

Stereochemistry of Chemical reactions

Lecture 8

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We have seen examples of **molecules with one chiral center** that exist in two **mirror-image configurations**, which we call **enantiomers**

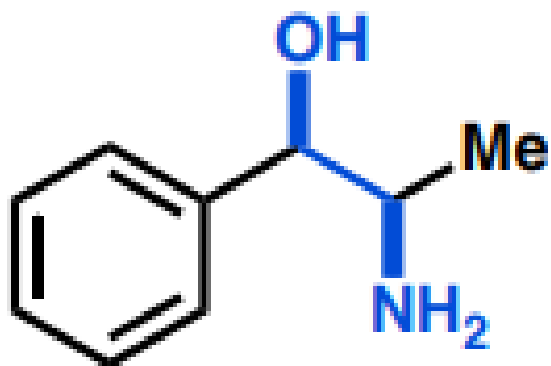
What happens when there is more than one chiral center? How many stereoisomers should we expect?

-Enantiomers differ only by their absolute stereochemistry (R or S etc)

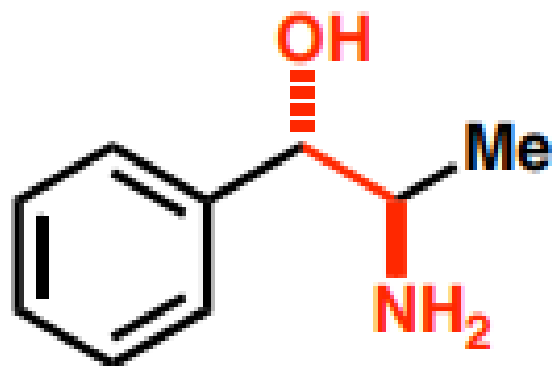
- **Diastereoisomers differ by their relative stereochemistry**

- **Relative stereochemistry** - defines configuration with respect to any other stereogenic element within the molecule.

In simple systems the two different relative stereochemistries are defined as below:



syn
same face



anti
different face

A molecule can only have one enantiomer but any number of diastereoisomers

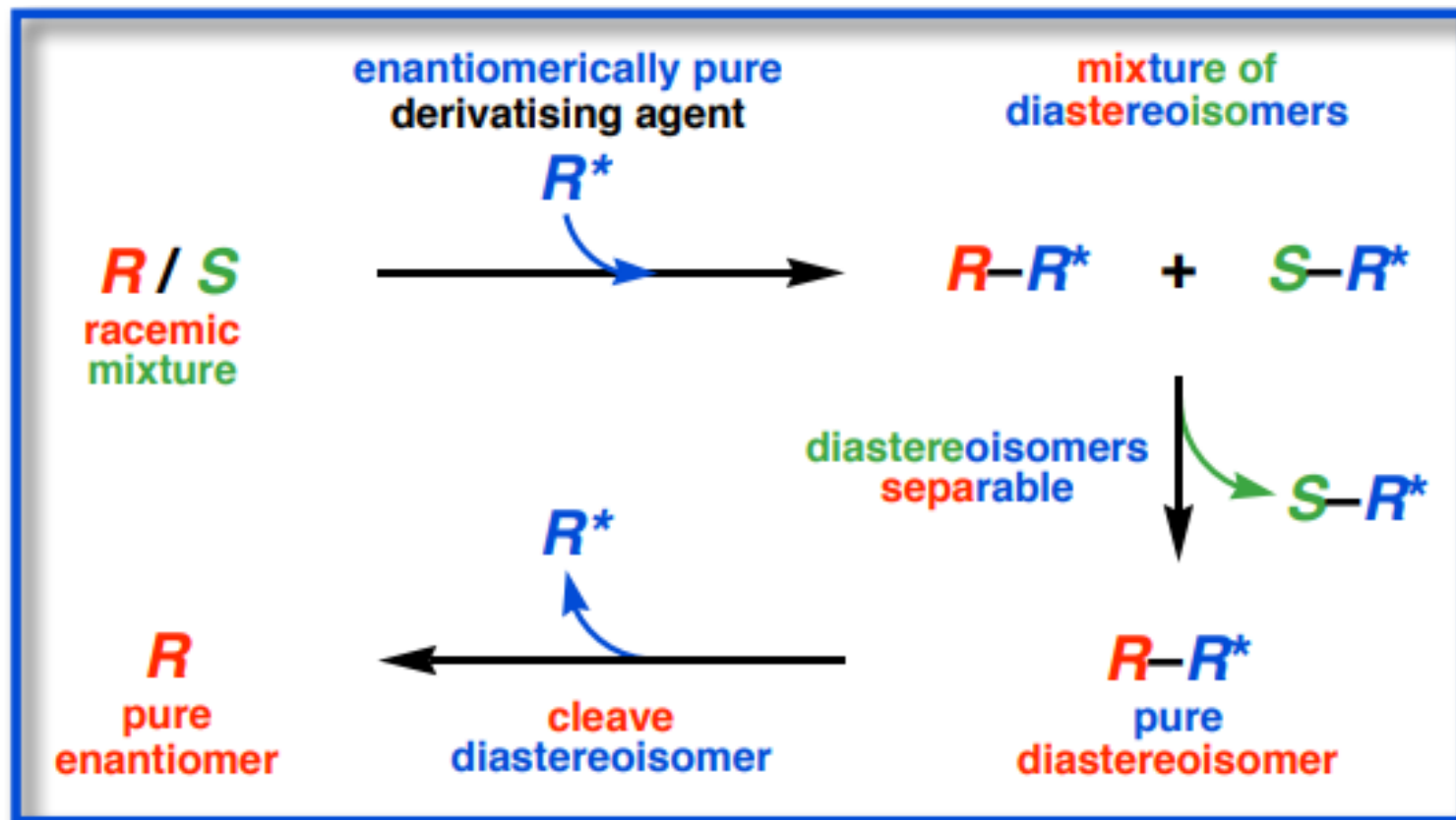
- The different physical properties of diastereoisomers allow us to purify them.
- The differences between diastereoisomers will be the basis for everything we do

If a molecule has **3 stereogenic centers** then it has potentially **8 stereoisomers** (4 diastereoisomers & 4 enantiomers)

- If a molecule has **n stereogenic centers** then it has potentially **2^n stereoisomers**
- Problem is, the molecule will never have more than 2^n stereoisomers but it might have less...

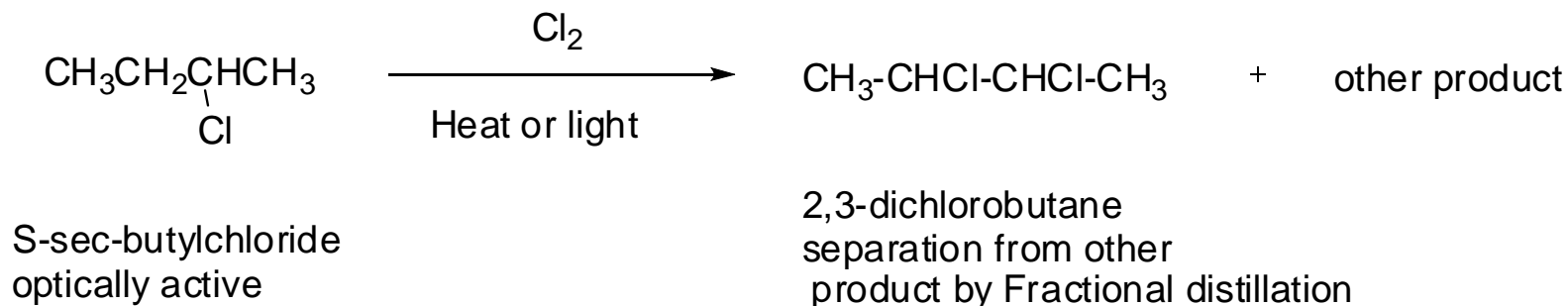
Chiral derivatizing agents

- Difference in diastereomers allows chiral derivatizing agents to resolve enantiomers



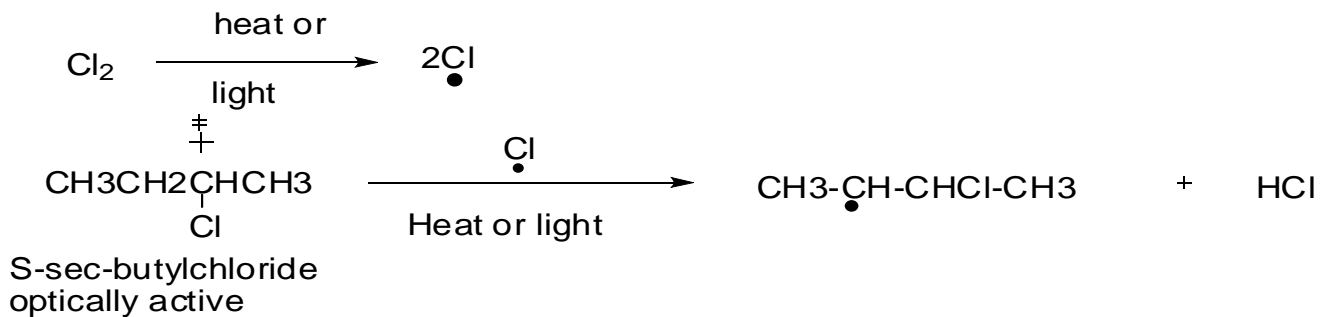
- **Remember a good chiral derivatizing agent should:**
- Be enantiomerically pure (or it is pointless)
- Coupling reaction of both enantiomers must reach 100%
- Coupling conditions should not racemize stereogenic center
- Enantiomers must contain point of attachment

