

## Module 2

# Stereoselectivity and Stereospecificity

### 1. What are Stereoselective and Stereospecific reactions?

Suppose we carry out a reaction and two or more stereoisomers can be generated from that reaction. If one stereoisomer is generated in greater percentage compared to other stereoisomers, then the reaction is called **stereoselective**. If the products are enantiomers of each other, then the reaction is called **enantioselective** and if the products are diastereoisomers of each other, then the reaction is called **diastereoselective**.

A stereoselective reaction is one in which there is a choice of pathway to generate different stereoisomers, but the product stereoisomer is formed due to its reaction pathway being more favourable than the others available. In a stereospecific reaction, only one stereochemistry of the reaction is favored. 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 one in which a single reactant can give two or more stereoisomeric products, and one or more of these products is preferred over the others - even if the preference is very small.**

**In a stereospecific reaction, one stereoisomer of the reactant gives one stereoisomer of the product, while a different stereoisomer of the reactant gives a different stereoisomer of the product.**

Now, how you can understand which reaction is stereospecific and which reaction is stereoselective?

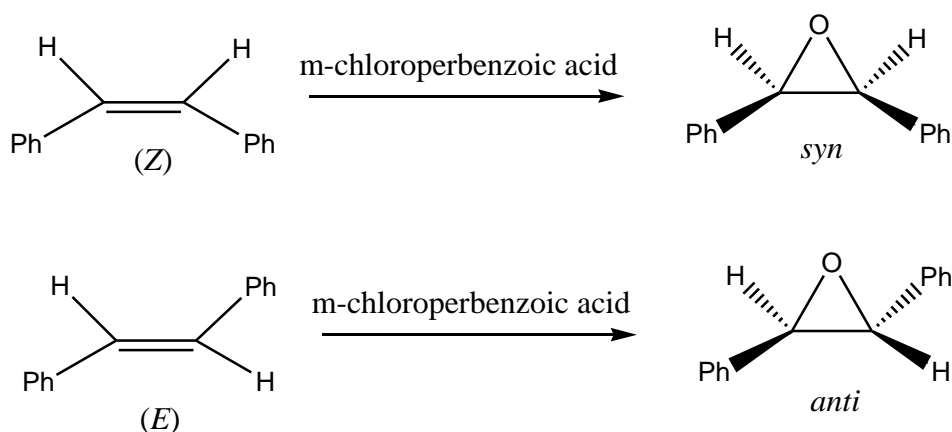
#### Steps:

1. Look at your reaction.
2. If multiple stereoisomeric products are possible, but one is produced in excess, the reaction is stereoselective.
3. Consider the stereochemical features of the reactants to determine stereospecificity:
  - If another stereoisomer of the reactant will give identical products in identical ratios, then the reaction is not stereospecific.
  - If a different stereoisomer of the reactant or reagent gives a stereoisomerically different product, then the reaction is stereospecific.

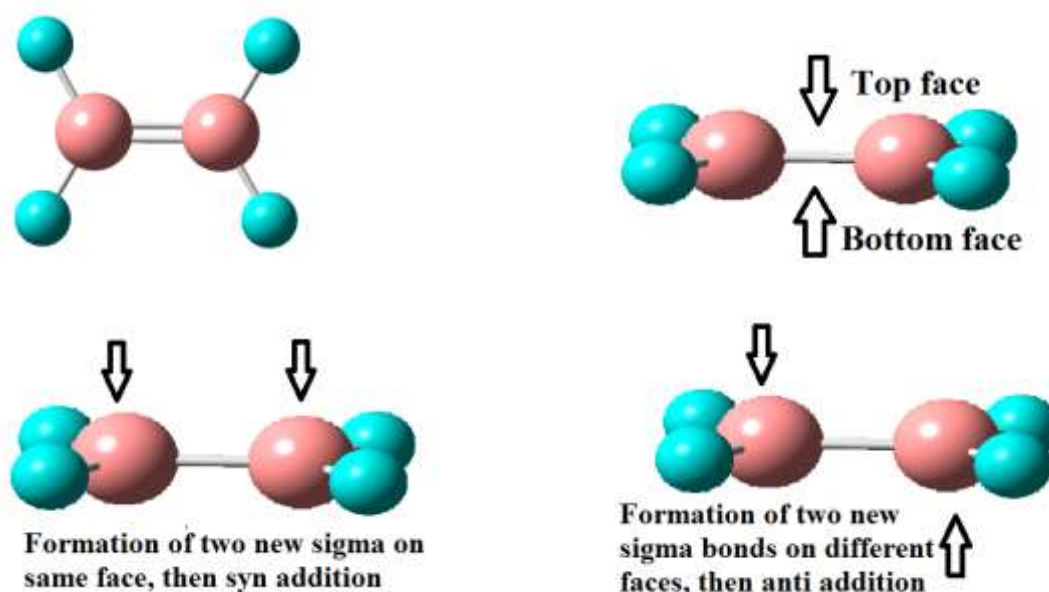
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Now, let us examine the electrophilic epoxidation of alkenes with peracids. It occurs via a concerted process and the geometry of the alkene determines the geometry of the product as shown below. *Z* isomer of the starting material gives the *syn* product and *E* isomer of the starting material gives the *anti* product. If a different stereoisomer of the reactant or reagent gives a stereoisomerically different product, then the reaction is stereospecific. So, this reaction is stereospecific and since the two products obtained are diastereoisomers, the reaction is diastereospecific.



