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SHAMBHUNATH INSTITUTE OF PHARMACY

Subject Code:BP401T   **Subject: Org Pharmaceutical Chemistry(III)**

B.Pharm.   SEMESTER: IV

FIRST SESSIONAL EXAMINATION, EVEN SEMESTER,(2019-2020)
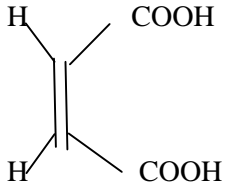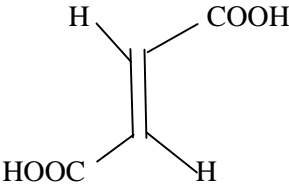
Time –1hr 30 min   *SOLUTION*   Maximum Marks – 30

SECTION –A

1. Attempt all questions in brief.   (1*5 = 5)

Q N	QUESTION
a.	**What are Meso compounds? Why are they optically inactive?** **SOLUTION:** An optical isomer containing more than one chiral carbon center but possessing any of the elements of symmetry (Plane or center) are known as Mesoform of the isomer. Meso compounds are optically inactive because of Mutual Internal Compensation, i.e. rotation caused by upper half of the molecule in one direction is cancelled out by the lower half of the molecule in opposite direction and in equal amount. This is also because of the achiral nature of the molecule due to presence of a plane of symmetry. COOH | H—C—OH | H—C—OH | COOH e.g. meso tartaric acid
b.	**What are the conditions for optical activity?** **SOLUTION:** For a compound to be optically active : (i) It should be asymmetric or chiral (ii) It must have no element of symmetry (iii) The mirror images should be non super-imposable COOH COOH | | H—C—OH HO—C—H | | CH₃ CH₃ D-lactic acid L-lactic acid e.g lactic acid
c.	**Discuss any TWO conditions necessary for Geometrical Isomerism.** **SOLUTION:** For being a geometrical isomer; (i) Since the rotation is supposed to be restricted, there should be a Double bond or a ring in the molecule. (ii) The two atoms or groups attached to each double bonded carbon should be different.

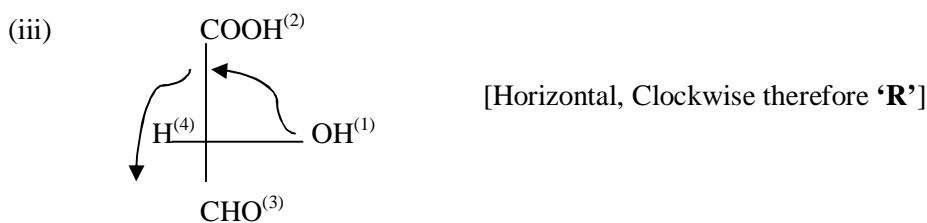|	(iii) The isomers should be non mirror images (also called Diastereomers)
	  Maleic acid Fumaric acid
d.	**Cis isomer of a geometrical isomer is lesser stable than trans isomer. Why?** **SOLUTION:** Cis isomer of a geometrical isomer is lesser stable than the trans form because in Cis form the bulky groups are packed closer and there is an element **of STERIC HINDERANCE**.
e.	**List the CIP sequence rule for priority assignment.** **SOLUTION:** RULE 1: If the four atoms attached to the chiral center are all different, priority depends on atomic number, with the atom of lowest priority number getting the lower priority and with highest atomic number getting highest priority. E.g. priority in the compound having Bromo, Chloro, Iodo and Methane will be: I(1), Br(2), Cl(3) and H(4) Similarly higher isotopes get higher priority. In groups, the order of priority is decided on the Basis of atomic number of first atom of the group. RULE 2: if two atoms attached to the chiral center are same, we compare the atoms attached next to these first atoms. RULE 3: When there is a double or a triple bond, both atoms are considered to be duplicated of triplicated

