SEMESTER –III

PAPER-2 MODERN ORGANIC SYNTHESIS

THEORY

Programme: M.Sc.
Course code: P20/CHE/DSC/302 **Hours: 60**
Course type: DSC – 10 **Hours per week:4**
No. of credits: 4 **Max. Marks: 100**

COURSE OBJECTIVES:

1. Asymmetric synthesis deals with the specification of absolute and relative configuration and the measurement of the selectivity of stereo selective reactions. This module also a general strategy of asymmetric synthesis and the classification into chira substrate, auxiliary, reagent and catalyst controlled processes.

2. Retro synthetic analysis is a problem solving technique for transforming target molecule to a sequence of simple structures along a path which leads to simple or commercially available starting materials for synthesis.

3. Organic synthesis is a special branch of chemical synthesis and is concerned with the intentional construction of organic compounds via new synthetic schemes.

4. Synthetic organic chemistry is to develop new and improved chemical reactions and processes as quickly as possible.

COURSE OUTCOMES

CO1: Explain Prostereoisomerism, prochiral nomenclature, conditions of stereo selectivity and analytical methods with brief introduction of stereo selective reactions.

CO2: Discuss the types of asymmetric synthesis controlled by chiral auxiliary, chiral catalyst, chiral substrate and chiral reagent with examples.

CO3: Discuss the terminology, criteria for selecting target, synthesis involving chemo and regioselectivity, reversal of polarity and cyclisation involved in retro synthesis analysis. Explain order of events, one bond and two bond C-C and C-X disconnection and control in carbonyl condensation with examples.

CO4: Define strategic bond and discuss guidelines for disconnection with greatest simplification using symmetry and corresponding to known reliable reactions, Retrosynthesis and synthesis of Retronecene, Longifoline.

CO5: Discuss new synthetic reactions involving c-c coupling reaction, c=c formation reaction, multi component reactions.

CO6: Discuss ring formation reactions, ring opening & closing, metathesis, 1,3 dipolar cycloaddition reaction

CO7: Apply Baldwin rules for cyclisation of various compounds and discuss Chiron approach in organic synthesis & determine the absolute configuration by Mosher's method

MODULE I - ASYMMETRIC SYNTHESIS (15Hrs)

Introduction: Brief revision of classification of stereo selective reactions Prostereoisomerism: Topicity in molecules Homotopic, stereoheterotopic (enantiotopic and diastereotopic) groups and faces- symmetry criteria.

Prochiral nomenclature: Pro chiraility and Pro-R, Pro-S, Re and Si.

Conditions forstereoselectivity: Symmetry and transition state criteria, kinetic and thermodynamic control.

Methods of inducing enantioselectivity. Analytical methods: % Enantiomeric excess and diastereomeric ratio. Determination of enantiomeric excess: specific rotation, Chiral NMR; Chiralderivatizing agents, Chiral solvent, Chiral shift reagents and Chiral HPLC.

Chiral Substrate controlled asymmetric synthesis: Nucleophilic additions to chiral carbonyl compounds. 1, 2- asymmetric induction, Cram's rule and Felkin-Anh model. Chiral auxiliary controlled asymmetric synthesis: α-Alkylation of chiral enolates, Evan's oxazolidinone, 1, 4-Asymmetric induction and Prelog's rule..

Chiral reagent controlled asymmetric synthesis: Asymmetric reductions using BINAL-H. Asymmetric hydroboration using IPC2 BH and IPCBH2.

Chiral catalyst controlled asymmetric synthesis: Sharpless epoxidation. Asymmetric hydrogenations using chiral Wilkinson biphosphin catalyst.

Asymmetric aldol reaction: Diastereoselective aldol reaction (achiral enolate& achiral aldehydes) its explanation by Zimmerman-Traxel model.

MODULE II – SYNTHETIC STRATEGIS (15 Hrs)

Introduction: Terminology, Target, synthon, synthetic equivalent, functional group interconversion (FGI), functional group addition. Criteria for selection of target. Linear and

convergent synthesis. Retrosynthetic analysis and synthesis involving chemoselectivity, region selectivity, reversal of polarity and cyclizations. . Order of events: S-Salbutamol, Propoxycaine..

One group C-C and C-X disconnections: Introduction .One group C-C disconnections in alcohols and carbonyl compounds. One group C-X disconnections in Carbonyl compounds, alcohols, ethers and sulphides.

Two group C-C and C-X disconnections: Introduction .Two group C-X disconnections in 1,1-difunctionalised, 1,2-difunctionalised and 1,3-difunctionalised compounds.
Two group C-C disconnections: Diels-Alder reaction, 1, 3-difunctionalised compounds, 1,5- difunctionalised compounds, Michael addition and Robinson annulation.
Control in carbonyl condensations: oxanamide and mevalonic acid.
Strategic bond: definition, guidelines for disconnection; disconnection of C-X bonds, disconnect to greatest simplification, using symmetry in disconnection, disconnection corresponding to known reliable reaction, high yielding steps and recognizable starting materials. Retrosynthesis of Retronecene, Longifoline.