Let us study study the addition to alkenes. When an alkene undergoes addition, two new  $\sigma$  bonds are formed. If we think of an alkene as having two faces, then the two new  $\sigma$  bonds can either both form on the same face, which we call *syn* addition, or they can be formed on different faces which we call *anti* addition.



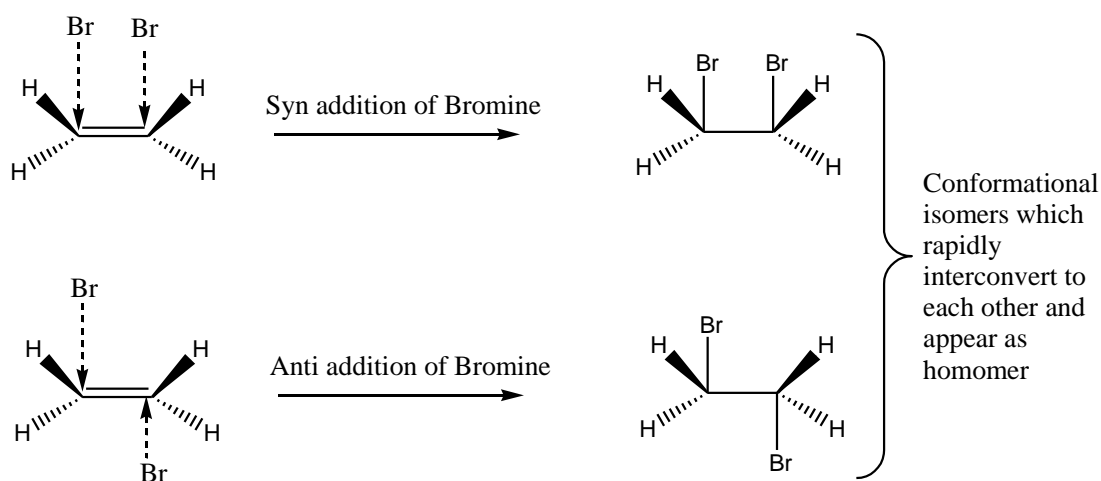
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Remember that an alkene unit is planar. The alkene has been drawn in such a style that the substituents on the C=C are into and out of the page. This means that the two faces of the alkene are above and below the where the alkene makes the horizontal plane.

**Syn** addition results when the two new bonds are both formed to the same face of the alkene, in this case they are shown to have formed on the top face. **Anti** addition results when the two new bonds have formed to opposite faces.