SECTION - B

2. Attempt any __TWO__ of the following.   (2*5=10)

Q N	QUESTION
a.	**What is Racemic modification? How can a recemic mixture be resolved?** **Solution: An equimolar mixture** of enantiomers is called racemic modification. It is supposed to be optically inactive because the rotation caused by a molecule of 1 isomer is exactly cancelled by an equal and opposite rotation caused by the other enantiomers. Racemic mixture is denoted by $\pm$ signs or (dl). The separation of racemic mixture into its (+) and (-) components is known as resolution. It is achieved by any of the following methods: 1. By mechanical separation for solid substances with well-definedcrystals. This is done by using hands magnifying glass and small forceps. The method is very tedious for practical purposes. 2. By bio-chemical methods using certain microorganism such as yeast, bacteria etc. which destroys one

		form selectively leaving the other in solution.
		3. By chemical methods using the racemic mixture to combine with another optically active compound and dissolving insolvents.
		4. Preferential Crystallisationof a super saturated solutions by seeding with a crystal of one of the two enantiomers.
		5. By kinetic method by considering the different rate of reactions of different enantiomers with an optically active substance.
		6. By complex formation
		7. By chromatography considering difference in affinity of stationary phase with the two enantiomers.
		8. By selective adsorption over a column of finally powdered optically active adsorbent
b.		**Assign R / S or E / Z, whichever is applicable to the following compounds.**

(i)

$F^{(1)}$ (2) (2) $OH^{(1)}$ **'Z'**

(ii)

$HO^{(2)}$ $CH_3^{(2)}$

$Cl^{(1)(1)}$ **'Z'**

(iii)

$COOH^{(2)}$

$H^{(4)}$ $OH^{(1)}$ [Horizontal, Clockwise therefore **'R'**]

$CHO^{(3)}$

(iv)

CH_2OH

H ———— Br   **'2R, 3S'**

H_3C NH_2
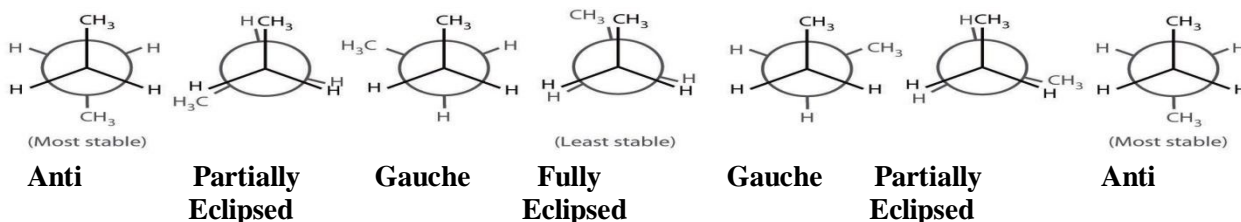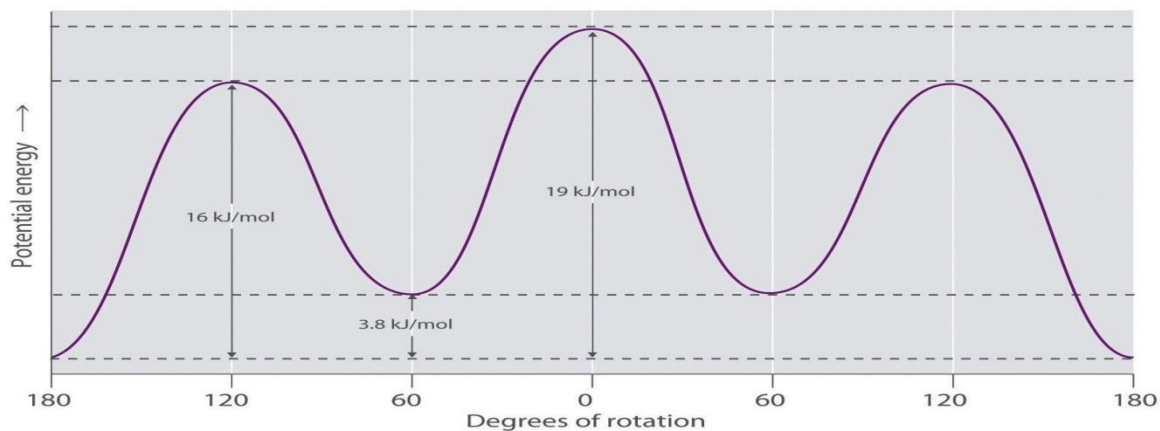
CHO

