SEMESTER -III

SYNETHETIC REAGENTS, ADVANCED NMR, CONFORMATIONAL ANALYSIS AND ORD

THEORY

Programme: M.Sc. **Max. Hours: 60**
Course Code: P20/CHE/DSC/301 **Hours per week: 4**
Type of course: DSC – 9 **Max. Marks: 100**
No. of credits: 4

COURSE OBJECTIVES

1. A protecting group or protective group is introduced into a molecule by chemical modification of a functional group to obtain chemoselectivity in a subsequent chemical reaction, Study of organometallics in the mechanisms of various organic syntheses are emphasised with prediction of stereo- or regio- chemical consequences.
2. Synthetic reagents mostly rely upon the selection and implementation of proper reagents, which may be either used under specific or variety of conditions.
3. Identification of compounds using ^{13}C NMR and 2D NMR experiments and elucidates the structure of organic compounds
4. 4. Conformational analysis deals with the understanding of the complex relationship among different types of strain, while also discussing the factors that determine stability of a particular conformation.

COURSE OUTCOMES

CO1: Discuss the protection of various functional groups like alcohols, 1,2-diols, carbonyls, carboxylic acids to get the desired result.

CO2: Explain methods of preparation and applications of organometallic reagents like organo lithium,organo copper,organo silicon,organo borane reagents in organic synthesis. Discuss the reagents used in reactions like Carbonyl methylenation, carbene insertion and C-H activation

CO3: Discuss different types of reagents used for oxidation reactions

CO4: Solve the problems related to reduction reactions.

CO5: Discuss types of CMR spectra and methods of recording CMR and 2D NMR spectra. Explain the factors affecting chemical shift and CMR and applications of CMR.

CO6: Solve the problems based on CMR and 2D NMR spectra.

CO7: Discuss the Conformational analysis of cyclic molecules. Write down the factors governing the reactivity of axial and equatorial substituents in Cyclohexanes.

CO8: Describe Optical Rotatory Dispersion and how it is used for the determination of structure of chiral molecules.

MODULE1 : SYNTHETIC REAGENTS- I — 15 Hrs

i) Protecting groups: a) Protection of alcohols by ether, silyl ether and ester formation

b) Protection of 1,2-diols by acetal, ketal and carbonate formation c) Protection of amines by benzyloxycarbonyl, t-butyloxycarbonyl, fmoc and triphenyl methyl groups. d) Protection of carbonyls by acetal, ketal and thiolacetal (Umpolung) groups. e) Protection of carboxylic acids by ester and ortho ester (OBO) formation.

ii) Organometallic Reagents: Preparation and application of the following in organic synthesis: 1) Organo lithium 2) Organo copper reagents3) Organo boranes in C-C bond formation 4) Organo silicon reagents: reactions involving β-carbocations and α-carbanions, utility of trimethylsilyl halides, cyanides and triflates.

iii) Carbonyl methylenation:a) Phosphorousylide mediated olefination 1) Witting reaction, 2) Horner-Wordsworth-Emmons reaction.b) Titanium- Carbene mediated olefination 1) Tebbe reagent, 2) Petasis reagent 3) Nysted reagent.

iv) Carbene insertions: Rh based carbene complexes, cyclopropanations.

v) C-H Activation: Introduction, Rh catalysed C-H activation.

MODULE 2: SYNTHETIC REAGENTS- II — 15 Hrs

i) Oxidations: a) Oxidation of active C-H functions: DDQ and SeO2.b) Alkenes to diols: Prevost and Woodward oxidation c) Alcohol to carbonyls:CrVI oxidants (Jones reagent, PCC, PDC) IBX, DMP, CAN, TEMPO, TPAP, Swern oxidation d) Oxidative cleavage of 1,2-diols: Periodic acid and Lead tetra acetate.

ii) Reductions: a) Catalytic hydrogenation: Homogenous (Wilkinsons's catalytic hydrogenation) and heterogeneous catalytic reduction. b) Non-metallic reductions: Diimide reduction c) Dissolving metal reductions: Birch reduction. d) Nucleophilic metal hydrides: LiAlH4, NaBH4, and their modifications. e) Electrophilic metal hydrides: BH3, AlH3 and DIBAL. f) Use of tri-n-butyl tin hydride: Radical reductions.