3- Generation of a second chiral center

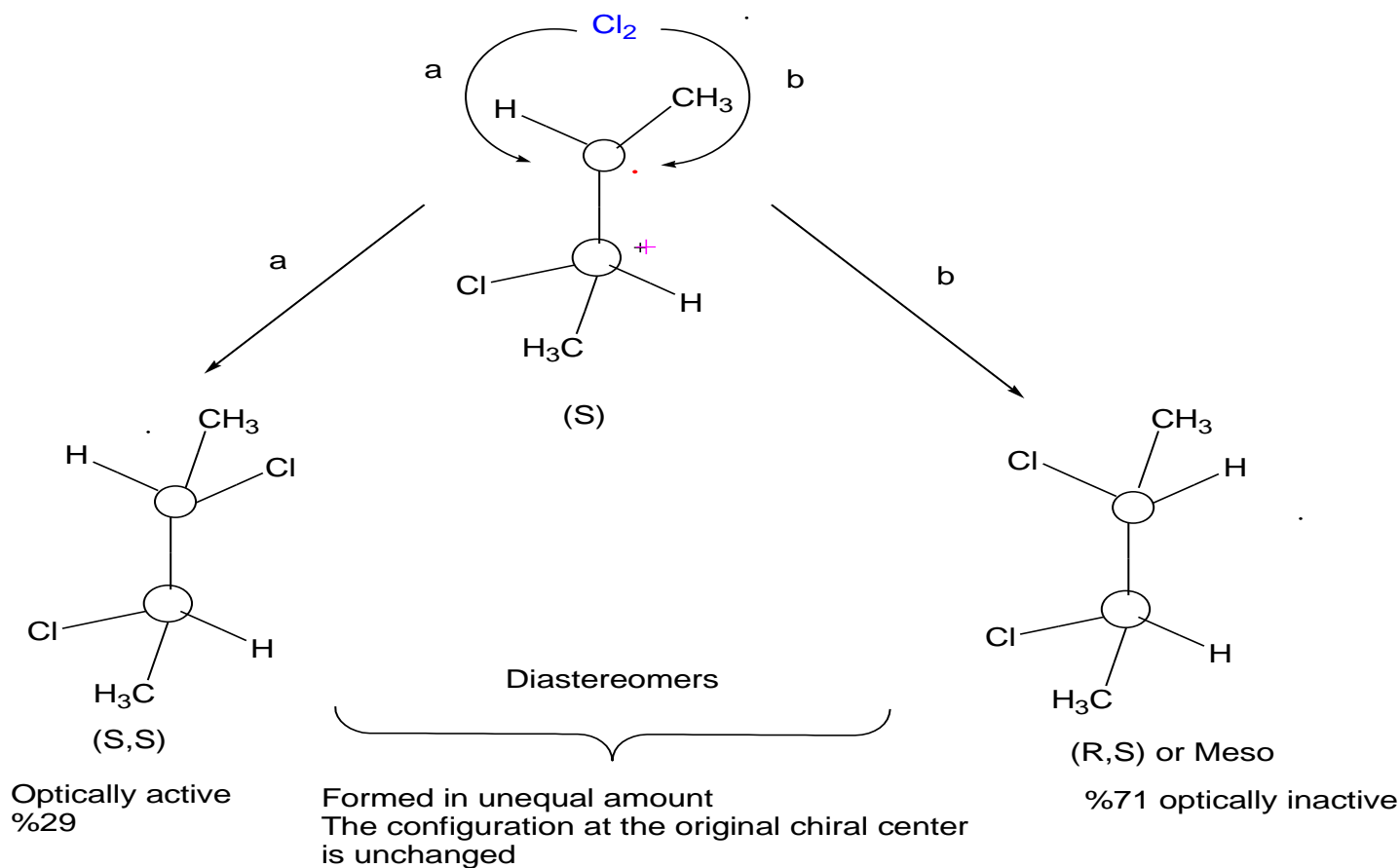


Note:- Configuration of original chiral center 2 will retained, since no bond to it was broken

Q) Is the product optically active or inactive?



attach on opposite sides of the Flat portion of the Free radical



**Q) Why are the Diastereomeric products
Formed in unequal amount?**

It's because the intermediate 3-chloro-2-butyl radical already contain a **chiral center**.

The Free radical is chiral and **lacks the symmetry** that is necessary for attach at the two faces to be equally likely.

In this case attach (a) and (b) are not equally likely. This must apply in all case where diastereomeric products are Formed.

Thus, generation of a new **chiral** center in a **optically active** compounds, yield an **optically active** product containing **unequal** amounts of **diastereomers**.

***Note:-* Some optically active compounds are obtained from natural source.**

Since living organism usually produce only one enantiomer of a pair.

Only (+) lactic acid ($\text{CH}_3\text{CHOHCOOH}$) is Formed in the *contraction of muscles*.

Only (-) malic acid ($\text{HOOCCH}_2\text{CHOHCOOH}$) is obtained from **fruit juice**.

Resume

What is Resolution?

It means separation of a racemic modification into enantiomers.

Racemic mixture and because of identical properties (physical properties) of both enantiomers of the mixture, it is not possible to separate them by usual methods like fractional distillation or Crystallization. Experiments carried out using optically active compounds or optically active reagent

like: (+)-sec-butanol; (-)-2-bromooctane;etc.

A racemic mixture is *converted* by an **optically active reagent** into a mixture of salts (*diastereomers*) which can then be separated.

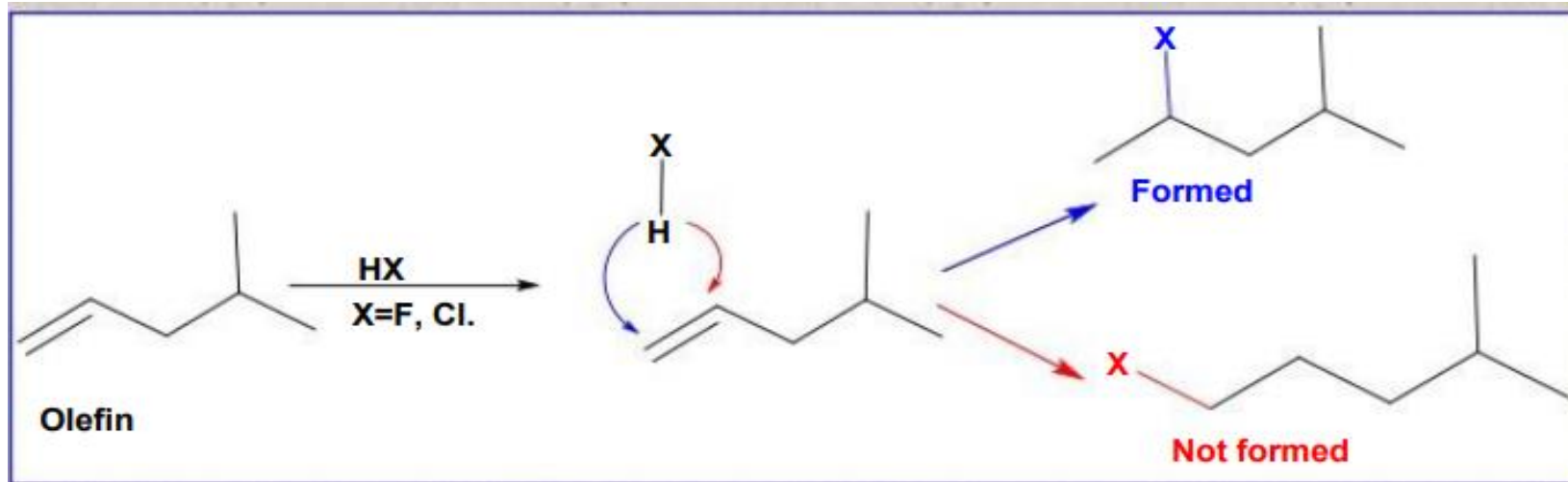
Stereochemistry of Addition Reactions:

