SEMESTER - IV

ADVANCED HETEROCYCLIC&NATURAL PRODUCTS-I

THEORY

Programme: M.Sc. **Max.Hours : 60**
Course Code: P20/CHE/DSE/401 **Hours per week: 4**
Type of course: DSE – 5 **Max.Marks: 100**
No. of credits : 4

COURSE OBJECTIVES:

- The rationalization of synthesisand reactivity of non aromatic three and four membered heterocyclic compounds with single and two hetero atoms.**Aromaticity** deals with classification of organic molecules into aromatic, non aromatic and anti aromatic compounds.
- This module deals with synthesis, reactivity and aromaticity of Five and six membered heterocyclics with two hetero atoms.
- Six membered heterocyclic compounds with more than two similar or different hetero atoms aromaticity, synthesis and reactivity
- Seven membered heterocyclic compounds containing one hetero atom are the Heterocyclicanalogues of 1,3,5 – cycloheptatrien. The interest of these compounds is of recent origin.

COURSE OUTCOME:

CO1 Outline the synthesis, reactivity and importance of ring systems like Azirines, Aziridines, Oxiranes, Thiiranes, Diazirenes, Diaziridines, Oxaziridines, Azetidines, Oxetanesandthietanes

CO2 Explain the criteria for aromaticity and Huckel's 4n+2 electron rule for benzene and non benzenoid aromatic compounds.

CO3 Outline the synthesis, reactivity, aromatic character and importance of five and six membered heterocyclics with two hetero atoms

CO4 Determine the biosynthetic mechanism, discuss biosynthetic precursors and feeding experiments of secondary metabolites.

CO5 Explain Acetate –malonate pathway, Shikimmic acid pathway and Mevalonic acid pathway of secondary metabolites with examples.

CO6 Discuss the total stereo selective synthesis including Nicalou's synthesis of Dynemycin A,andTaxol, Corey's Synthesis of Prostaglandins and Pacoriflorin.

CO7 Discuss Sharpless synthesis of L-Hexoses, Danishefsky synthesis of Indolizomycin.

CO8 Discuss Takasago synthesis of Menthol, Hoffmann-LaRoche synthesis of Biotin

MODULEI NONAROMATIC HETEROCYCLICS& AROMATICITY (15 Hrs)

Different types of strains, interactions and conformational aspects of nonaromatic heterocycles. Synthesis, reactivity and importance of the following ring systems.Azirines, Aziridines, Oxiranes, Thiiranes, Diazirenes, Diaziridines, Oxaziridines, Azetidines, Oxetanesandthietane

Aromaticity: Introduction, Aromatic and anti aromatic compounds. Criteria for aromaticity. Huckel's 4n+2 electron rule for benzene and non benzenoid aromatic compounds. Eg. Cyclopropenium ion, cyclopentadienyl ion, cycloheptatrienium ion, azulene and annulenes.

MODULE II FIVE AND SIX MEMBERED HETEROCYCLICS WITH TWO HETERO ATOMS (15 Hrs)

Synthesis, reactivity, aromatic character and importance of the following heterocycles:Pyrazole, Imidazole, Oxazole, Thiazole, Isoxazole, Isothiazole, Pyridazine, Pyrimidine. Pyrazine,Oxazine, thiazine, benzimidazole, benzoxazoleand benzthiazole.

MODULE III BIOSYNTHESIS OFNATURALPRODUCTS: (**15 Hrs)**

Biosynthesis of secondary metabolites: Introduction,Difference between Laboratory synthesis and biosynthesis. Methods for determination of biosynthetic mechanism. Isolation and identification of Biosynthetic precursors, Feeding experiments – use of radioisotopes Measurement of incorporation – absolute incorporation, specific incorporation. Identification of the position of labels in labeled natural products by chemical degradation and spectral methods. Major biosynthetic pathways: 1) Acetate-Malonate pathway: Biosynthesis of aromatic compounds, 2) Shikimic acid pathway ; Biosynthesis of essential amino acids – phenylalanine, tyrosine and tryptophan, carboxylic acid derivatives, flavonoids and morphine alkaloids. 3) Mevalonic acid pathway : Biosynthesis of terpenes – mono,sesqui, di, tri (β-amyrin) and carotenoids, steroids – cholesterol.