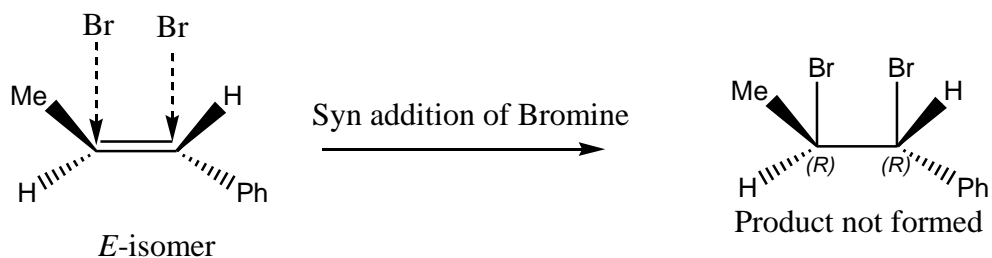
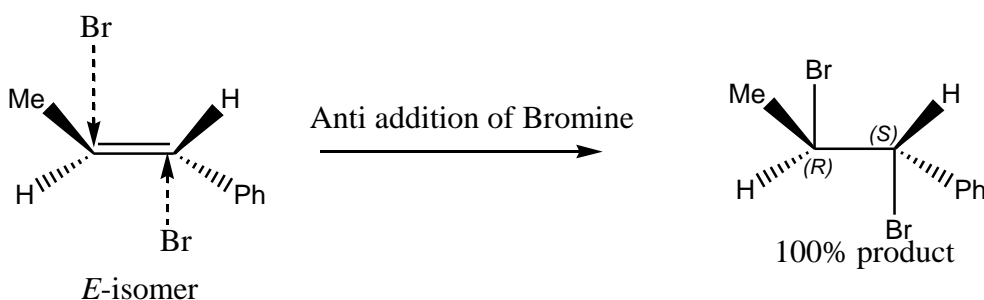
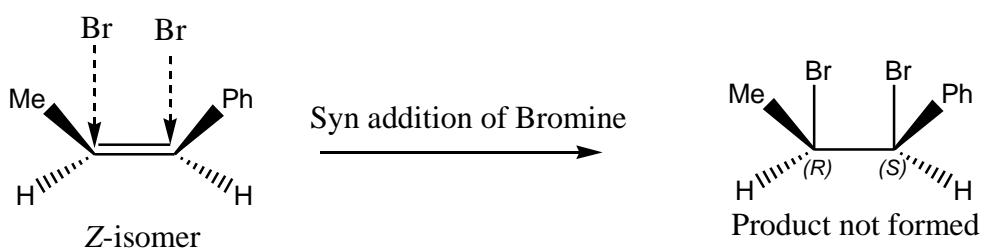
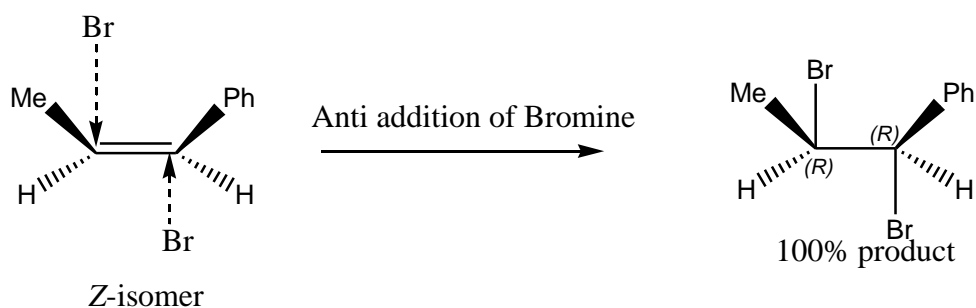
Suppose, we have the simplest alkene, ethylene, for syn and anti addition of bromine as shown below:



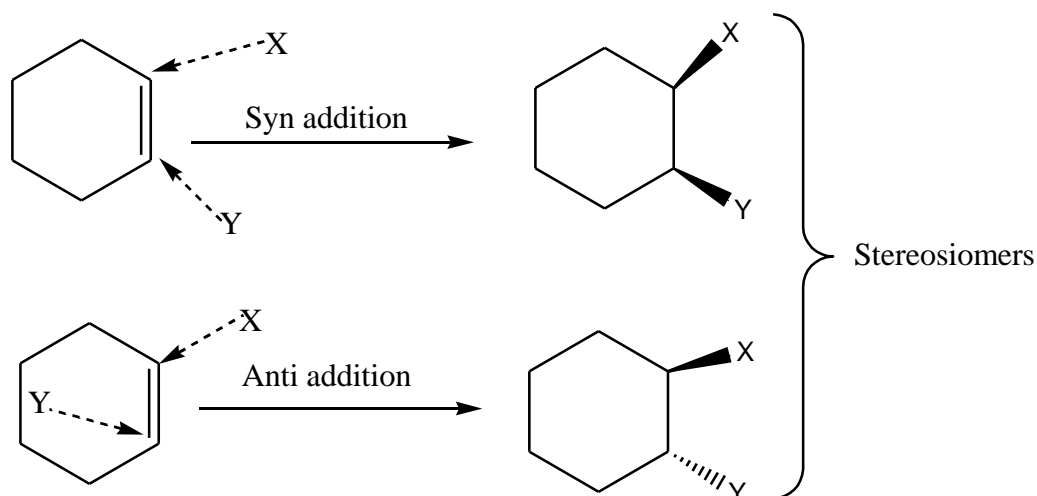
Reaction is not stereoselective because in the case of a simple alkene like ethene, the free rotation of the C-C bond means that the two product structures are conformational isomers and rapidly interconvert.