Stereochemistry of Addition Reactions: Addition of halogen to Alkenes

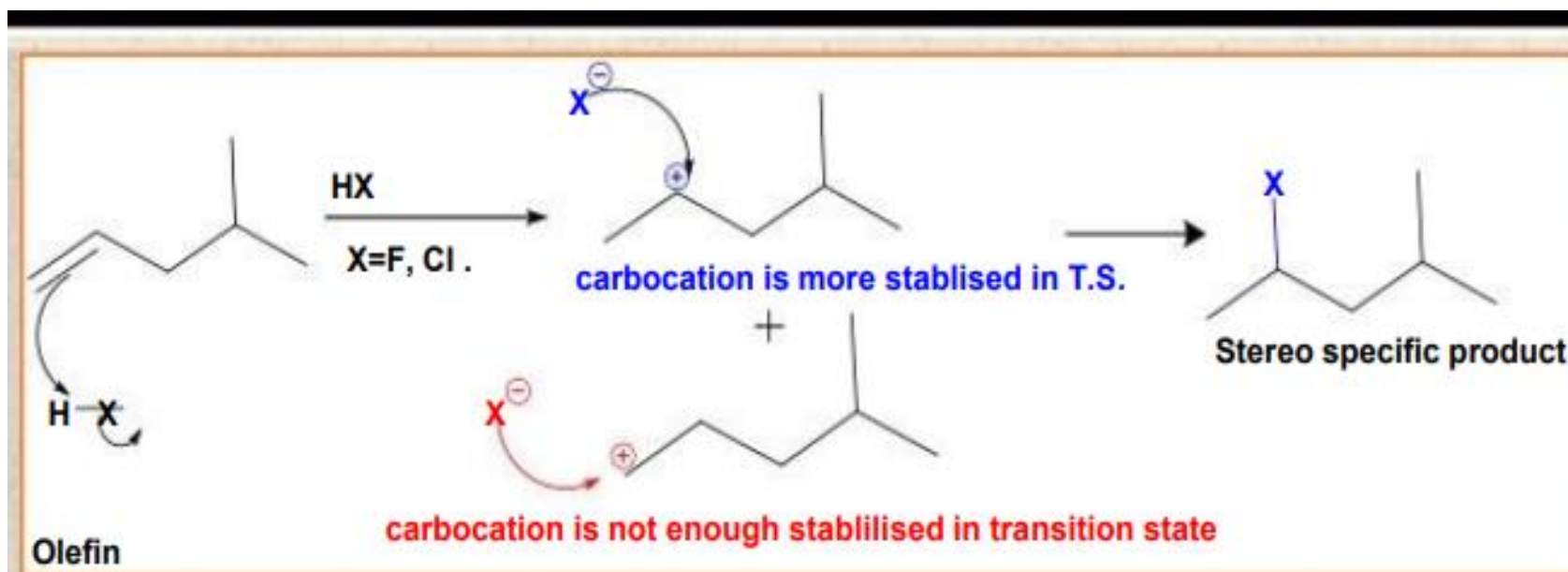
markovnikov' additions Rules

Addition of hydrogen to an unsymmetrical olefin occurs at those carbon atoms with maximum number of hydrogen atoms. (i.e., the carbon with least substitution).

- Electronegative group goes to more substituted carbon atom.
- Such an addition leads to a stabler carbocation.
- Such a reaction may lead to **constitutional isomers** but actually one of the products is formed **as major product**.



Origin



Alkenes-some facts

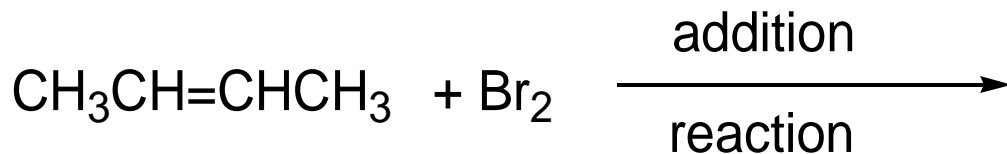
- Due to **trigonal planer geometry of olefine** carbon atoms the addition can occur on the same side (syn periplanar) or on opposite sides (anti periplanar).
- Alkenes are generally Nucleophilic.
- Electron donating groups increase the rate for Electrophilic attack as they assist in carbocation and **positive charge stabilization** in the TS

Stereochemistry of Addition Reactions:

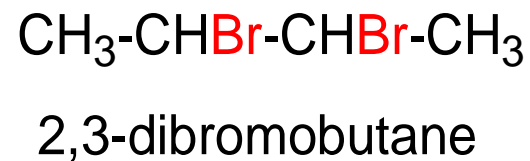
Addition of halogen to Alkenes

- The reactants exist as stereoisomers : *a pair* of geometric isomers, *cis and trans*.
- Addition of bromine to 2-butene yields 2,3-dibromobutane
- The products have two *chiral center* and the product can exist as a pair of enantiomers and a Meso form

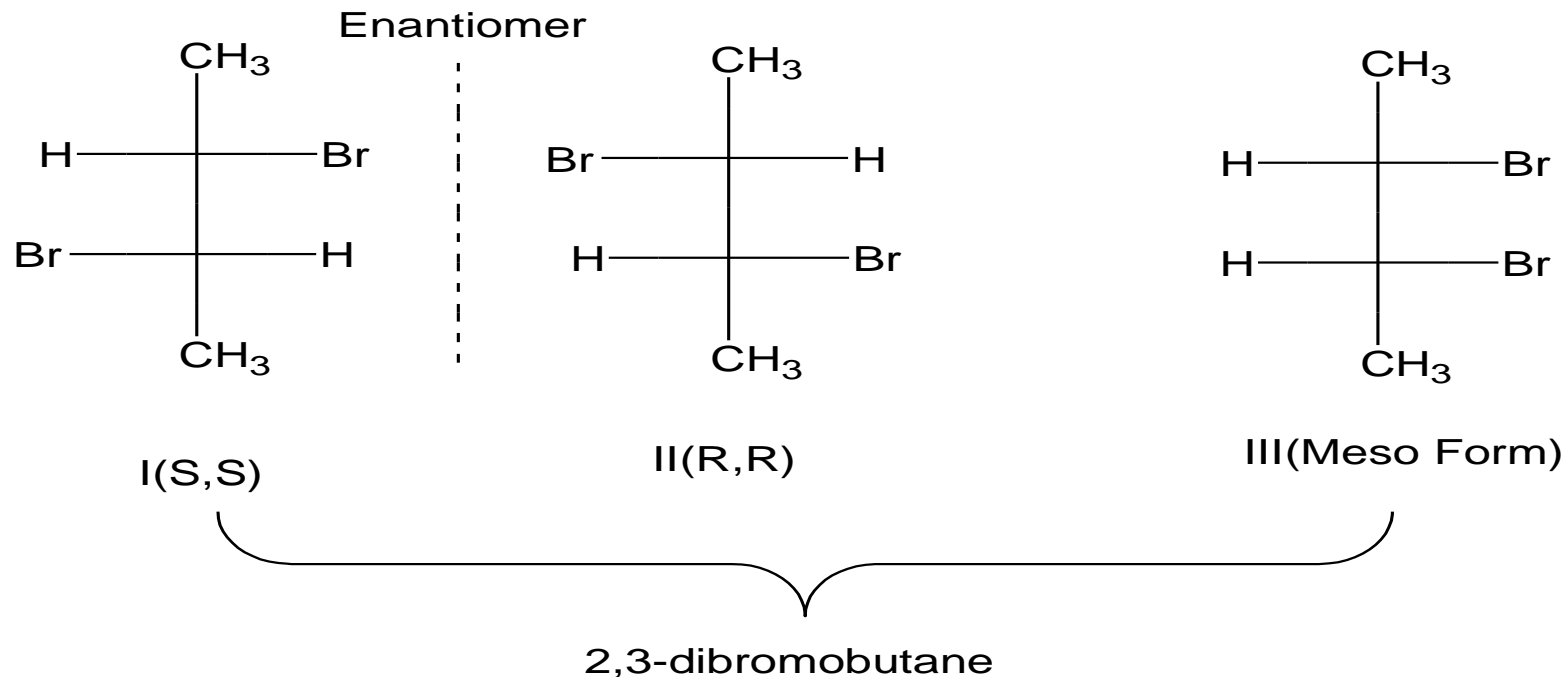
achiral molecule



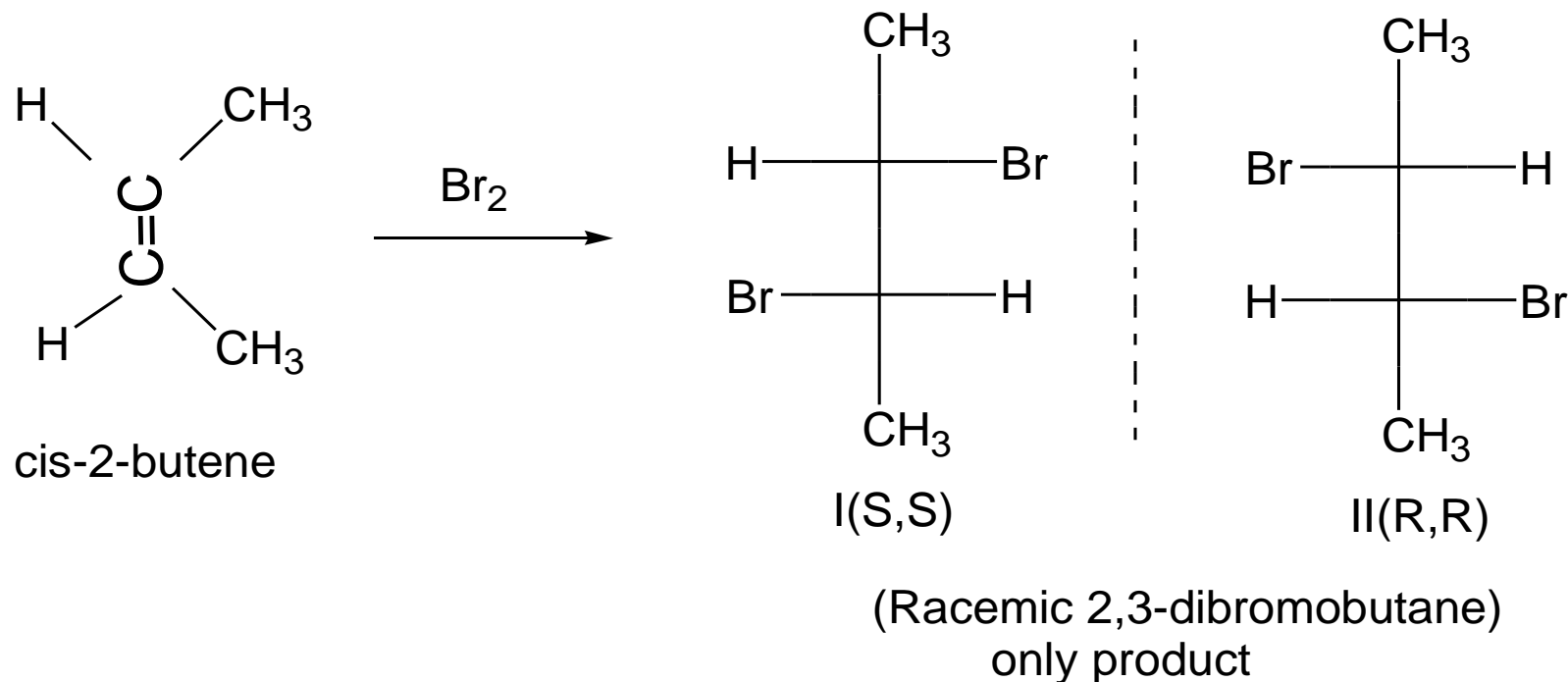
chiral molecule
optically inactive



exist as a pair of
geometric isomer
cis and trans



Q) If we start with cis-2-butene, which stereoisomer we get?

