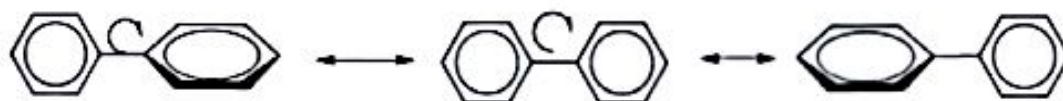
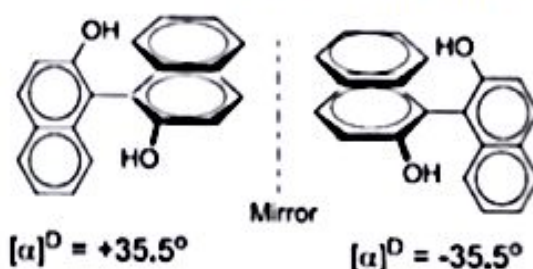


❖ Atropisomerism

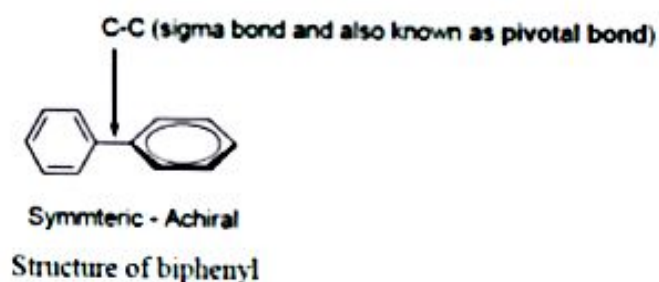
- **Biphenyls** are compounds whereby a phenyl ring is connected to another through a central σ bond.



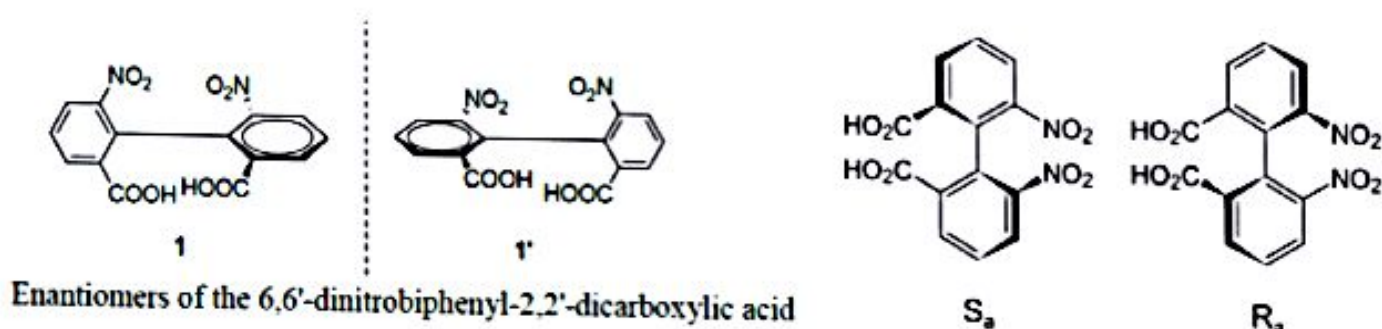
- In unsubstituted biphenyl, there is sufficient amount of freedom of rotation around the central single bond to allow for free interconversion between the various conformers or rotamers so that the various rotamers cannot exist independently.
- However, **biphenyls** with large substituents at the **ortho** positions on either side of the **central σ bond** experience restricted rotation along this bond due to **steric hindrance**. If the substituents are different, a chiral molecule existing as a pair of enantiomers called **atropisomers** is obtained.
- Polynuclear aromatic systems such as binol also exist as enantiomers.



- Atropisomerism are stereoisomers as a result of restricted rotation about a single bond.
- Atropisomers are stereoisomers resulting from hindered rotation about single bonds where the steric strain barrier to rotation is high enough to allow for the isolation of the conformers (from Greek, a = not and tropos = turn).
- If bulky group on **ortho** position of **bi-phenyl** or strained ring structural features. Bulky substituents or strained rings may enhance the barrier to rotation between two distinct conformations to such an extent as to allow observation of **atropisomers**.
- **Atropisomerism** is also called **axial chirality** and the chirality is not simply a centre or a plane but an axis.