Now, let us consider the case of substituted alkene as 1-phenyl propene. The starting material can have *Z* and *E* configurations. For *Z*-configuration, syn addition gives rise to the *R,S* product and in case of anti addition, *R,R* product is the formed. For *E*-configuration, syn addition gives rise to the *R,R* product and in case of anti addition, *R,S* product is the formed.

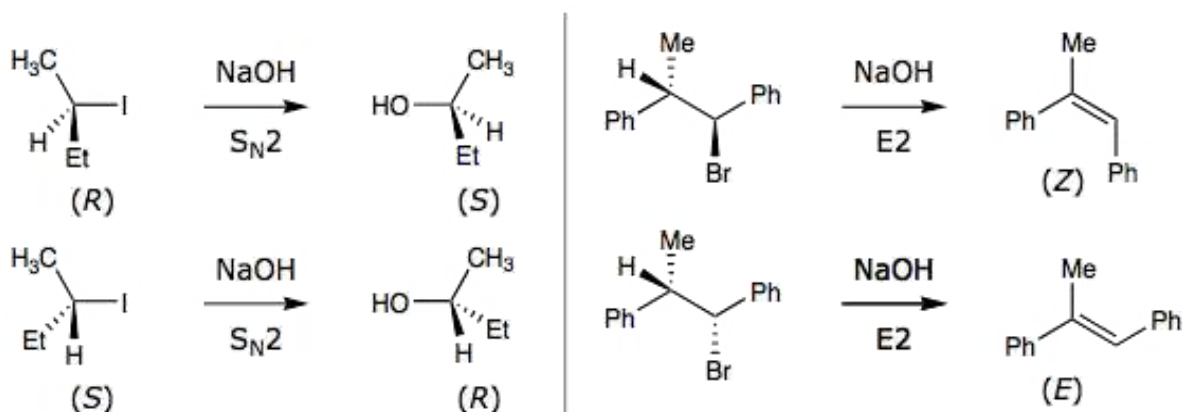
We all know that bromination of alkene proceeds through formation of bromonium ion and undergoes anti addition exclusively. Hence, bromination of *Z*-configuration gives rise to *R,R* product exclusively and bromination of *E*-configuration gives rise to *R,S* product exclusively. If a different stereoisomer of the reactant or reagent gives a stereoisomerically different product, then the reaction is stereospecific. So, this reaction is stereospecific and since the two products obtained are diastereoisomers, the the reaction is diastereospecific.



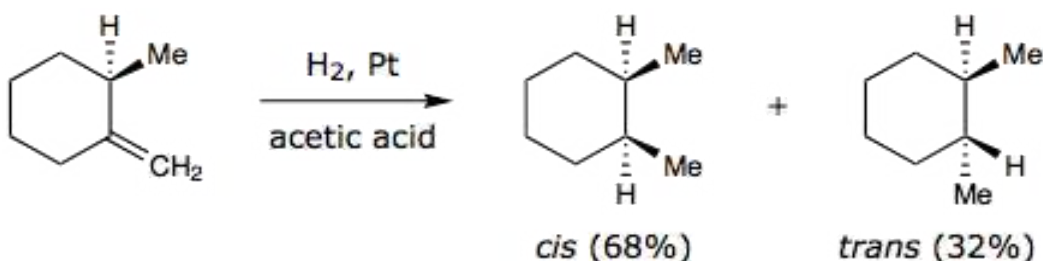
If we have a cyclic alkene such as cyclohexene, then the reaction is stereoselective for syn addition and anti addition. Both the products are stereoisomers of each other. and hence the reactions are stereoselective which favour one addition out of syn and anti as the major pathway of attack.



The best known example of stereospecific reaction is  $S_N2$  reaction. It always proceeds with the inversion of configuration at the reacting centre. E2 reaction is also stereospecific since it always occurs via anti-periplanar transition state.