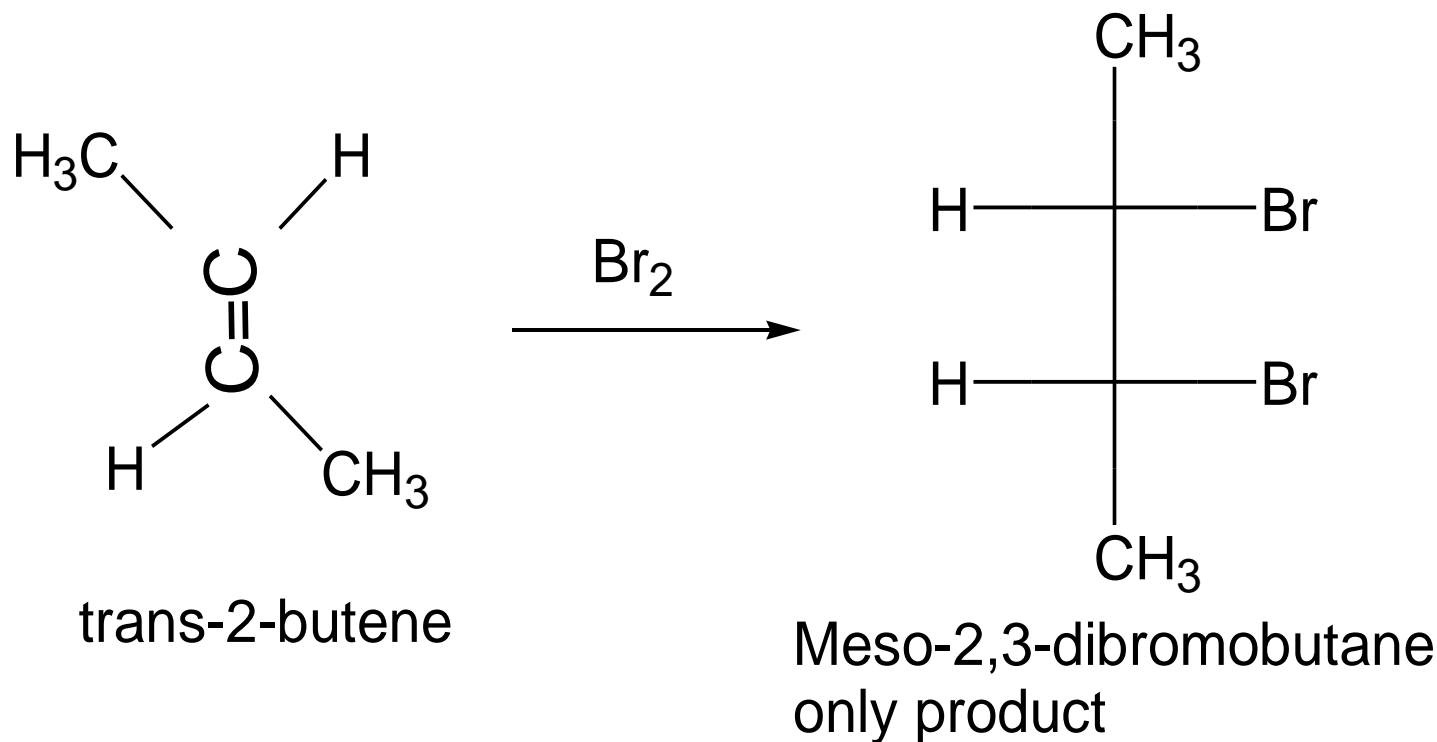


A reaction that yields mainly *one stereoisomer* (or one pair of enantiomers) of several possible diastereomers is called a **stereoselective reaction**.

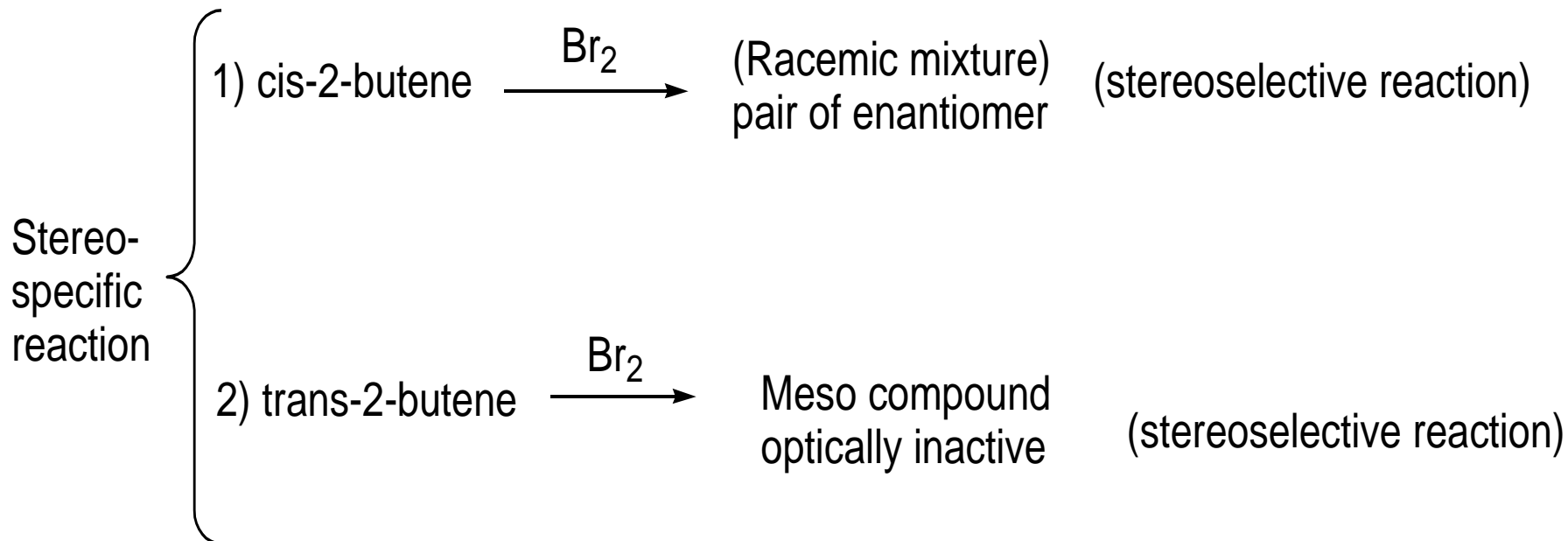
If we start with **trans-2-butene**. Which stereoisomer we get?

Does this too yields the racemic dibromide? **NO**

- The trans alkene yields only *Meso-2,3-dibromo butane*.



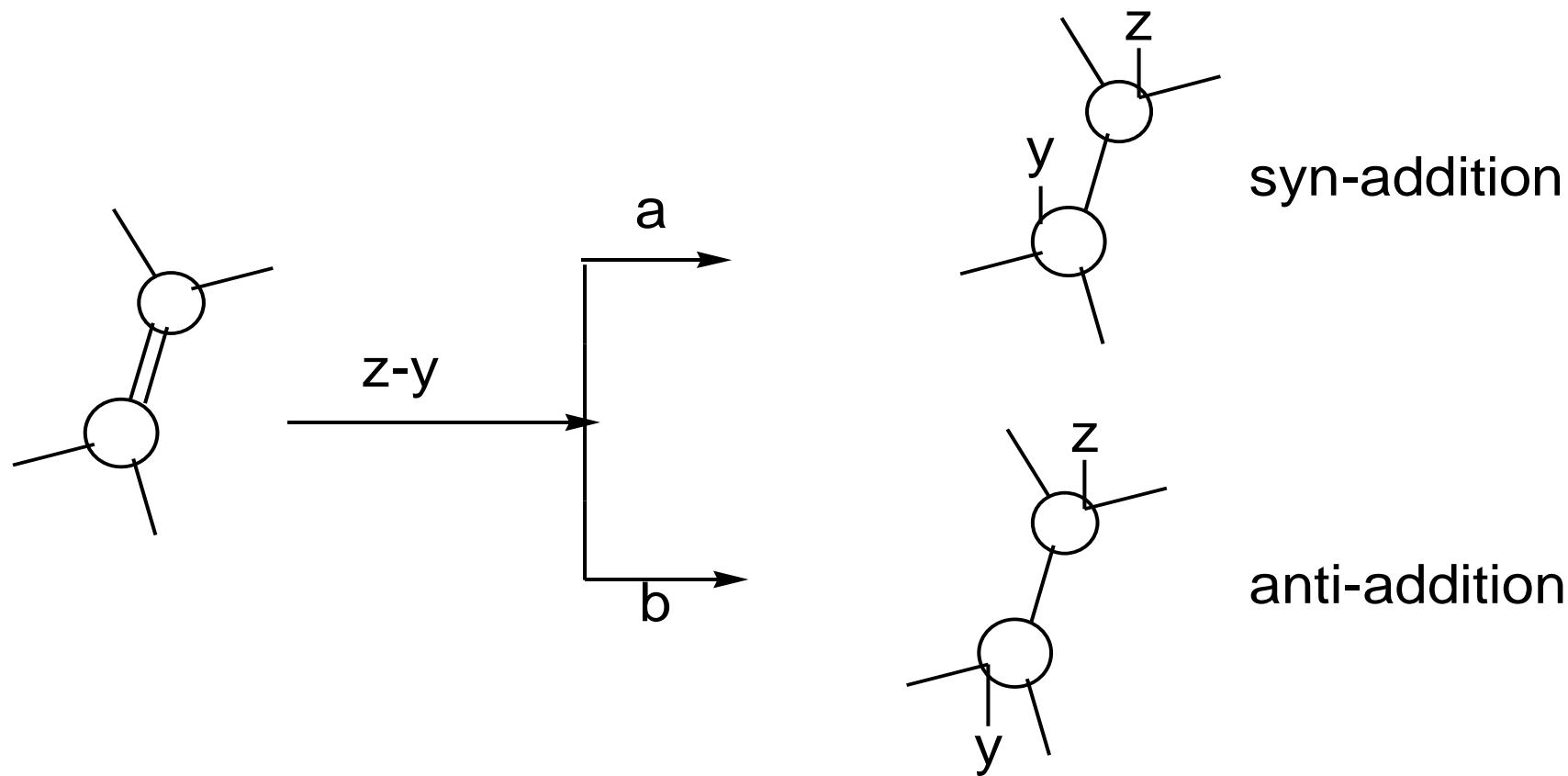
Just which product we obtain depends upon which stereoisomer we start with