(v)

OH

NH_2

H   **'S'**
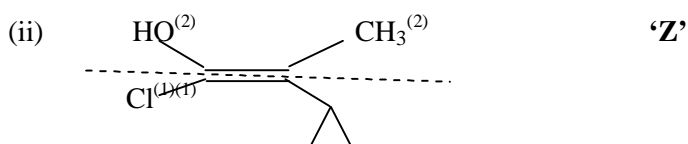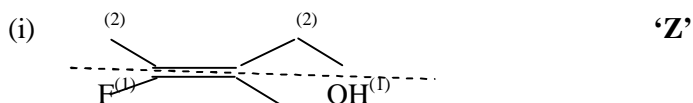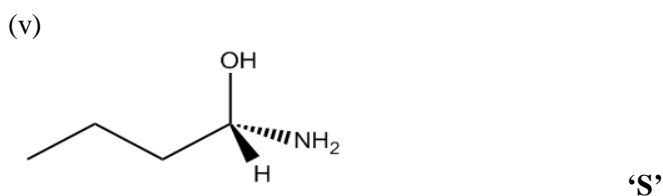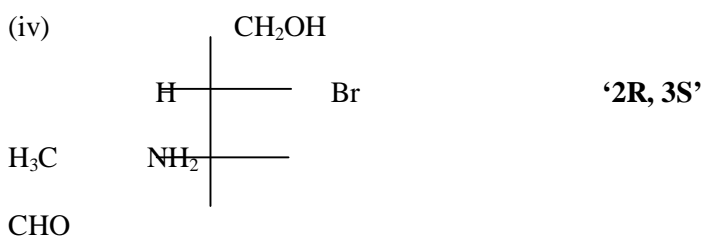
| **c.** | | **Give all conformational isomers of n-butane and express their stability in terms of the energy profile diagram.**
 SOLUTION: |

| Anti | Partially Eclipsed | Gauche | Fully Eclipsed | Gauche | Partially Eclipsed | Anti |

As is evident from the energy profile diagram above the anti - form is the most stable while the fully eclipsed form is the least. The intermediate forms of partially eclipsed and gauche have intermediate energies so intermediate stability. This stability of the different forms is due to the steric hindrance and the torsional strain on the C-C bond.

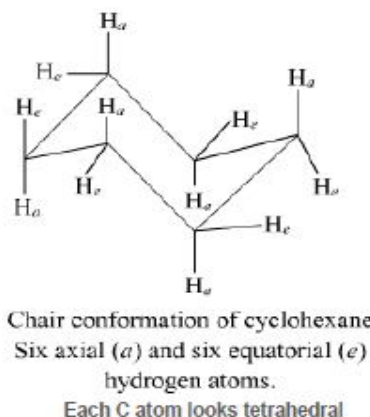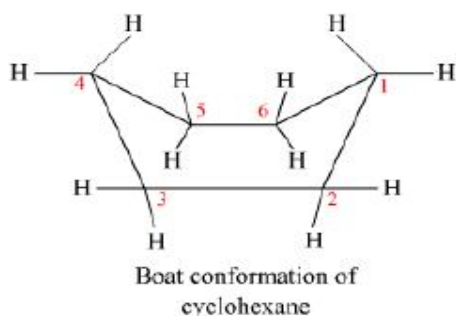| d. | **Discuss all the optical isomers of Tartaric acid.**
SOLUTION:
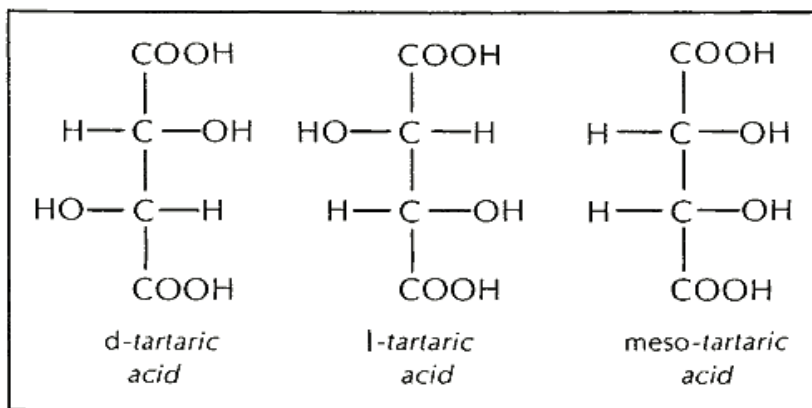
Str.1　　　**Str.2**　　　**Str.3**
Of the three forms of tartaric acid Structure1 and 2 are non- superimposable mirror images of each other and are thus optically active .But the structure 3 is optically inactive due to the presence of plain of symmetry and internal compensation.Also this mesoform(Structure 3) is a diastereomer of structure 1 and structure 2 in addition to these three forms tartaric acid also exists in optically active racemic modification($\pm$) |

