at centers, axis, planes and helices and determine the absolute configuration.	**K2 & K3**
CO5	Acquire good foundation about conformational analysis and to differentiate the reactive intermediates can be differentiated by their unique properties through various reaction pathways to develop new and notable aromatic organic compounds	**K3 & K4**

*CO-Course Outcomes

Knowledge level K1-Remember; K2-Understand; K3-Apply; K4-Analyze

MAPPING WITH PROGRAM OUTCOMES

COS	PO1	PO2	PO3	PO4	PO5	PO6
CO1	M	S	S	M	M	M
CO2	M	S	M	M	S	M
CO3	M	M	M	S	S	M
CO4	M	S	S	S	S	M
CO5	M	M	S	S	S	M

UNIT-I: AROMATICITY AND REACTION MECHANISM **12 hours**

Aromaticity of benzenoid, heterocyclic and non – benzenoid compounds – Huckel's rule – Annulenes. Kinetic and Non-kinetic methods of determining organic reaction mechanisms – Isolation and trapping of intermediates – Isotopic labeling studies – Primary Kinetic Isotopic effect. Generation of Kinetic and Thermodynamic enolates – Hammett equation-simple problems and Taft equation. Significance of reaction as well as substituent constants – Ambident nucleophiles such as CN^-, NO_2^-, phenoxide and ambident dianions – Williamsons ether synthesis.

UNIT-II: ALIPHATIC NUCLEOPHILIC SUBSTITUTION **12 hours**

Mechanism of nucleophilic substitution reaction: S_N1, S_N2 and S_Ni mechanisms – Solvent and leaving group effects and neighbouring group participation (NGP) – Substitution at carbonyl, vinylic and bridgehead system – Substitution with ambident nucleophiles- "O" Vs "C"alkylation. Role of LDA – crown ethers and phase transfer catalysts (PTC) in nucleophilic substitution reactions.

Generation of enolates – enolate selectivity (Kinetic Vs Thermodynamic) – alkylation of enolates and stereochemistry of enolate alkylation – Mechanism of ester hydrolysis – Alkylation of active methylene compounds. Asymmetric alkylation (Evans, Enders and Meyers procedures) – Preparation and synthetic utility of enamines, Finkelstein reaction – Wurtz coupling.

UNIT-III: AROMATIC ELECTROPHILIC AND NUCLEOPHILIC SUBSTITUTION REACTIONS **12 hours**

Aromatic electrophilic substitution: mechanism of nitration, sulfonation, Friedel – Crafts alkylation and acylation reactions – Synthesis of di and trisubstituted benzenes from benzene or monosubstituted benzenes (symmetrical tribromo benzene, 2-amino 5-methylphenol, 3 - nitro 4-bromobenzoic acid, 3, 4-dibromonitrobenzene, 1,2,3 – trimethylbenzene) – Hammett and Hammett-Taft equation – Haworth reaction (for naphthalene), Scholl reaction, Vilsmeier-Haack formylation, Gattermann reaction, Reimer– Tiemann and Bischler – Napieralski reactions.

Aromatic nucleophilic substitution in aryl halides by Meisenheimer complex mechanism and benzyne mechanism. Reactions of aryldiazonium salts – Zeigler alkylation, Vicarious Nucleophlic Substitution (VNS), Chichibabin and Schiemann reactions.

UNIT-IV: STEREOCHEMISTRY **12 hours**

Chirality, Symmetry elements, Asymmetric and Dissymmetric chiral molecules – Calculation of number of optical isomers – Stereochemistry of mono and disubstituted cyclopropane, cyclobutane, cyclopentane and cyclohexane – Stereochemistry of tri-substituted cyclopentane, trisubstituted pentane and tetrasubstituted hexane. Description of various types of optically active compounds including allenes, cumulenes, spiranes, biphenyls, *trans* – cyclooctene.