Stereo specific reaction:-

A reactions in which stereochemically different molecules react and give stereochemically different products

To describe the kinds of stereochemistry possible in addition reactions, the concept of *syn-addition* and *anti-addition* are used.

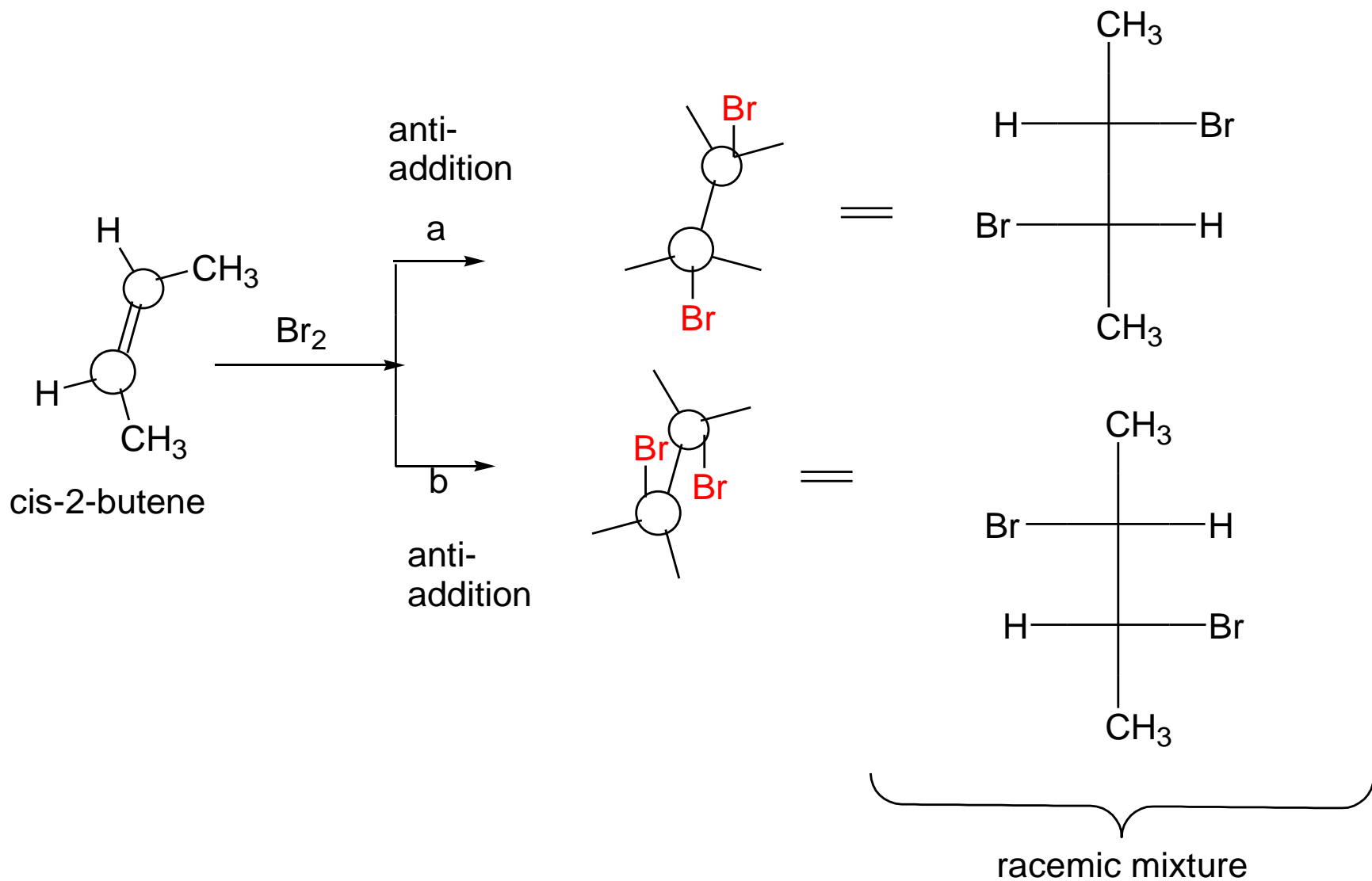


Syn-addition--→ means the added groups to the double bond is attached to the **same face**.

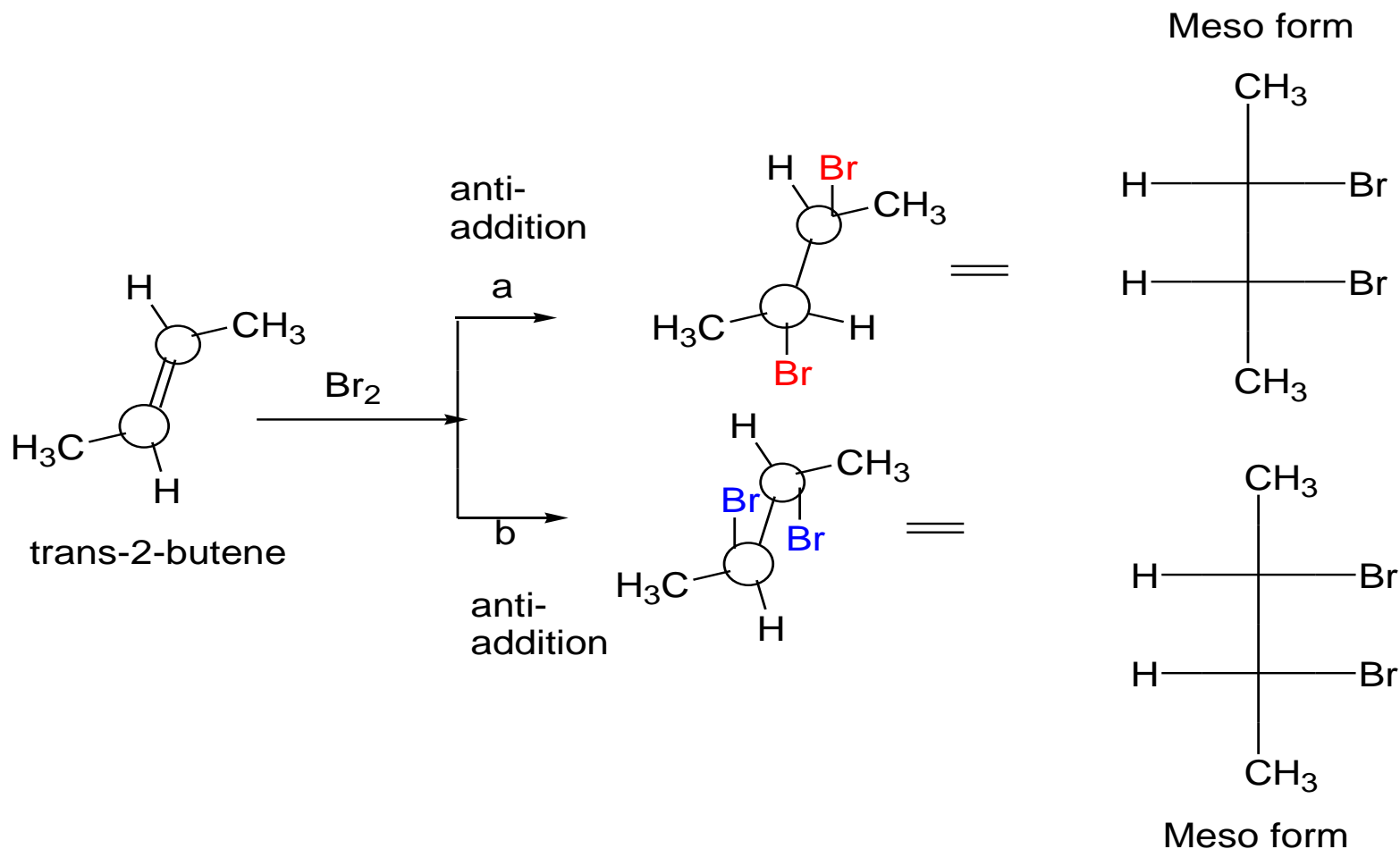
Anti- syn addition -→ means the added groups to the double bond is attached to **opposite face**.