- Biphenyl substituted on **ortho** position, which contains a chiral axis along the biphenyl linkage. The biphenyl rings are perpendicular to each other in order to minimize steric clashes between the four ortho substituents meaning that rotation about the biphenyl bond through pivotal bond is restricted.

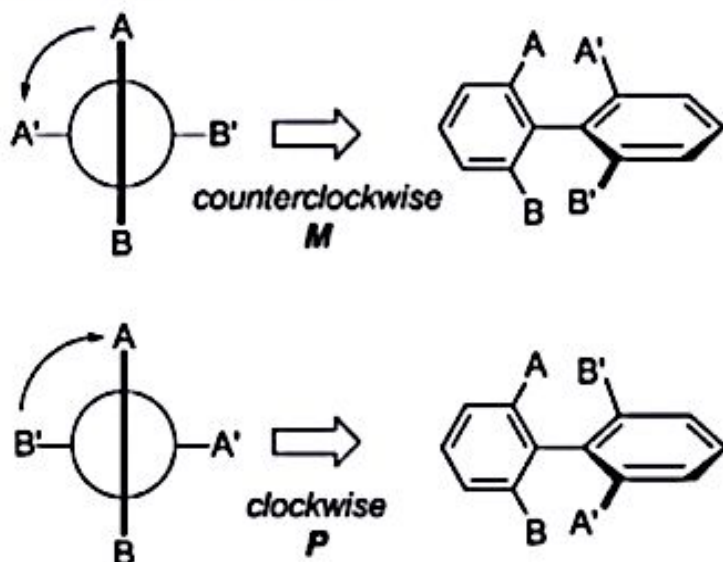


- **Conditions of Atropisomerism:**

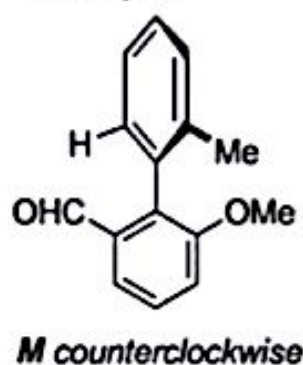
1. A rotationally stable axis
2. Presence of different substituents on both sides of the axis
3. The configurational stability of axially chiral biaryl compounds is mainly determined by three following factors:
 - i. The combined steric demand of the substituent in the combined steric demand of the substituents in the proximity of the axis.
 - ii. The existence, length and rigidity of bridges.
 - iii. Atropisomerisation mechanism different from a merely physical rotation about the axis, e.g. photochemically or chemically induced processes.

- **Stereochemical assignment**

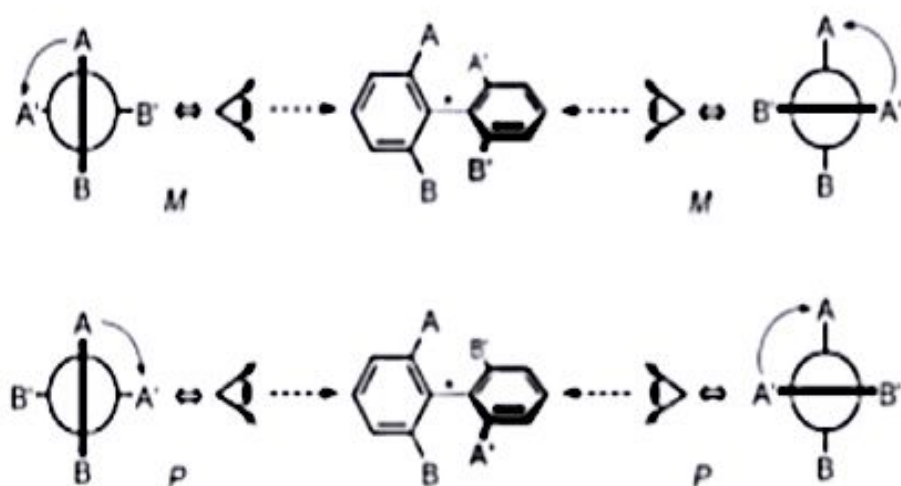
- o Determining the axial stereochemistry of biaryl atropisomers can be accomplished through the use of a Newman projection along the axis of hindered rotation.
- o The ortho, and in some cases *meta* substituents are first assigned priority based on Cahn–Ingold–Prelog priority rules.
- o Starting with the substituent of highest priority in the closest ring and moving along the shortest path to the substituent of highest priority in the other ring, the absolute configuration is assigned **P** or **Δ** for clockwise and **M** or **Λ** for counterclockwise.