Now, let us consider an example of diastereoselective reaction as shown below:



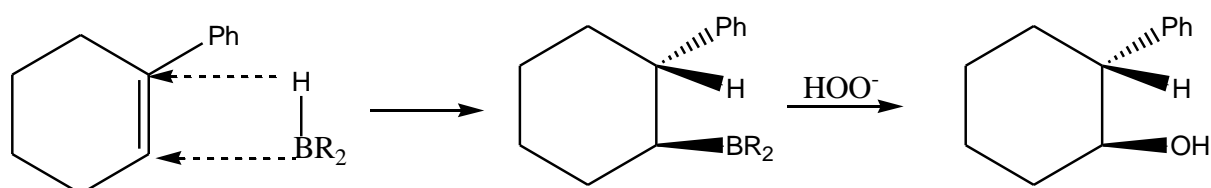
In this reaction, both *cis* and *trans* products are formed from the same starting material and the products are diastereomers of each other. One stereoisomer is formed in greater percentage than the other. A stereoselective reaction is one in which a single reactant can give two or more

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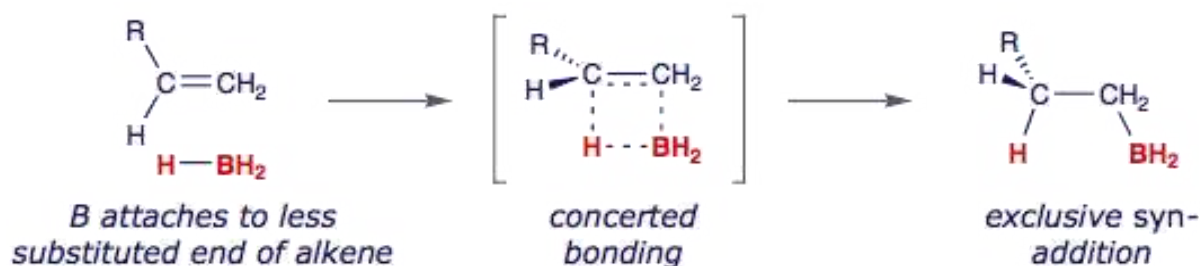
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stereoisomeric products, and one or more of these products is preferred over the others – even if the preference is very small. Hence the reaction is diastereoselective in nature.

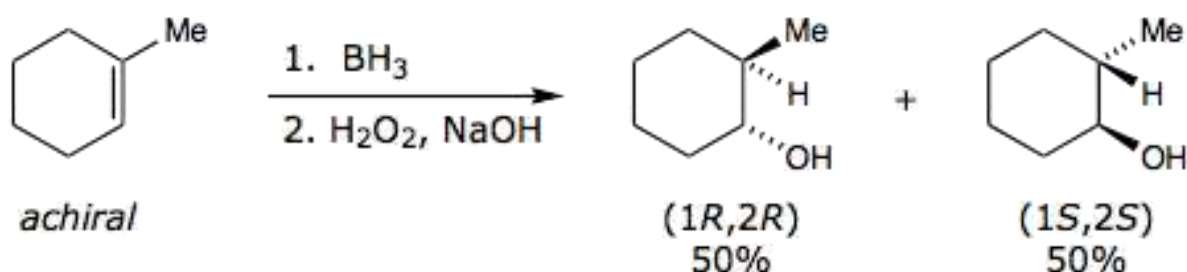
Hydroboration is also a stereospecific reaction. In case of hydroboration, bonds are made and broken at the same time. Syn addition of hydrogen and boron takes place in this reaction and there is retention of stereochemistry in case of the final product. Out of the two options of addition, the syn attack is exclusively followed. Hence, the reaction is stereospecific reaction.



Hydroboration of reactions is regioselective since B adds to the least substituted end of the alkene. So, we can classify hydroboration as a regioselective and stereospecific reaction.