Note:- Addition of Bromine to (2-butene) involve
anti- addition

Anti-addition of Br₂ to cis-2-butene



Anti-addition of Br₂ to trans-2-butene



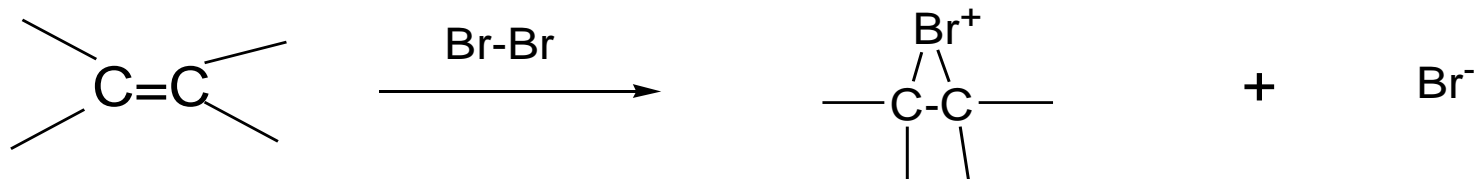
Both compound have a *plane of symmetry* and they are the same compound and it is **Meso form**

Mechanism of halogen addition

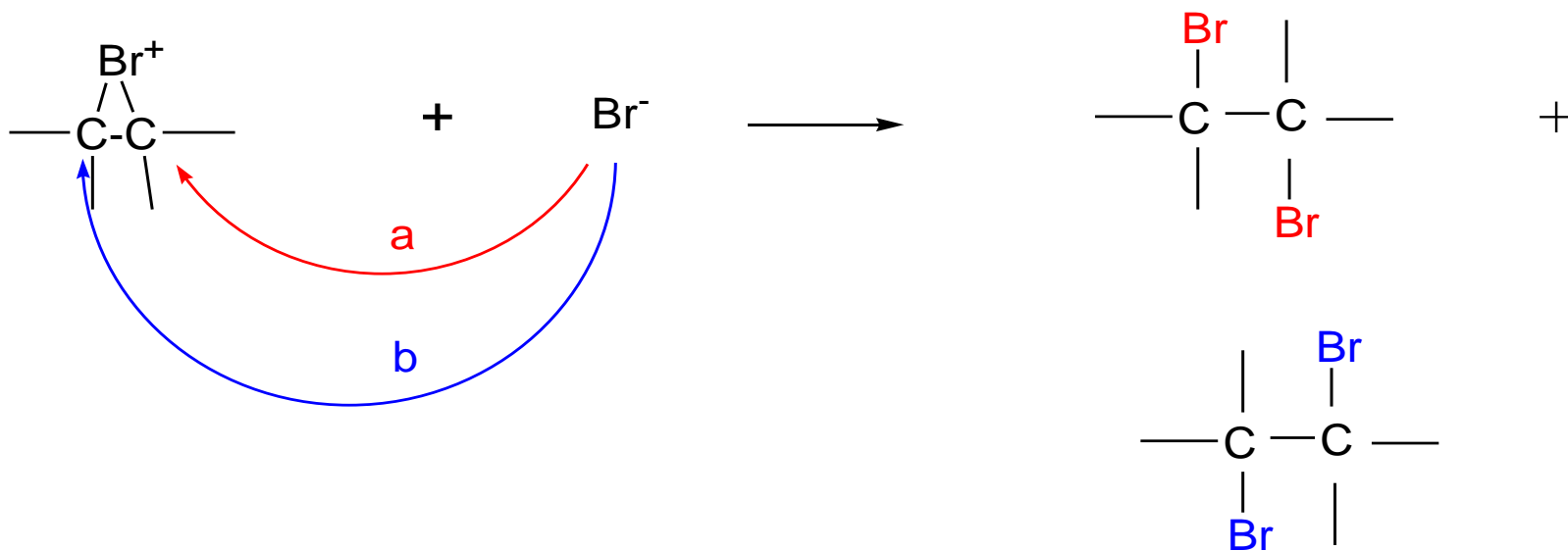
Bromonium ion mechanism

The last mechanism suggested by Robert 1937 for the addition of Bromine or halogen on the double bond