MODULE 3: ^{13}CNMR AND 2D NMR SPECTROSCOPY 15 Hrs

i) ^{13}C NMR spectroscopy: Introduction, Types of ^{13}CNMR spectra: undecoupled, proton decoupled and off-resonance decoupled (ORD) spectra. ^{13}C chemical shifts, factors affecting the chemical shifts, chemical shifts of organic compounds. Calculation of chemical shifts of alkanes, alkenes and alkynes. Homonuclear (^{13}C, ^{13}C J) and heteronuclear (^{13}C, ^{1}H J and ^{13}C, 2H J) coupling. Applications of 13C-NMR spectroscopy: Structure determination, stereochemistry, reaction mechanisms and dynamic processes in organic molecules. 13C-NMR spectral editing techniques: principle and applications of APT, INEPT and DEPT methods.

ii) 2D-NMR spectroscopy: Principles of 2D NMR, Classification of 2D-experiments. Correlation spectroscopy (COSY) HOMOCOSY (1H-1H COSY) , TOCSY (Total Correlation Spectroscopy), HeteroCOSY (1H,13C COSY,HMQC), long range 1H,13C COSY (HMBC), Homonuclear and Heteronuclear 2D-J-resolved spectroscopy, NOESY and 2D- INADEQUATE experiments and their applications.

MODULE 4 CONFORMATIONAL ANALYSIS (CYCLIC SYSTEMS) &ORD

15 Hrs

Conformational analysis (Cyclic systems)

Study of conformations of cyclohexane, mono, di and tri substituted cyclohexanes, (1,3,5-trimethyl cyclohexanes and Menthols), cyclohexanone (2-alkyl and 3 -alkyl ketone effect), 2-halocyclohexanones, cycloheptane . Stereo chemistry of bicyclo[3,3,0]octanes, hydrindanes, decalins and perhydroanthracenes. Conformational structures of piperidine, N-Methylpiperidine, tropane, tropine, pseudotropine, decahydroquinoline and quinolizidine. Factors governing the reactivity of axial and equatorial substituents in cyclohexanes. (oxidation, SN2 reaction, rearrangements, Ester hydrolysis) Stereochemistry of addition to the carbonyl group of a rigid cyclohexanone ring.

Optical Rotatory Dispersion (ORD) and CD Spectroscopy: Optical rotation, circular birefringence, circular dichroism and Cotton effect. Plain curves and anomalous curves. Empirical and semiempirical rules-The axial haloketone rule, the octant rule, Helicity rule, Exciton chirality method. Application of the rules to the study of absolute configuration and conformations of organic molecules.

Recommended Books:

1.Some modern methods of organic synthesis by W. Carruthers
2.Guidebook to organic synthesis, by R K Meckie, D M Smith & R A Atken
3.Organic Synthesis by O House
4.Organic synthesis by Micheal B Smith
5.Reagents for organic synthesis, by Fieser&Fieser, Vol 1-11 (1984)
6.Organic synthesis by Robert E Ireland
7.Handbooks of reagents for organic synthesis by Reich and Rigby, Vol-I-IV
8.Organic chemistry by Jonathan Clayden, Nick Greeves and Stuart Warren
9.Organic Reactions and their mechanisms by P.S.Kalsi
10.Organic reaction mechanisms by V.K.Ahulwalia and Rakesh Kumar Parashar
11.Spectroscopic identification of organic compounds by RM Silverstein, G C Bassler and T B Morrill
12. Organic Spectroscopy by William Kemp
13. Spectroscopic methods in Organic chemistry by DH Williams and I Fleming
14. Modern NMR techniques for chemistry research by Andrew B Derome
15. NMR in chemistry - A multinuclear introduction by William Kemp
16. Spectroscopic identification of organic compounds by P S Kalsi
17. Introduction to organic spectroscopy by Pavia
18. Carbon-13 NMR for organic chemists by GC Levy and O L Nelson
19. Nuclear Magnetic Resonance Basic principles by Atta-ur-Rahman
20. Basic one and two-dimensional NMR spectroscopy by Horst Friebolin
21. NMR spectroscopy by H.Gunther
22. Stereochemistry of organic compounds — Principles & Applications by D Nasipuri
23. Stereochemistry of Carbon compounds by Ernest L Eliel& Samuel H. wilen
24. Stereochemistry: Conformation & Mechanism by P S Kalsi
25. The third dimension in organic chemistry, by Alan Bassendale
26. Stereo selectivity in organic synthesis by R S Ward.
27. Advanced organic chemistry. Part A Structure & Mechanism by Francis A. Corey and Richard J. Sundberg
28. Optical rotatory dispersion by C Djerassi
29. Optical rotatory dispersion and circular dichroism by P Crabbe
30. Mechanism and Structure in Organic chemistry by S Mukherjee

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SYNTHETIC REAGENTS, ADVANCED NMR, CONFORMATIONAL ANALYSIS AND ORD

MODEL THEORY QUESTION PAPER

Course Code: **P20/CHE/DSC/301** **Max. Time: 2½** Hrs
Credits: 4 **Max. Marks: 60**

SECTION –A

I. Answer the following Questions:- **4X10=40M**

1. (a) Expalin the synthetic applications of Gilmans Reagent**.(CO2)**
   (b) Discuss about protection of carbonyl group by acetal, ketal and thioacetal. **(CO1)**

OR

2. (a) Describe the synthetic applications of petasis reagent **.(CO2)**
   (b) Give synthetic applications of organoboranes in C-C bond formation**. (CO2)**

3. (a) Write a note on oxidation using SeO2**. (CO3)**
   (b) Explain the reduction of aromatic hydrocarbons using Birch reduction and explain the regioselectivity. **(CO4)**

OR

4. (a) Compare woodward and prevost oxidations. **(CO3)**
   (b) Discuss the mechanism involved in homogenous hydrogenation using Wilkinson's catalyst. **(CO4)**

5. (a) How do you calculate the ^{13}C chemical shifts of Alkanes, Alkenes and Alkynes with suitable examples? **(CO5)**
   (b)What is an APT spectrum? Explain with suitable example. **(CO6)**

OR

6. (a) What is Hetero COSY? Explain the spectrum and its use with one example. **(CO6)**
   (b) What are NOESY and 2D-INADEQUATE experiments? Outline their applications giving examples. **(CO5)**

7. (a) Discuss the stereochemistry of addition to the carbonyl group in a rigid cyclohexanone. **(CO7)**
   b) Discuss the stereochemistry of Decalin. **(CO7)**

OR

8. (a) Explain Cotton effect **(CO8)**
   (b) Explain Octant rule with suitable examples **(CO8)**

SECTION-B

II Answer any <u>FIVE</u> questions **5 X 4= 20 M**

9. Illustrate the use of Fmoc and CBZ as protecting groups. **(CO1)**
10. Write a brief note on the mechanism involved in the Wittig reaction. **(CO2)**
11. Explain the oxidative cleavage of 1,2diols by periodic acid. **(CO3)**
12. Write a brief note on reductions using AlH_3. **(CO4)**
13. Give the applications of DEPT by taking two examples? **(CO5)**
14. Draw the HOMO-COSY spectrum of ethylchloride. **(CO6)**
15. What is 2-alkyl ketone effect? **(CO7)**
16. Explain the application of CD curves to study the absolute configuration and conformation of organic molecules with examples