example:



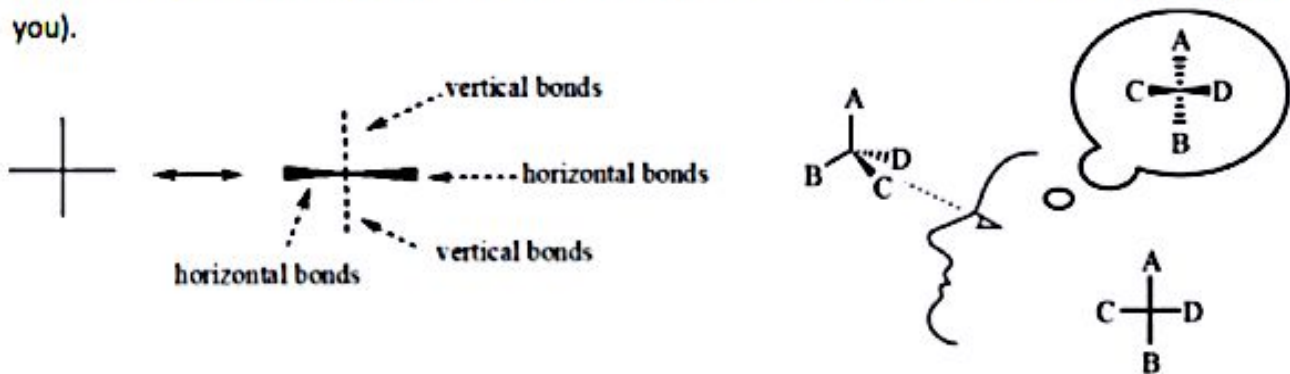
chirality in biaryl compounds (priority: A > B):



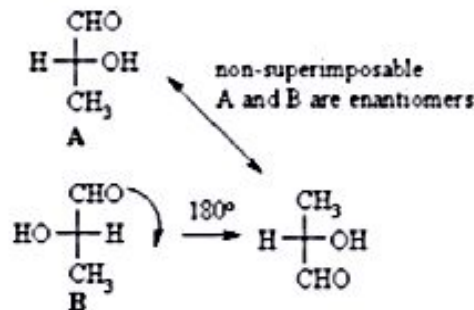
counterclockwise : **M** (minus)
clockwise : **P** (plus)

❖ Fischer Projection

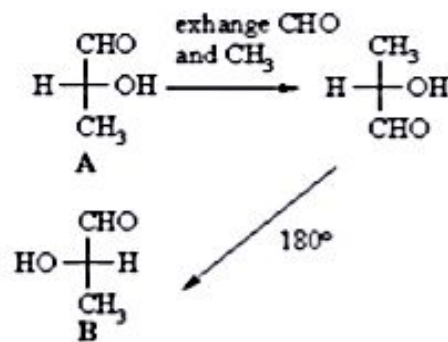
- Fischer Projections are abbreviated structural forms that allow one to convey valuable stereochemical information.
- The definition is that every carbon is specified completely by a cross designating the carbon (at the center) and the four bonds to that carbon. The stereochemistry of the bonds is defined (now) as the **horizontal bonds are in front of the plane** (coming toward you, the viewer); the **vertical bonds are behind the plane** (going away from you).