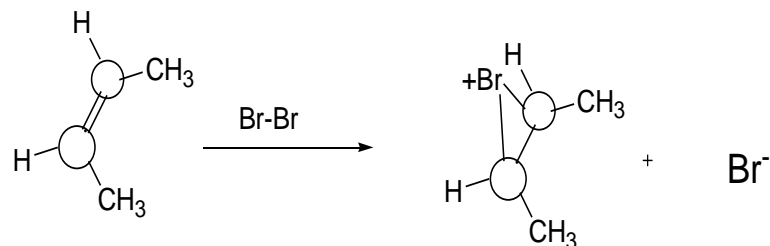
Bromonium ion mechanism



cyclic structure
prevent the free rotation

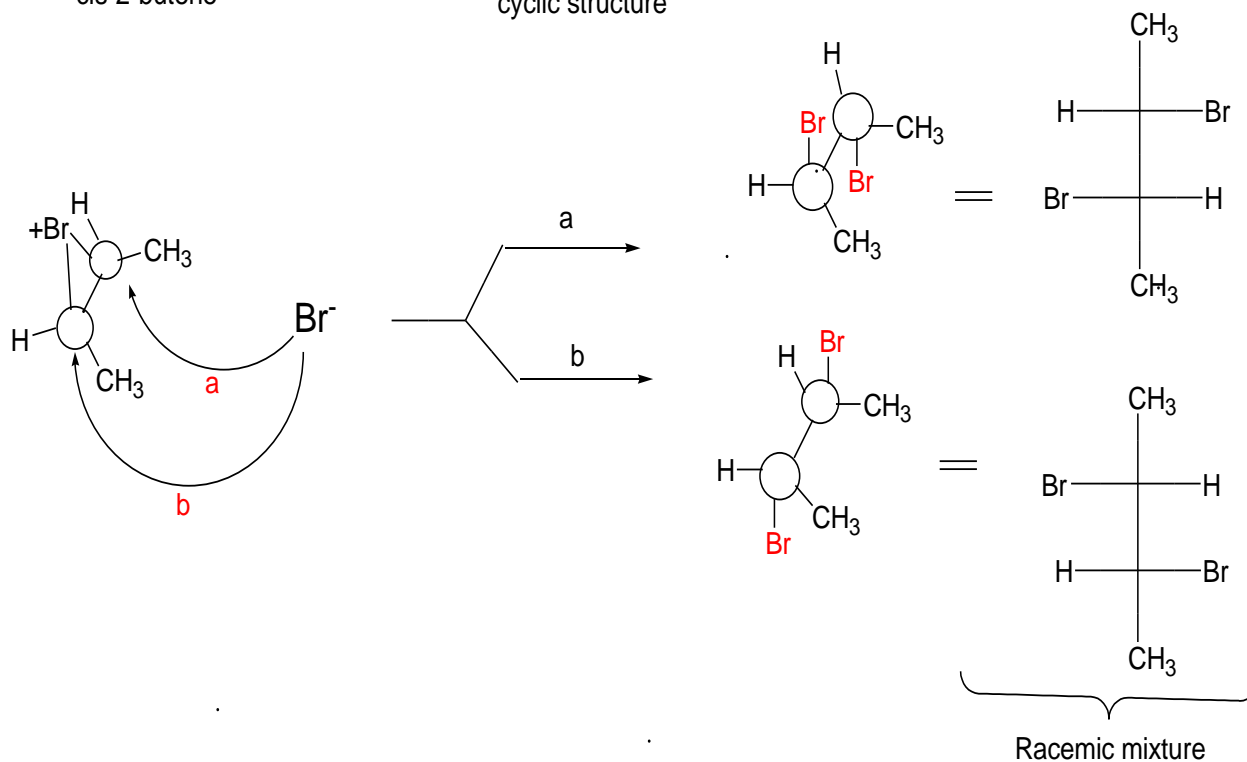


For applying the mechanism in stereochemistry

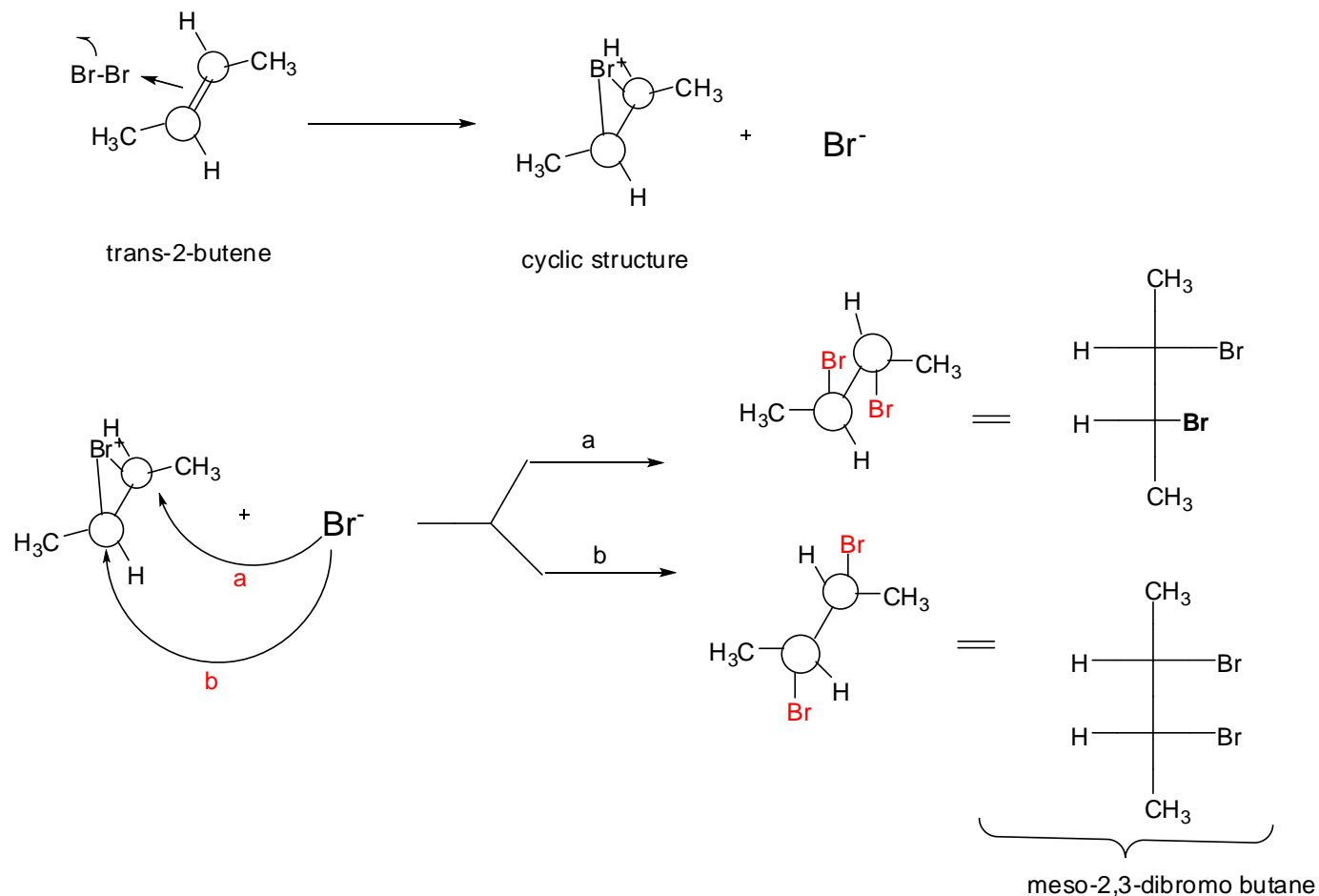


cis-2-butene

cyclic structure

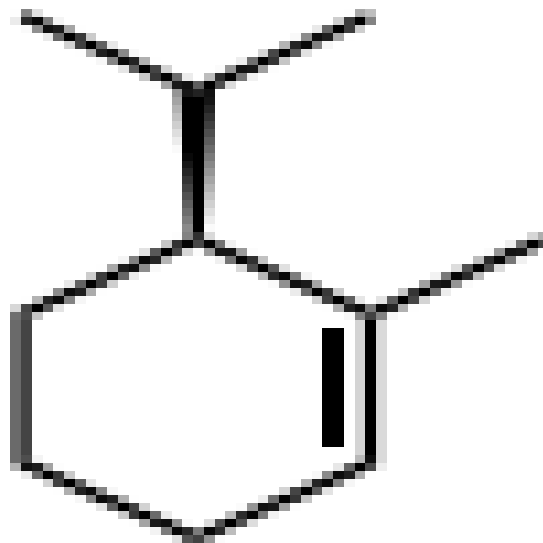


Now let us carry the same operation on trans-2-butene

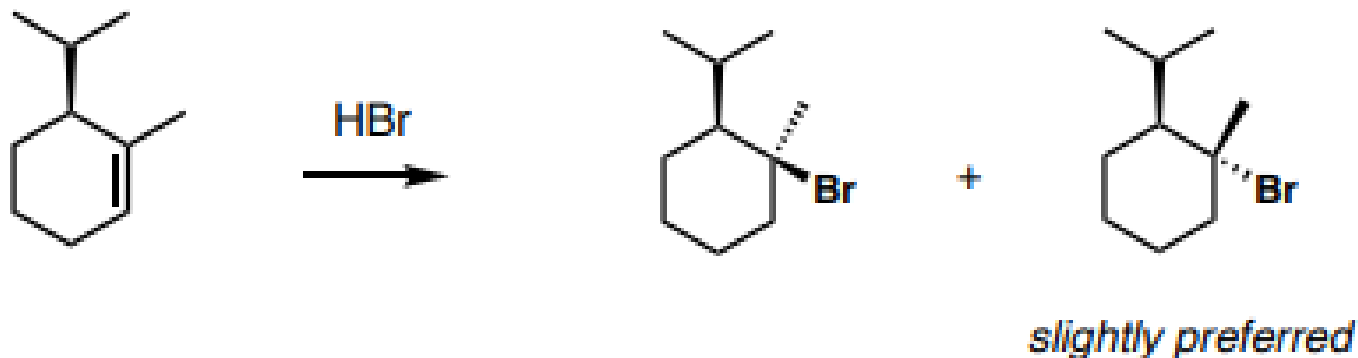


- Addition of bromine to trans-2-butene via a cyclic bromonium ion
- opposite-side attacks give the same product

Alkene with an asymmetric center



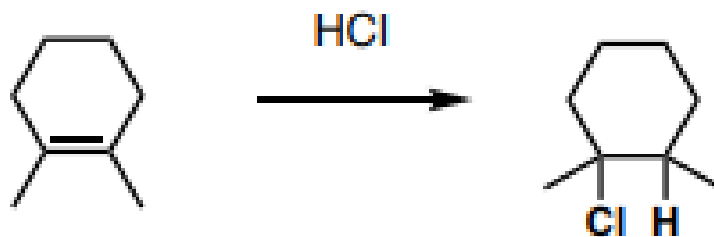
Alkene now has an asymmetric center



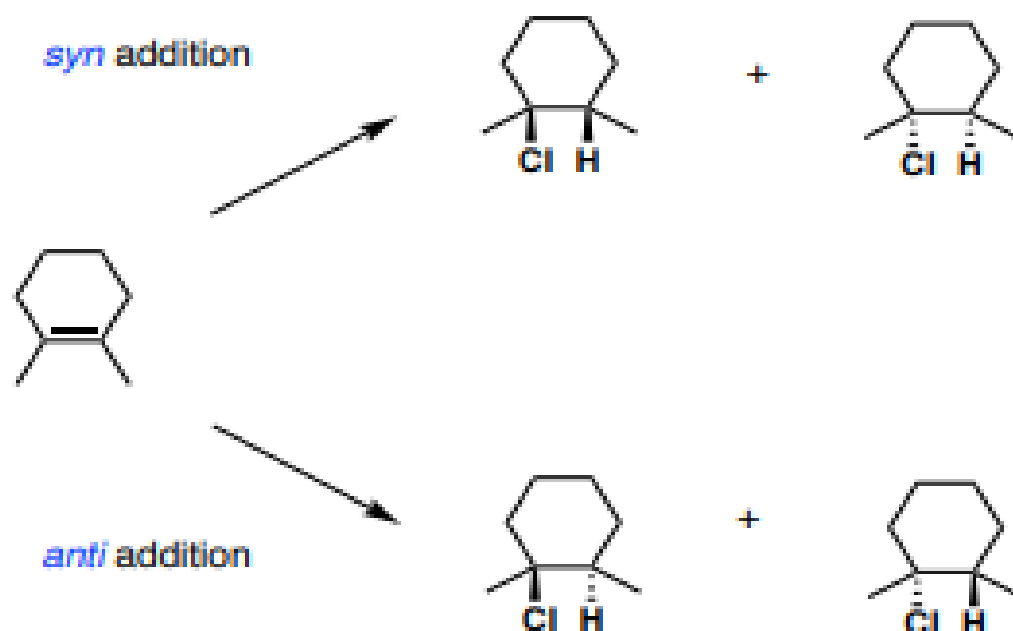
If the starting compound has an **asymmetric center** and the reaction forms a product with a new asymmetric center, **the product will be a pair of Diastereomers**

Example:

How many new Asymmetric Centers are formed?