Hydroboration is stereospecific and it is essential to note that with an achiral alkene, the addition takes place with equal facility and gives rise to two enantiomers with equal proportion as shown below:

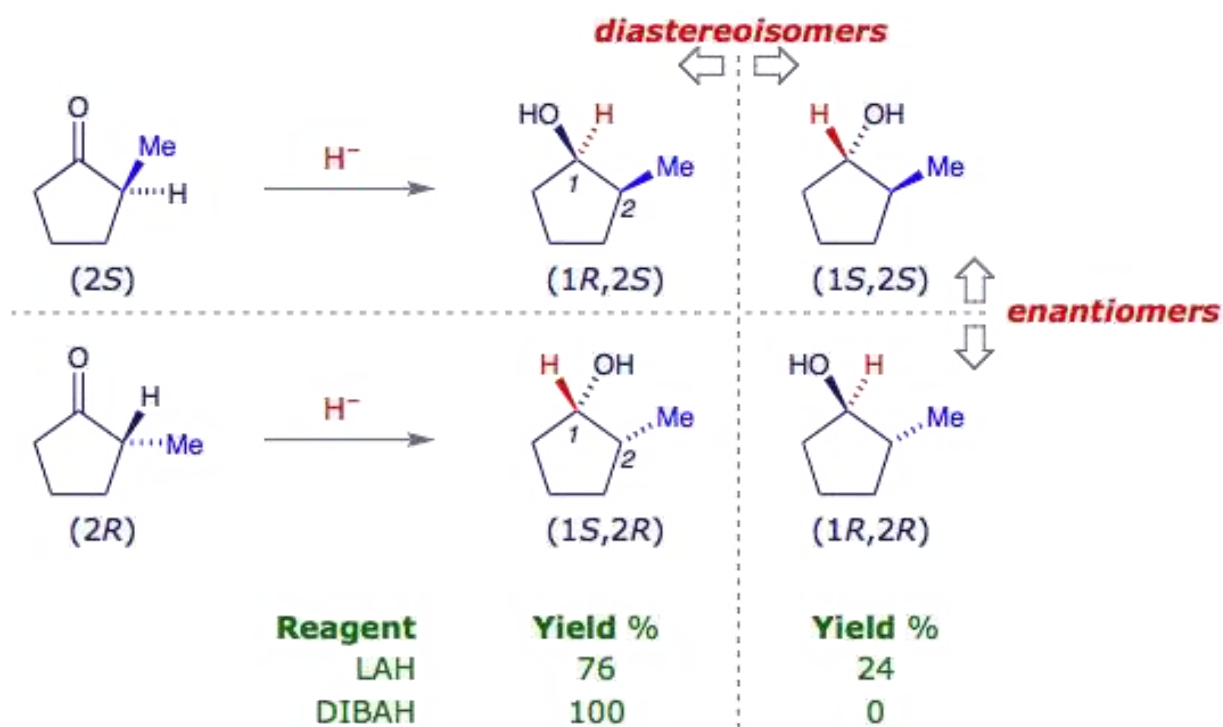


Selectivity of reactions changes with the use of different reagents. In the following example, diastereoselective reduction of cyclic ketones is shown. With lithium aluminium hydride, the percentage is 76% of (1R,2S) and 24% for (1S,2S) and with DIBAL (Di-isobutyl aluminium hydride), only one diastereoisomer (1R,2S) is obtained in case of 2(S) isomer of the ketone. On the other hand,

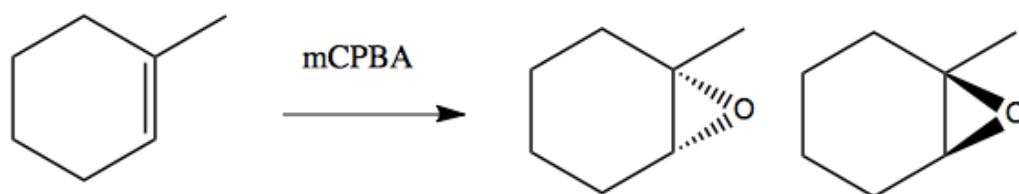
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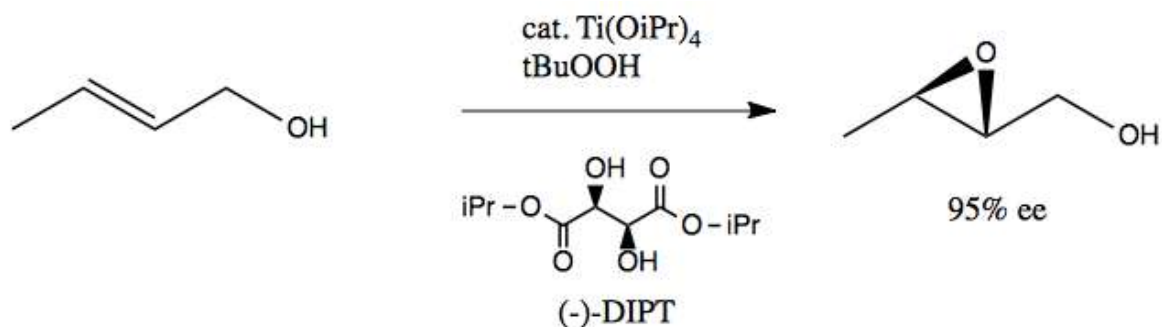
With lithium aluminium hydride, the percentage is 76% of (1S,2R) and 24% for (1R,2R) and with DIBAL (Di-isobutyl aluminium hydride), only one diastereoisomer (1S,2R) is obtained in case of 2(R) isomer of the ketone. Thus, in the previous case with LAH, the reaction is stereoselective and in the second case it is diastereospecific.