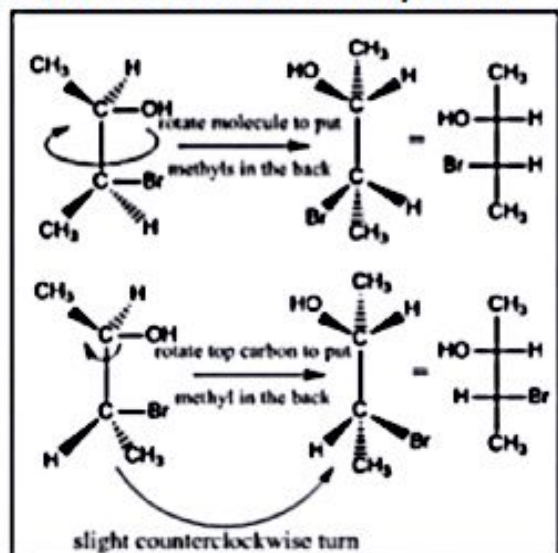
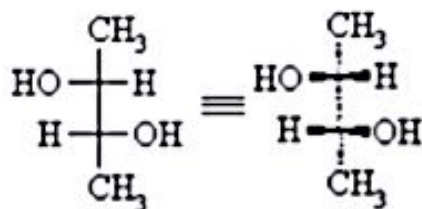
- When relating one Fischer projection to another, it's important to realise that it may only be manipulated within the 2D plane



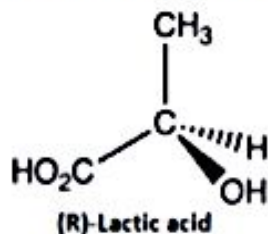
- Why we can't rotate 90°? A 90° rotation is equivalent to breaking bonds and exchanging two groups, which would result in the formation of the other enantiomer.



- Fischer projections can also be used to represent molecules with more than one chirality center.



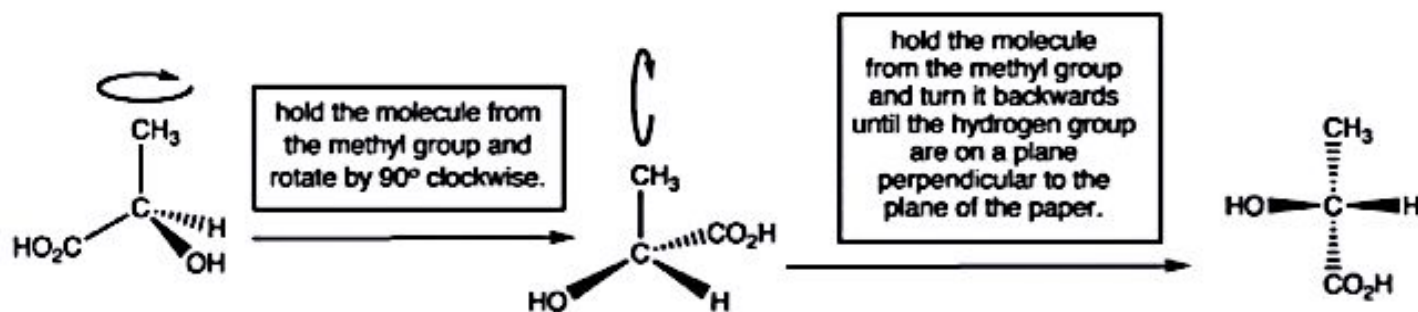
- A Fischer projection or Fischer projection formula is a convention used to depict a stereo-formula in two dimensions without destroying the Stereochemical information, i.e., absolute configuration, at chiral centers.



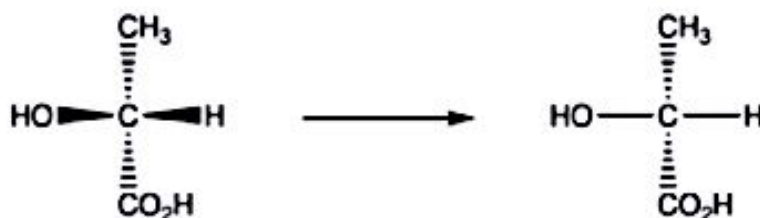
- o To convert this stereofomula into a Fischer projection use the following procedure
[Fischer Projection of (R)-Lactic acid]