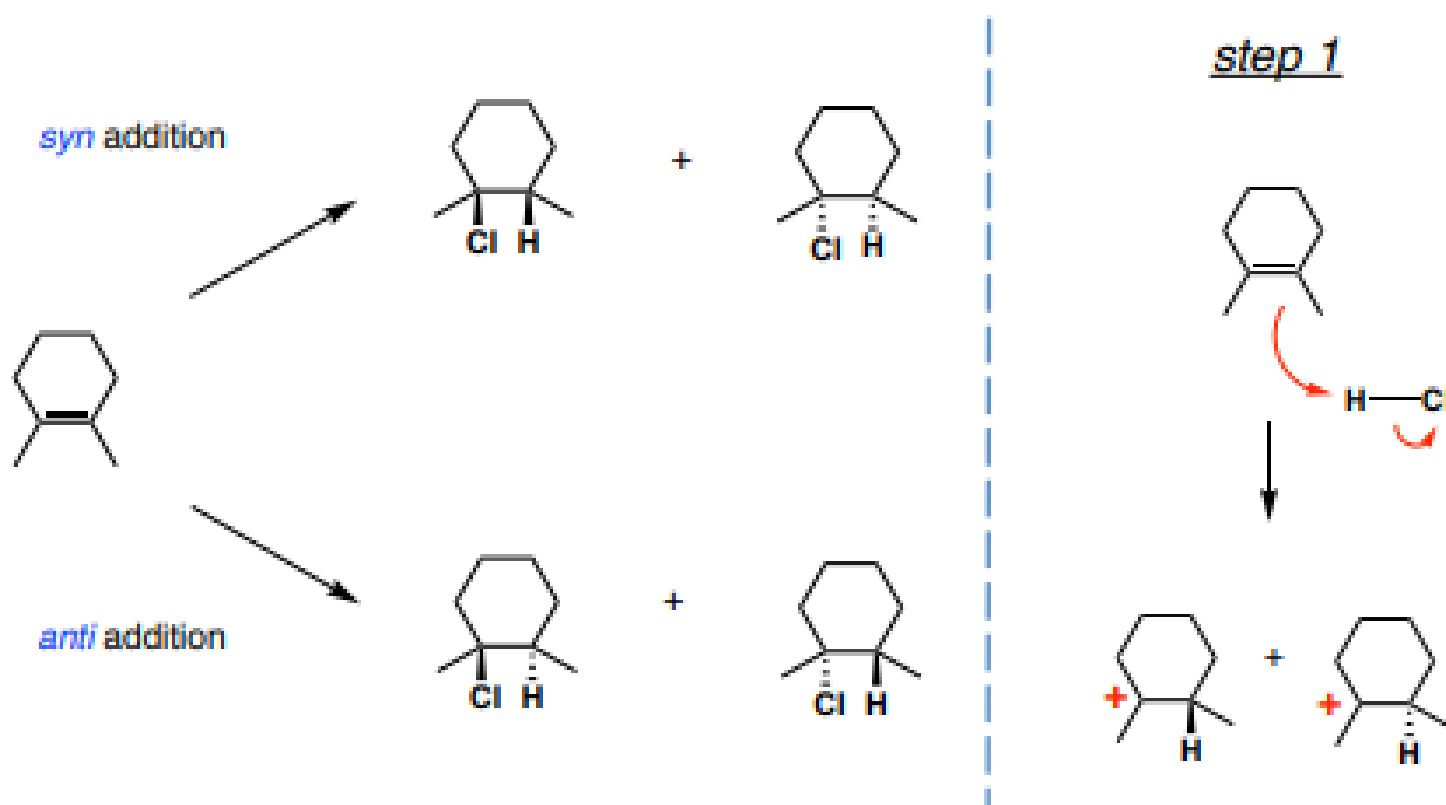
Syn and *Anti* Additions



syn addition: new bonds on the same side of the double bond

anti additions: new bonds on the opposite side of the double bond

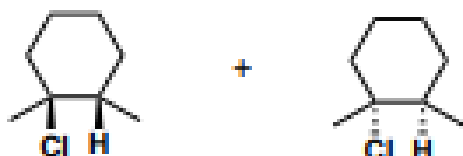
Four Stereoisomers are Obtained if the Reaction Forms a Carbocation Intermediate



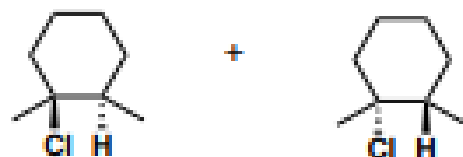
The stereoisomers obtained as products depend on the mechanism of the reaction.

Four Stereoisomers are Obtained if the Reaction Forms a Carbocation Intermediate

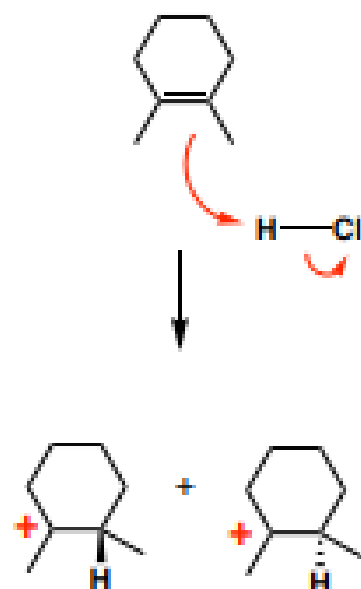
syn addition



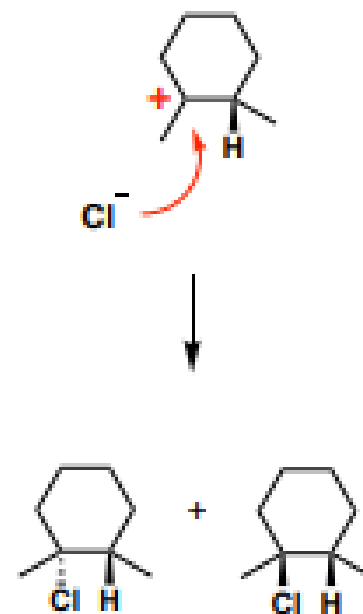
anti addition



step 1



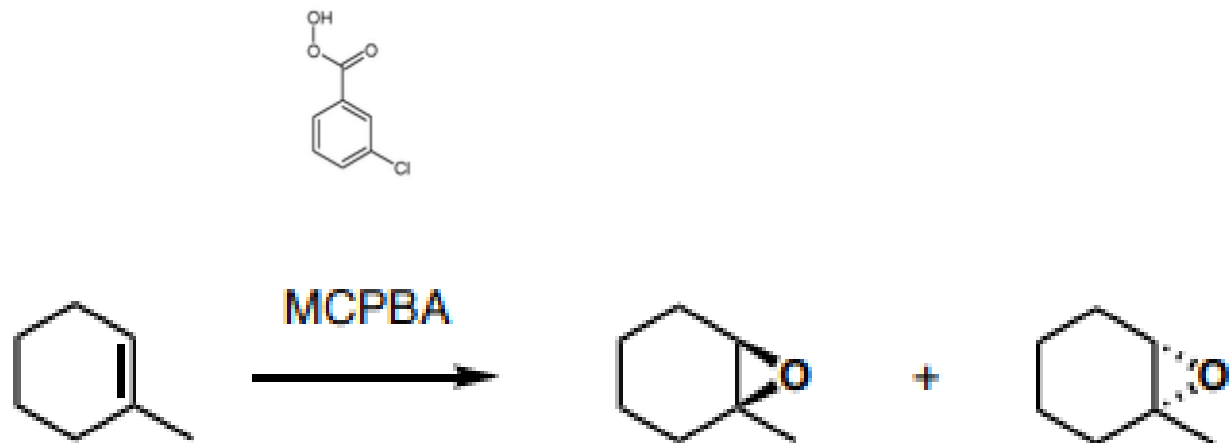
step 2



same for the enantiomeric cation

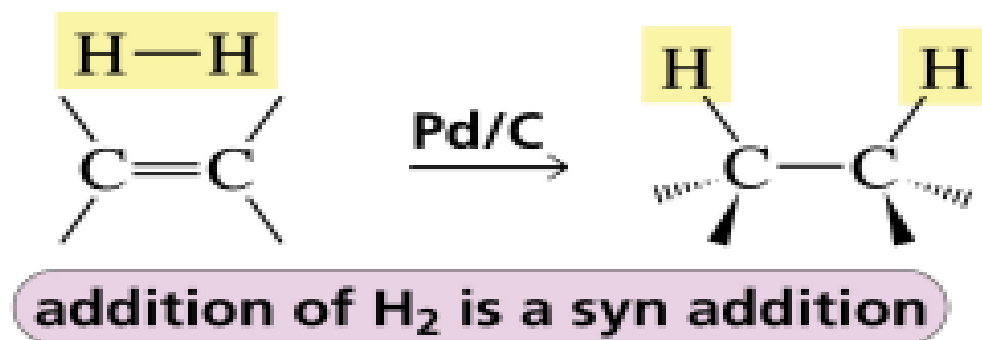
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Epoxidation: syn or anti addition?



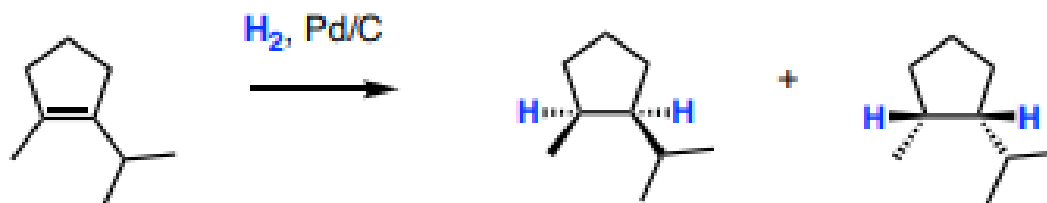
only syn addition

The Stereochemistry of Hydrogen Addition

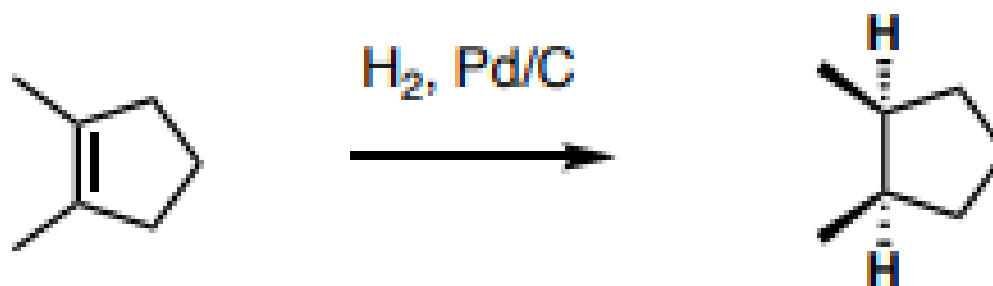


only syn addition

Syn H₂ Addition Forms Only the Cis Stereoisomers..



**If the Substituents are the Same,
The Cis Stereoisomer gives a *Meso* compound**



Thank you for your attention