SECTION - C

3. Attempt any ONE part of the following:　　　(1*5 = 5)

Q N	QUESTION
a.	**Explain stability of cycloalkanes based on Sachse Mohr's theory.**

Sachse-Mohr Theory (Theory of Strainless Rings)

According to Baeyer, the carbon atoms of a ring are all in the same plane. The strain was calculated on the assumption that cyclic rings are planer. The strain is minimum for cyclopentane and goes on increasing as the size of the ring increases. Hence, members higher than cyclopentane should be increasingly unstable but Hermann Sachse, soon pointed out that large rings need not be strained, because the carbons need not be coplanar.

Sachse Mohr's theory proposed that higher member ring can become free from strain if all the ring carbons are not forced into one plane. They exhibit in two non-planar 'folded' or 'puckered' conformations both of which are completely free from strain. These are strainless as the carbon atoms lie in different planes and the normal valency angle (109.5°) is retained. These are called the 'Chair' Form or the 'Z' Form and the 'Boat' Form or the 'C' Form because of their shapes.


Boat conformation of cyclohexane

Chair conformation of cyclohexane
Six axial (a) and six equatorial (e) hydrogen atoms.
Each C atom looks tetrahedral

The chair confirmation is the most stable confirmation. In this, there are two types of positions, Axial and Equatorial. The Axial position point perpendicular to the plane of ring while the Equatorial position are around the plane of ring. In both the forms Carbon 2, 3, 5, and 6 are in the same plane. In the boat form, Carbon 1 and 4 are above the plane. While in the chair form, Carbon 1 is above the plane and 4 is below the plane.