Step 1: Hold the molecule so that

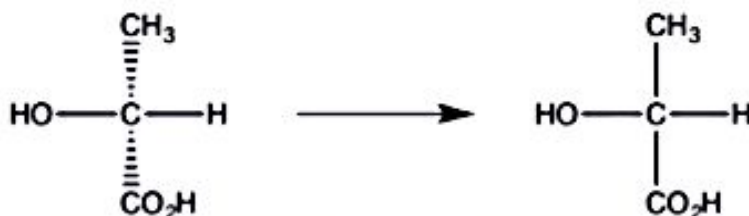
- (i) The chiral center is on the plane of the paper,
- (ii) Two bonds are coming out of the plane of the paper and are on a horizontal plane,
- (iii) The two remaining bonds are going into the plane of the paper and are on a vertical plane.



Step 2: Push the two bonds coming out of the plane of the paper onto the plane of the paper.



Step 3: Pull the two bonds going into the plane of the paper onto the plane of the paper.



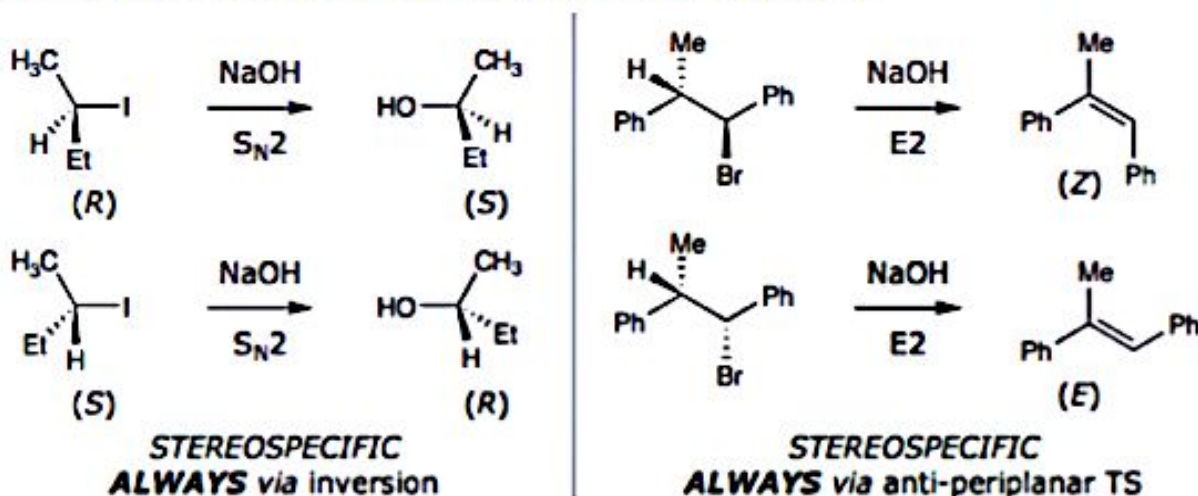
Step 4: Omit the chiral atom symbol for convenience.



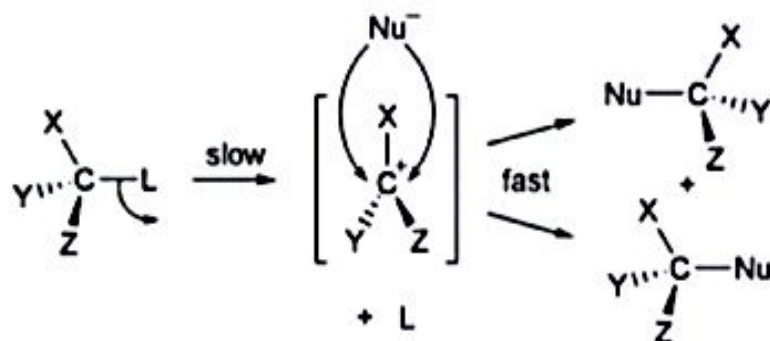
❖ Stereospecific and Stereoselective Reactions