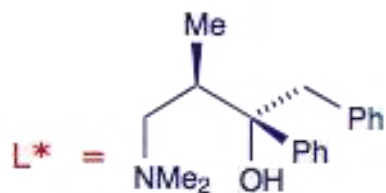
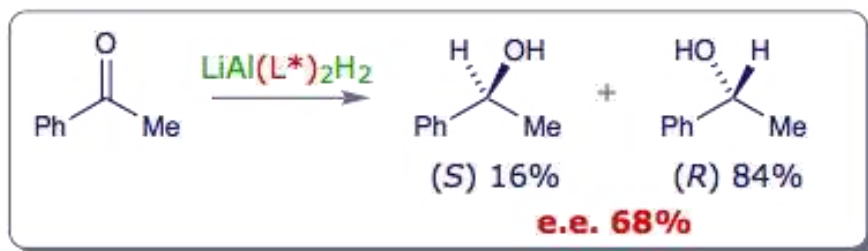
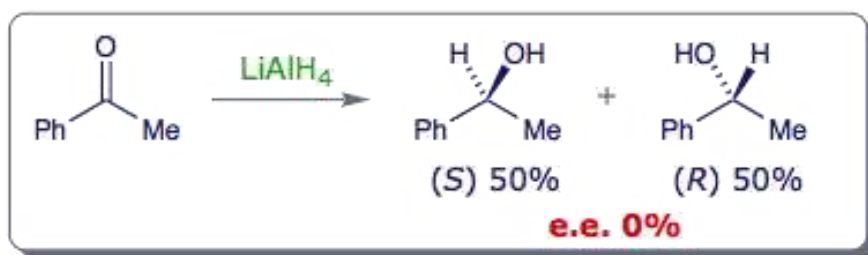
Now, let us study an example of enantioselective reaction. In case of enantioselective reaction, two enantiomers are formed in such a proportion that one enantiomer predominates over other. The enantiomeric excess is greater than 0. In the following example, there is no enantioselectivity, you get both products about equally:



Enantioselective reactions are generally carried out by using chiral reagents. Sharpless asymmetric epoxidation is a way of epoxidating allylic alcohols by enantioselective process. It uses a titanium catalyst derived from a tartrate.



In the example given below, the first reaction is not enantioselective since both enantiomers are formed in 50% yield. The second reaction is enantioselective and it involves use of a chiral reagent and one enantiomer predominates over the other with enantiomeric excess of 68%.



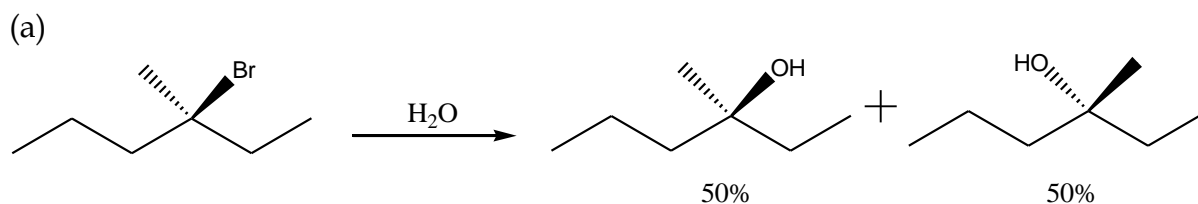


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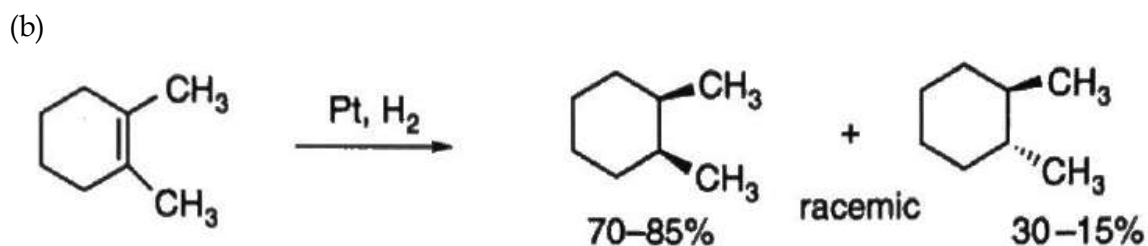
### Stereoselectivity and Stereospecificity