Compounds containing two asymmetric centers; Erythro and threo isomers – Conversion of Fischer projection into perspective forms – Erythro and Threo – Inter conversion of Fischer to Sawhorse and Newman projections – Zig-Zag representation of glucose – Interpretation of homotopic, enantiotopic and diastereotopic atoms and faces – Pro-chiral carbon – Concept of *Re*- and *Si*- faces – R and S nomenclature of simple compounds – allenes, spiranes and biphenyls – Stereospecific and Stereoselective reactions – Asymmetric Synthesis-Crams rule and Felkin-Anh model. E-Z nomenclature of olefins.

UNIT-V: REACTIVE INTERMEDIATES AND CONFORMATIONAL ANALYSIS

12 Hours

Organic reactive intermediates: Generation, stability and reactivity of carbocations, carbanions, free radicals, carbenes, carbenoids, benzynes and nitrenes.

Conformation of some simple 1, 2 – disubstituted ethane derivatives – Conformational analysis of disubstituted cyclohexane and their stereochemical features (geometric and optical isomerism (if shown) by these derivatives) – Conformation and reactivity of substituted cyclohexanol (oxidation and acylation) – cyclohexanone. (reduction) and cyclohexane carboxylic acid derivatives (esterification and hydrolysis) – Conformation and stereochemistry of cis and trans decalin and 9 – methyldecalin.

Distribution of Marks: Theory-80% and Problems-20%

TEXT BOOKS

S.No	Authors	Title	Publishers	Year of publication
1.	S.M. Mukherji and S.P. Singh	Organic Reaction Mechanism	McMillan India Ltd., Chennai	1990
2.	Stanley Pine	Organic Chemistry	V Edition, Tata McGraw-Hill Pub.,	1990
3.	Jerry March	Advanced organic reaction mechanism and structure	Tata McGraw-Hill Pub.,5th edition	2001
4.	Mc Murray	Organic Chemistry	V-edition, Thomson Asia Pvt., Ltd.	2001
5.	Graham Solomons	Organic Chemistry	John Wiley & Sons Ltd.,	2000
6.	P.S. Kalsi	Stereochemistry, Conformation analysis and Mechanism	2nd Edition, Wiley Eastern Limited, Chennai.	1993
8.	P.S. Kalsi	Stereochemistry and Mechanism through solved problems	Wiley Eastern Ltd	1994
9.	R.K. Bansal	Organic Reaction Mechanism	IV Edition, New Age Int.,(P) Ltd.,	2003
11.	Peter Sykes	A Guidebook to mechanism in organic chemistry	Orient Longman Ltd.	1999

REFERENCE BOOKS

S.No	Authors	Title	Publishers	Year of publication
1.	F. Carey and R. J. Sundberg	Advanced Organic Chemistry-Part A and B	Springer Science + Business Media, 5 th Ed	2007
2.	M. B. Smith and Jerry March	Advanced Organic Chemistry	John Wiley & Sons, 5th Ed	2001
3.	J. Clayden, N. Greeves and S. Warren	Organic Chemistry	Oxford University Press 2nd Ed	2012
4.	M. B. Smith	Organic Synthesis	Academic Press, 3rd Ed	2011
5.	R. O. C. Norman and J. M. Coxon,	Principles of Organic Synthesis	Chapman & Hall, 3rd Ed	1993

6.	Stuart Warren	Organic Synthesis: Disconnection Approach	Wiley India (P) Ltd	2007
7.	I. L. Finar	Organic Chemistry Vol 2: Stereochemistry and the Chemistry of Natural product	Dorling Kindersley India (P) Ltd	2009
8.	E. N. Eliel	Stereochemistry of Carbon Compounds	Tata McGraw Hill Ed, Reprint	2008
9.	D. Nasipuri	Stereochemistry of Organic Compounds	New Age International (P) Ltd, Reprint	2005
10.	E. L. Eliel and S. H. Wilen	Stereochemistry of Organic Compounds	Wiley India Ed	2008

TEACHING METHODOLOGY:

- PowerPoint presentation
- Models
- Group discussion
- Seminar and Assignments
- Animated videos
- Board and chalk

SYLLABUS DESIGNERS:

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