• STEREOSPECIFIC REACTIONS

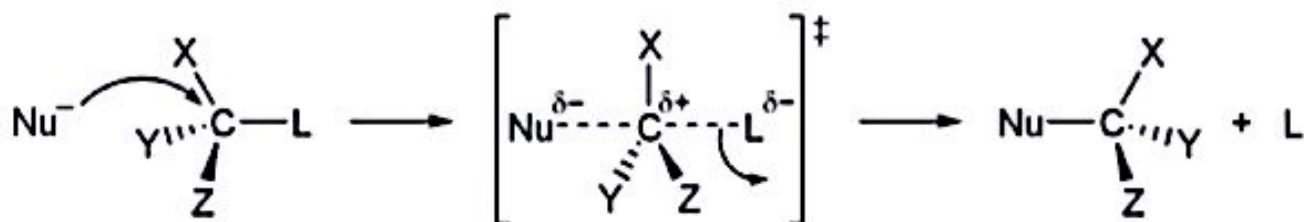
- A stereospecific reaction is one which, when carried out with stereoisomeric starting materials, gives a product from one reactant that is a stereoisomer of the product from the other.
- '*Stereospecific*' relates to the mechanism of a reaction, the best-known example being the S_N2 reaction, which always proceeds with inversion of stereochemistry at the reacting centre.



- *Stereospecificity in substitution reactions :*



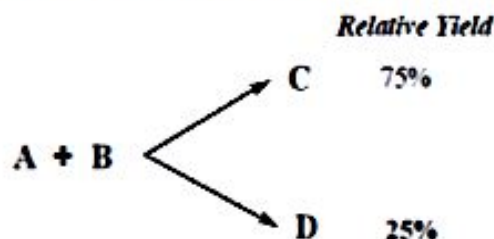
S_N1 mechanism non-stereospecific



S_N2 mechanism stereospecific

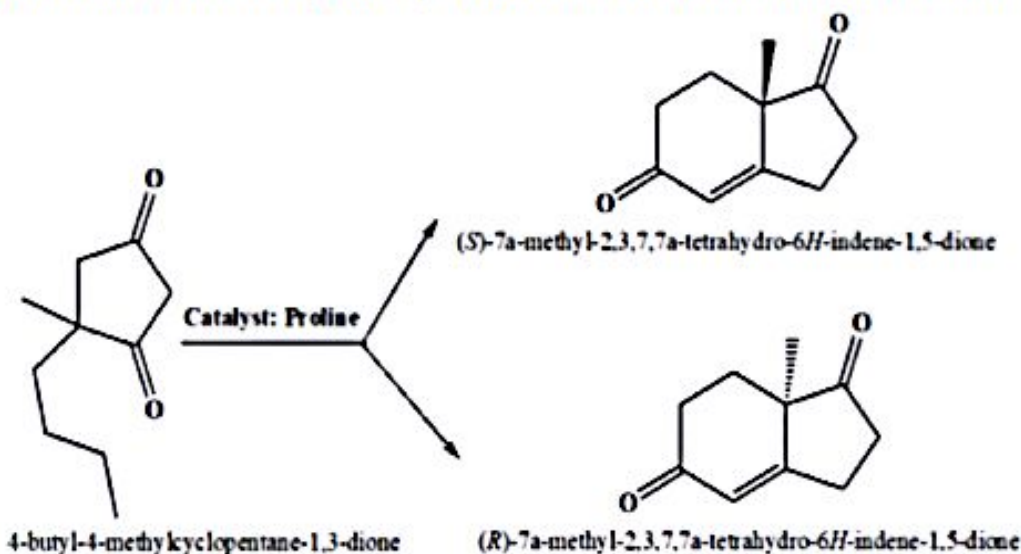
• STEREOSELECTIVE REACTIONS

- A stereoselective process is one in which one stereoisomer predominates over another when two or more may be formed.
- If more than one reaction could occur between a set of reactants under the same conditions giving products that are stereoisomers and if one product forms in greater amounts than the others, the overall reaction is said to be stereoselective.