b.	**Write a note on Stereospecific and Stereoselective reactions.** **SOLUTIONS:** **Stereospecific Reactions:** This reaction specifies the reactions which are related more to the reactant. Here, a particular stereo isomer of a reactant participates in the reaction and the other form has very less or almost nill participation or if at all it shows a different products. In this type of reaction the stereo chemistry of the reactant completely determines the stereo chemistry of the products. e.g. Anti elimination is shown my cis isomer while trans isomer does not show such eliminate reaction
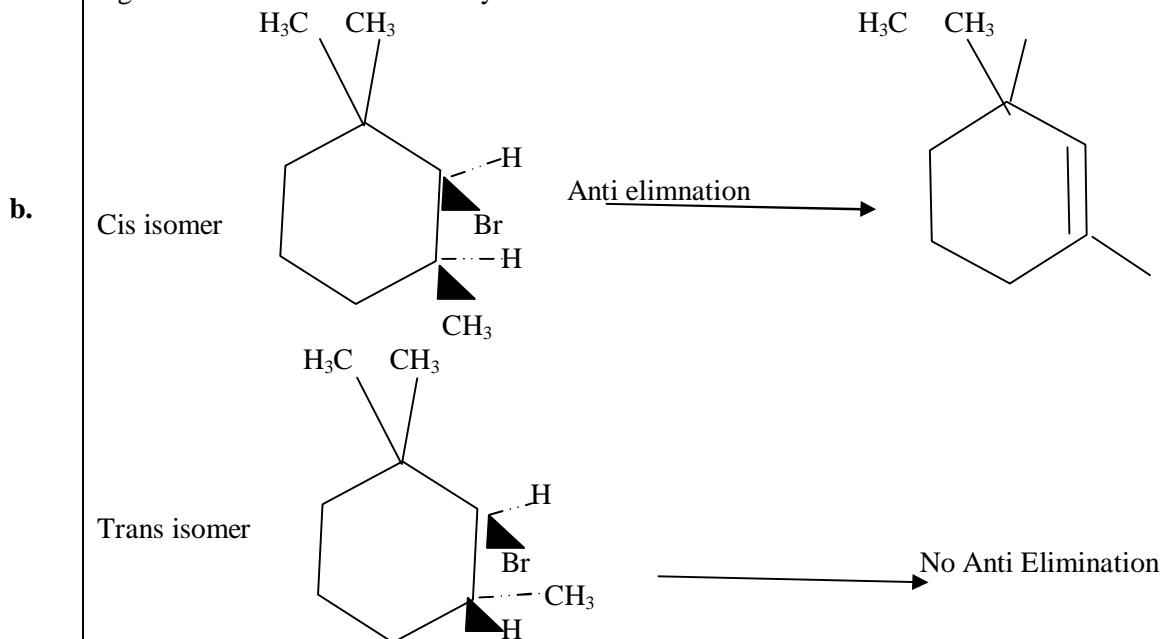
Stereoselective reactions: This reaction specifies the reactions which are related more to the product which means the products are found in uneven amount. One streoisomer is formed predominantly out of several diastereomers. There is also a choice of pathway but the product is defined by the most favorable pathway.

e.g. elimination reaction of 2-iodobutane(1) in presence of specific reagents gives 3 products namely, trans-2-butene (2), cis-2-butene(3) and 1-butene(4) with product (2) being the major product

2 – iodobutane	trans-2-butene	cis-2-butene	1-butene
(1)	(2)	(3)	(4)
	60%	20%	20%

4. Attempt any ONE part of the following: (1*5 = 5)

Q N	QUESTION
a.	**Discuss stereoisomerism in bi-phenyl compounds with examples.** **SOLUTION:** Ortho-Ortho-tetrasubstituted biphenyls become non-planar at room temperature in order to have minimum electronic repulsion among substituents.In this orientation(phenyl planes perpendicular to each other) the free rotation of C-C single bond is restricted and molecule shows optical activity due to molecular disymmetry. The two phenyl rings become perpendicular to each other thus leading to disymmetry which in turn leads to optical activity(chirality). Conditions for biphenyls to be chiral: **1st condition for optical activity of Biphenyls** ▸ The substituent in the ortho_position must have a large size. If three bulky groups present on ortho position they cause restriction. The groups are large enough to interfere mechanically i.e. to behave as obstacles then free rotation about the single bond is restricted. Thus the two benzene rings cannot be co-planner. ▸

2nd condition for optical activity of Biphenyls.

▸ Resolvable biphenyls must contain different ortho substituted on each ring if one or both rings contain two identical substitution the molecule is not chiral, in other words plane of symmetry must be absent in biphenyls.