MODULE IV TOTAL STEREOSELECTIVE SYNTHESIS OF NATURAL PRODUCTS (15 Hrs)

Nicalou's synthesis of DynemicinA , Corey's synthesis of prostaglandins (E2, F2α) and paeoriflorin, Sharpless synthesis of L-hexoses, Nicolaous synthesis of taxol, Danishefsky synthesis of indolizomycin, Takasago synthesis of menthol, Hoffmann-LaRoche synthesis of Biotin

Recommended Books:

1. .Heterocyclic Chemistry, T.Gilchrist
2. An introduction to the Chemistry of heterocyclic compounds, R.M.Acheson
3. Heterocyclic Chemistry, J.A.Joule&K.Mills
4. Principles of Modern Heterocyclie Chemistry, A.Paquette
5. Handbook of Heterocyclic Chemistry, A.R.Katritzky
6. The aromaticity III level, units 17-19 British open university volumes
7. Aromatic character and aromaticity by G.M.Badger
8. Non-benzenoid aromatic compounds by D.Ginsberg
9. Nonbenzenoid compounds by Lloy
10. Textbook of organic chemistry, Vol II by I L Finar
11. Chemistry of natural products, Vol 12, by Atta-Ur-Rahman
12. An introduction to the chemistry of terpenoids and steroids, by William templeton
13. Systematic identification of flavonoid compounds by Mabry &Markham
14. Steroids by Fieser arid Fieser
15. Alkaloids by Manske
16. Alkaloids by Bentley
17. The chemistry of terpenes by A Pinder
18. The terpenes by Simenson
19. Terpenoids by Mayo
20. Alkaloids by Pelletier
21. Total synthesis of Natural Products by ApsimonVol 1-5
22. Biosynthesis by Geismann
23. Principles of organic synthesis 3rdEd.R O C Norman and J M Coxen
24. One and two dimensional nmr spectroscopy by Atta Ur Rahman
25. Classics in total synthesis K C Nicolaou and E J Sorenson
26. Spectrometric identification of organic compounds by Silverstein and Webster

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MODEL QUESTION PAPER

THEORY

Course Code:P20/CHE/DSE/401 **Max Marks: 60**
Credits :4 **Time: 2½Hours**

SECTION –A (Essay Questions)

I. Answer the following **4 x 10 = 40 M**

1. (a) Outline the synthesis of Diazridine ring system. (CO1)
   (b) Discuss the reactivity of Oxetanes. (CO1)

   OR

2. (a) Discuss the reactivity of Azetidines. (CO1)
   (b) Outline the synthesis of Thiiranes. (CO1)

3. (a) Explain electrophilic and nucleophilic substitution reactions of imidazole. (CO3)
   (b) Outline the synthesis of pyrazine. (CO3)

   OR

4. (a) Discuss the reactivity of benzimidazole. (CO3)
   (b) Discuss the synthesis of thiazole. (CO3)

5. (a) Describe the shikimic acid pathway for the biosynthesis of aromatic compounds. (CO5)
   (b) Suggest the biosynthetic pathway of flavonoids. (CO5)

   OR

6. (a) Discuss the biosynthesis of Morphine. (CO5)
   (b) How do you identify the position of labeled precursors by chemical degradation method.(CO4)

7. Explain the Danishefsky synthesis of Indolizomycin. (CO7)

   OR

8. (a)Write the Corey's synthesis of Prostaglandins. (CO6)
   (b) Discuss the Sharpless synthesis of L-Hexoses. (CO7)

SECTION –B

II Anwer any five **5 x 4 = 20 M**

9. Discuss the fragmentation reactions undergo by aziridines. (CO1)
10. Discuss the aromaticity of [12],[14] & [16]-Annulenes. (CO2)
11. Discuss the aromaticity and synthesis of isoxazole. (CO3)
12. Explain the reactivity of pyrimidine. (CO3)
13. What are the differences between a laboratory synthesis and biosynthesis? (CO4)
14. How a biosynthetic pathway determined by use of radioisotopes? Give one example. (CO4)
15. Explain the Takasago synthesis of Menthol. (CO8)
16. Write the synthesis of Hoffmann -LaRoche synthesis of Biotin. (CO8)