#### Assignments

1. Classify which of the following reactions are stereoselective/ stereospecific /both or none of the two with explanation:

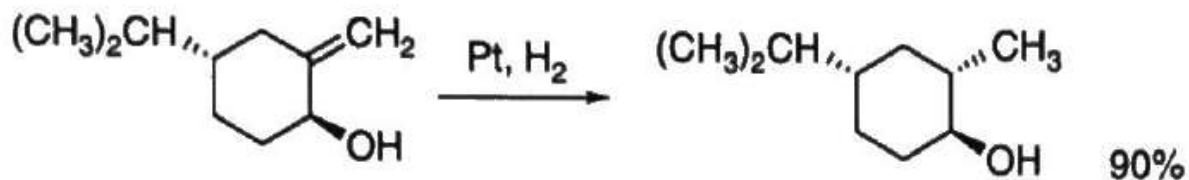


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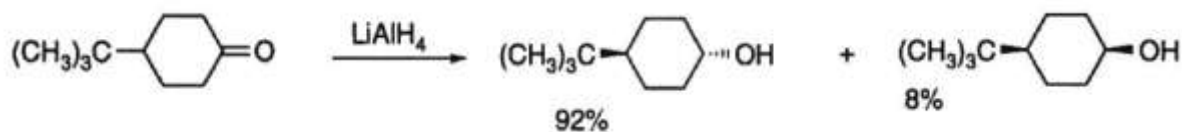
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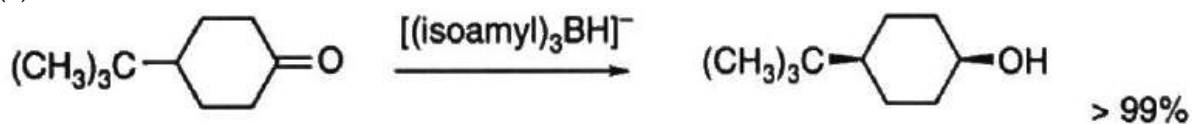
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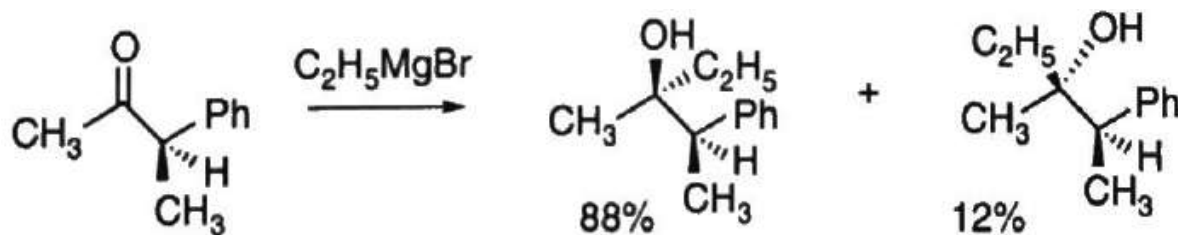
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Ans: \_\_\_\_\_  
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Ans:

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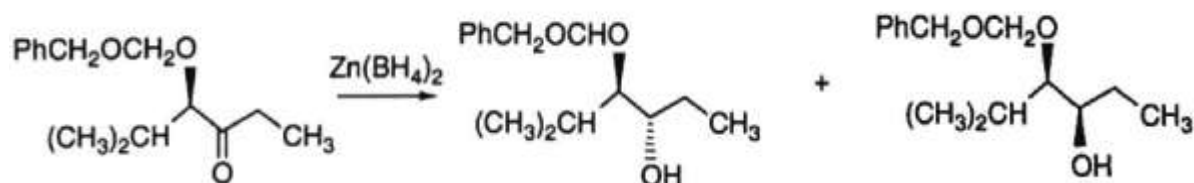
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(g)



Ans:

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