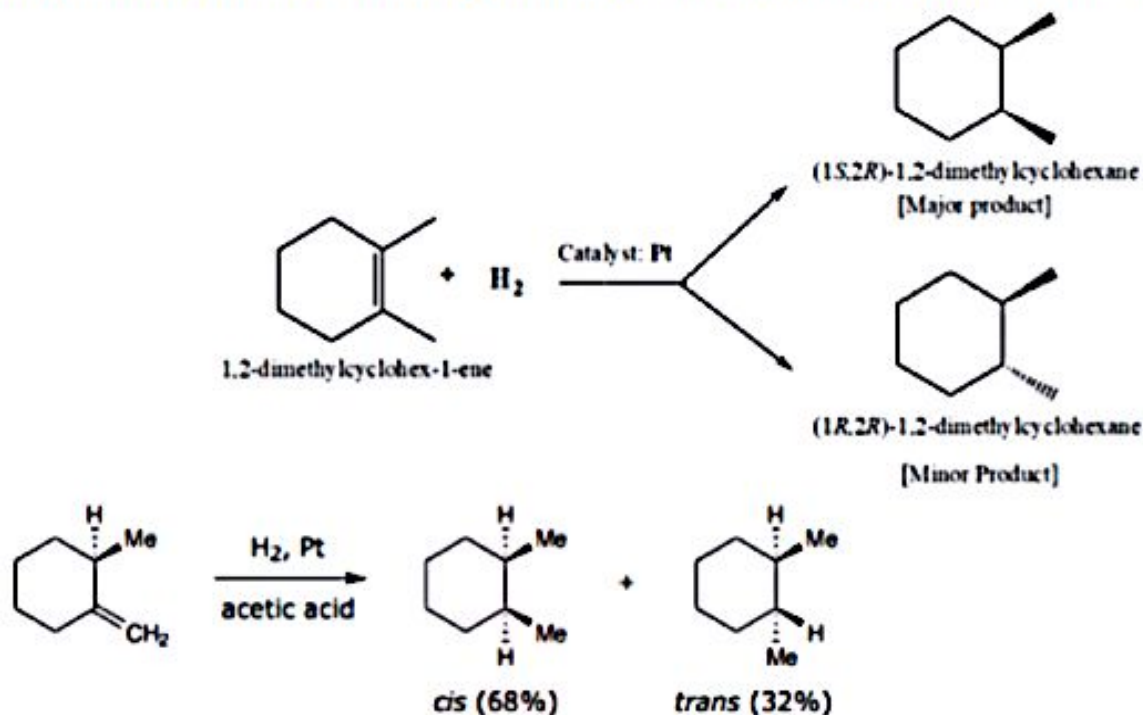


The overall reaction between A and B is stereoselective.

- A *stereoselective reaction* in which the possible products are enantiomers is said to be **Enantioselective**.



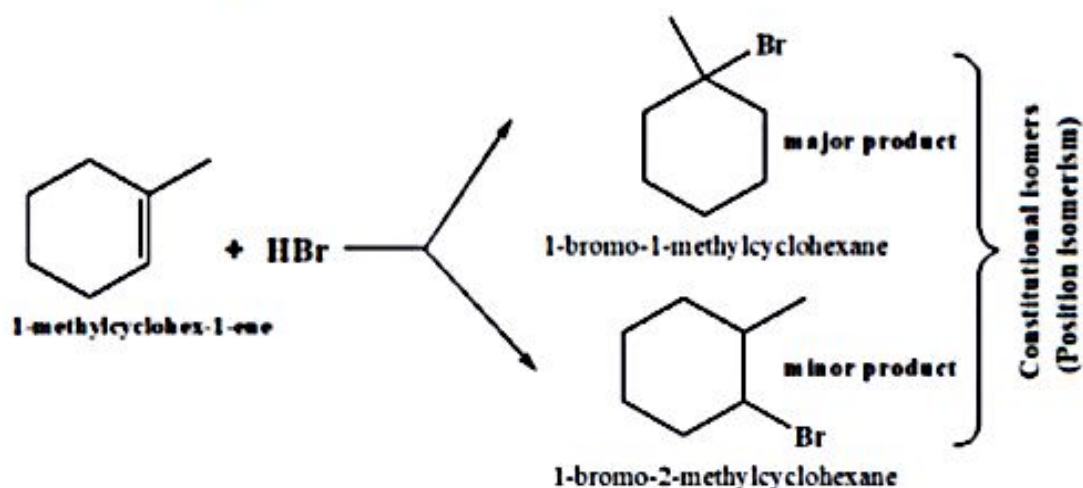
- A *stereoselective reaction* in which the possible products are diastereomers is said to be **Diastereoselective**.