MODULE III - NEW SYNTHETIC REACTIONS **(15 Hrs)**

1. Metal mediated C-C and C-X coupling reactions: Suzuki, Heck, Stille, Sonogishira cross coupling, Buchwald-Hartwig and Negishi-Kumada coupling reactions.
2. C=C Formation Reactions:Shapiro, Bamford-Stevens, McMurreyr eactions,Julia- Lythgoeo lefination and Peterson's stereoselective olefination.
3. Multicomponent Reactions:Ugi, Passerini, Biginelli, Bergman and Mannich reactions.
4. Ring Formation Reactions:Pausan-Khand reaction, Nazerov cyclisation.
5. Click Chemistry:Click reaction, 1,3-dipolar cycloadditions.
6. Metathesis: Grubb's 1st and 2nd generation catalyst, Olefin cross coupling metathesis(OCM), ring closing metathesis(RCM), ring opening metathesis(ROM), applications.
7. Other important synthetic reactions: Baylis-Hilman reaction, Eschenmoser- Tanabe fragmentation, Mitsunobu reaction, Stork-enamine reaction and Michael reactions.

MODULE IV - NEW TECHNIQUES AND CONCEPTS INORGANICSYNTHESIS

(15 Hrs)

1. Techniques in peptide synthesis: Solid phase peptide synthesis, commonly used resins (Rink resin, Wang resin and Ellmanresin, synthesis of cross linked Merrifield resin and drawbacks of solid phase synthesis.
2. Solid phase oligodeoxynucleotide synthesis: Phosphotriester, phosphitetriester and phosphoramidite pathway
3. Oligosaccharide synthesis:Glycosidation:cylicoxocarbeniumion, glycosyl donors and glycosyl acceptors, Kahneglycosidation, convergent and linear oligosaccharide synthesis.
4. Phase Transfer catalysis: Onium and crwon ethers as PTC.
5. Tandem synthesis: Tandem reactions; conjugate addition-aldol reaction, polymerization-cyclisation, elctrocylic-Diels Alder reaction.
6. Baldwin Rules: Exo and Endo cyclisation, tetrahedral, trigonal and diagonal systems, favoured and disfavoured cyclisations.

7. Chiron approach in organic synthesis: Nature's chiral pool, carbohydrates, amino acids, hydroxy acids, terpenes as chiral precursors. Synthesis of shikimic acid from D-arabinose, furanonycin from D-glucose, S-(-)-ipsenol from S-leucine.
8. Determination of absolute configuration: Mosher's method.

REFERENCES BOOKS:

1.Asymmetric synthesis by Nogradi

2.Asymmetric organic reactions by J D Morrison and H S Moschcr

3.Principles in Asymmetric synthesis by Robert E. Gawley&Jeffreyaube

4.Stereo differentiating reactions by Izumi

5.Some modern methods of organic synthesis by W Carruthers

6.Guidebook to organic synthesis, by R K Meckie, D M Smith & R AAtken

7.Organic synthesis by Michael B Smith

8.Organic Synthesis-The disconnection approach by S Warren

9.Organic Synthesis by C Willis and M Willis

10. Problems on organic synthesis by Stuart Warren

11.Organic chemistry Jonathan Clayden, Nick Greeves and Stuart Warren

12.The logic of chemical synthesis by Elias James Corey and Xue-Min Cheng

13. Name reactions by JieJacj Li

SEMESTER-III MODERN ORGANIC

SYNTHESIS MODEL THEORY

QUESTION PAPER

Course code: P20/CHE/DSC/302 **Max. Time:2½**
No. of credits:4 **Max. Marks:60**

1. a) Write a brief note on the following techniques in the determination of enantioselectivity. (CO2)
(i) Specific rotation (iii) Chiral Lanthanoid shift reagents
(ii) Chiral HPLC
b) Write an account on enantiotopic ligands and faces. (CO1)

OR

2. a) Explain the asymmetric epoxidation by Sharpless procedure with examples (CO2)
b) What is chiral reagent controlled asymmetric synthesis. Explain asymmetric reductions using BINAL-H (CO2)

3. a) Discuss the terms Functional group addition and Chemo selectivity with suitable examples. (CO3)
b) Explain Robinson annulation with suitable example.(CO3) OR

4. a) Explain the concept of two group C-X disconnections using 1,2 and 1,3-difunctionalised compounds. (CO3)
b) What is meant by control in carbonyl condensation? Explain taking Oxanamide (CO3)

5. a) Formulate Baylis –Hilmann reaction and its mechanism (CO5)
b) Give an account of Shapiro reaction with mechanism. Explain its region selectivity with respect to unsymmetrical hydrazones. (CO5)

OR

6. a) What is Metathesis? Explain Ring opening and Ring closing metathesis reactions examples (CO6)
b) Explain the mechanism involved in Suzuki reaction (CO5)

7. a) Discuss Convergent Oligosaccharide synthesis (CO7)
b) State Baldwin rules for five and six membered ring formation with examples. (CO8)

OR

8. a) How do you plan the synthesis of tripeptide by solid phase method? (CO7)
b) Determine the absolute configuration of a chiral compound by Moscher's method. (CO8)

SECTION-B

II. Answer any five **5 x 4 = 20 M**

9. Define substrate selectivity, product selectivity with one example each. (CO1)
10. Explain cram's cyclic model with examples? (CO2)
11. Write the retro synthesis and synthesis of Salbutamol. (CO3)
12. Define strategic bond and discuss the guidelines for the disconnection of C-X bondsusing symmetry in disconnection. (CO4)
13. Explain McMurrey reaction (CO5)
14. Explain the Click reaction of 1, 3-dipolar cycloadditions (CO6)
15. Explain Glycosyl donor and Glycosyl acceptor with suitable examples. (CO7)
16. What is Tandam synthesis? Explain with one example. (CO7)