▸
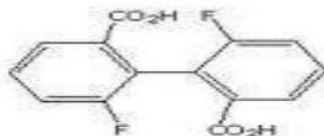
Explain Partial and Absolute Asymmetric synthesis with examples.
SOLUTION:
When a chiral olecule is synthesized from an achural molecule the product obtained is bound to be an optically inactice racemic mixture containing an equal amount of a pair of enantiomers
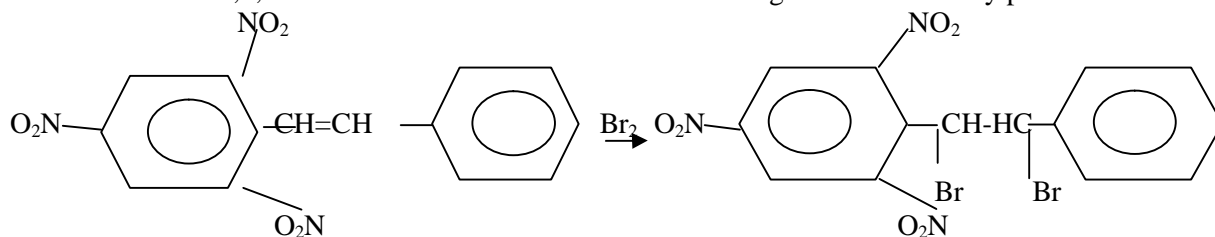
e.g. propionic acid $\longrightarrow$ $(\pm)$ α-bromo propionic acid

However, an optically active (chiral) compound can also be synthesized directly from an optically inactive compound in presence of a suitable optically active reagent. The process in which an optically active compound (asymmetric) compound is synthesized from an Achiral molecule under the influence of some optically active substance is known as Asymmetric synthesis.

    (i)   There must be a prochiral unit in the substrate molecule
    (ii)   Either the substrate, or reagent, or solvent or the catalyst must be a pure enantiomer.
          Based on these,the partial asymmetric synthesis can be categorized.

e.g. CH3COCOOH + (-)-menthol $\longrightarrow$ CH3COCOO – (-)-menthyl $\xrightarrow[\text{(ii) hydrolysis}]{\text{(i) LiAlH4}}$ CH3CHOHCOOH
   pyruvic acid   lactic acid (leavo)

Absolute Asymmetric synthesis: the synthesis in which intermediate active reagents are not used for the synthesis of optically active products form achiral substances is known as Absolute asymmetric synthesis. E.g. addition to bromine 2,4,6-trinitro stilbene in a controlled condition gave dextrorotatory products.


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5. Attempt any ONE part of the following :   (1*5 = 5)

Q N	QUESTION
a.	**Discuss Optical isomerism with examples.** **SOLUTION:** Compounds having same molecular formula and structural formula but differ in action towards plane polarized light are known as optical isomers. The property of certain compounds in solution to rotate plane of monochromatic plane polarized light either clockwise or anti-clockwise is known as Optical activity. The isomers are non-superimposable and non- inter convertible by rotation around C-C bond. It is possible only by breaking and reformation of bonds. The isomers should have no element of symmetry and are mirror images. If the rotation of the plane of plane polarized light is to the right or clockwise , it is denoted as Dextrorotatory

and represented by 'd' or (+)

While the isomer which rotates it to the left or anti clockwise are denoted Leavorotatory and represented by 'l' or (-)

An equimolar mixture of the above is called Racemic mixture and it in incapable of rotating light due to external compensation.

e.g.

COOH   COOH
 | |
H — C — OH   HO — C — H
 | |
CH₃   CH₃
D-lactic acid   L-lactic acid

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b.
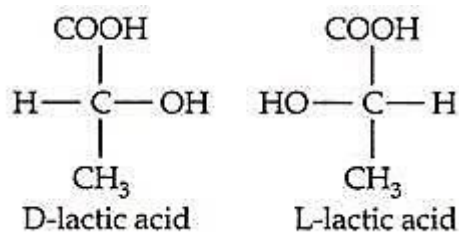
What are the methods of determination of configurations of Geometrical isomerism?

SOLUTION:

Depending on the nature of compound, following methods are used for determination of configuration of geometrical isomers.

1. Physical methods: by spectroscopy or X-Ray analysis.
2. On basis of higher melting point and intensity of absorption of trans isomer than that of cis. This is due to more regular and symmetrical structure of trans they are able to pack more compactly and have greater intermolecular force.
3. Trans isomer has lower boiling point, heat of combustion, heat of hydrogenation, refractive index and dipole moment.
4. By cyclisation. On heating Maleic acid forms anhydride while Fumaric acid does not.
5. By conversion into compound of known configuration
6. Determination of configuration of oxime.