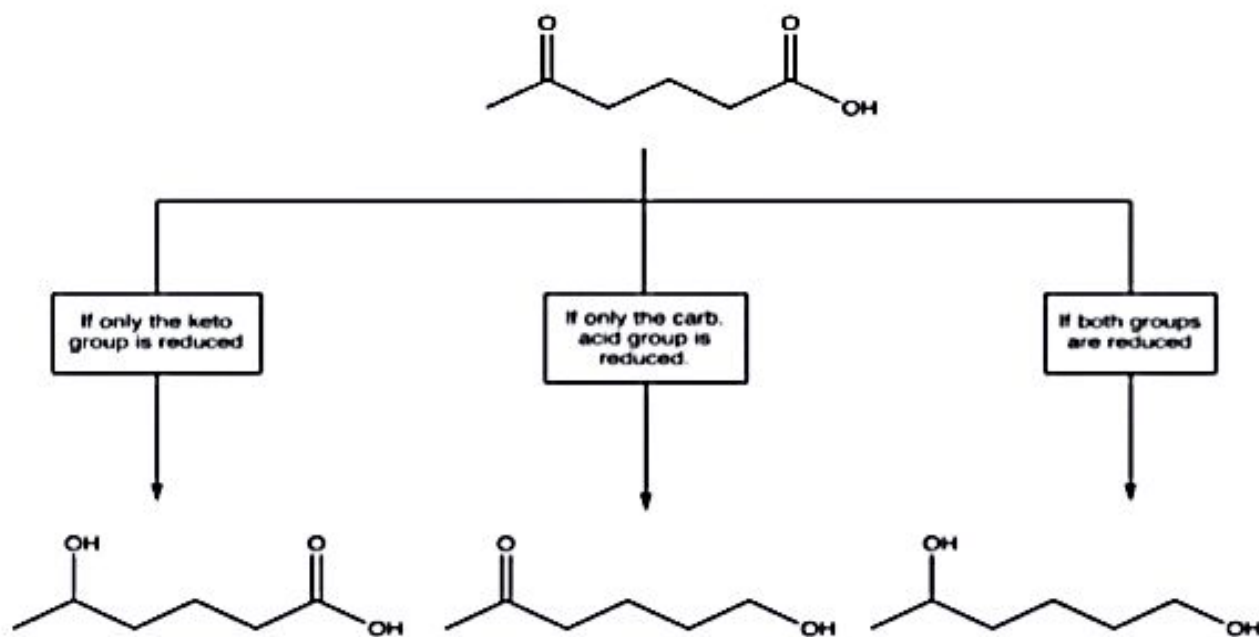
DIASTEREOSELECTIVE

Two diastereoisomers from one starting material

- **Regioselective:** If more than one reaction could occur between a set of reactants under the same conditions giving products that are constitutional isomers and if one product forms in greater amounts than the others, the overall reaction is said to be regioselective.



- **Chemoselective:** If an organic compound contains more than one different functional groups or more than one like functional groups that are not equivalent (see equivalent ligands), and, if a reagent reacts exclusively or predominately with one of them, the reaction is said to be Chemoselective.



• Difference Between Stereospecific and Stereoselective Reactions

	Stereospecific Reactions	Stereoselective Reactions
Definition	A stereospecific reaction is a reaction in which the stereochemistry of the reactant completely determines the stereochemistry of the product without any other option.	A stereoselective reaction is a reaction in which there is a choice of pathway, but the product stereoisomer is formed due to its reaction pathway being more favorable than the others available.
Number of Products	A stereospecific reaction gives a specific product from a certain reactant.	A stereoselective reaction can result in multiple products.
Effects	The final product of a stereospecific reaction depends on the stereochemistry of the reactant.	The selectivity of the reaction pathway depends on differences in steric effects (presence of bulky groups cause steric hindrance) and electronic effects.