Stereochemistry of Chemical reactions

Lecture 10

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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**

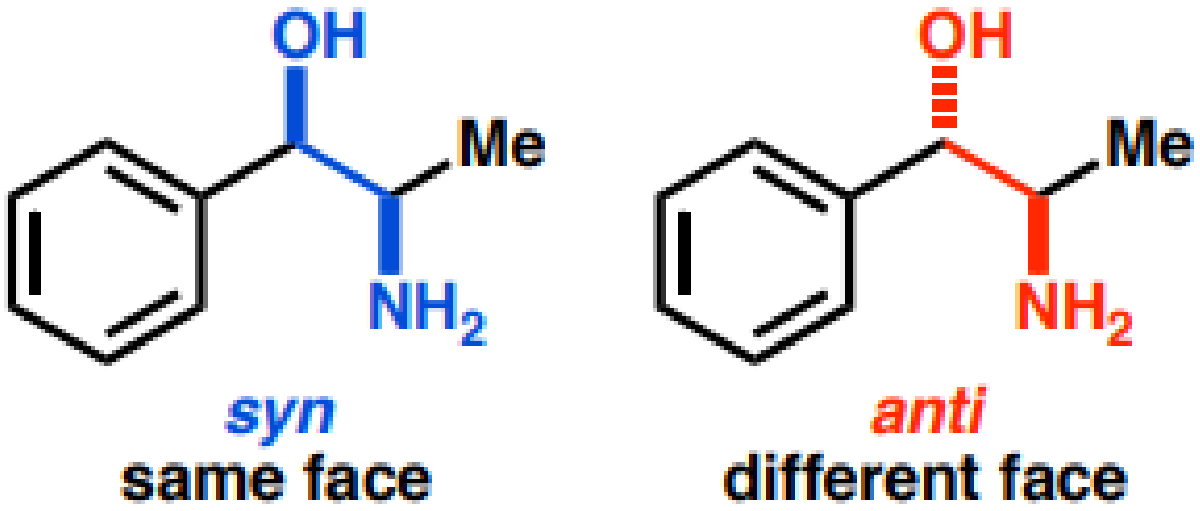
What happens when there is more than one chiral center? How many stereoisomers should we expect?

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

- **Diastereoisomers differ by their relative stereochemistry**

Relative stereochemistry - defines configuration concerning any other stereogenic element within the molecule.

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



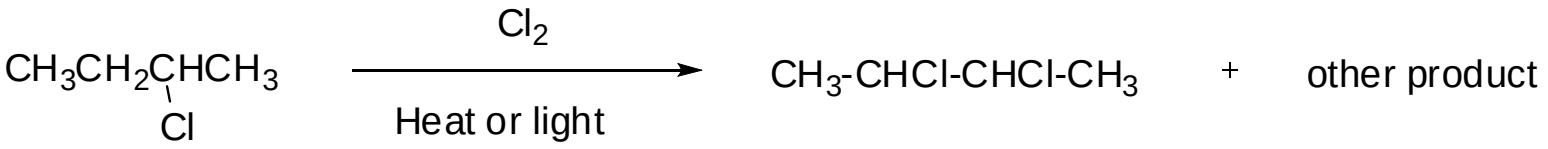
A molecule can only have one enantiomer but any number of diastereoisomers

- 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 **2n stereoisomers**
- Problem is, the molecule will never have more than 2n stereoisomers but it might have less...

Generation of a second chiral center

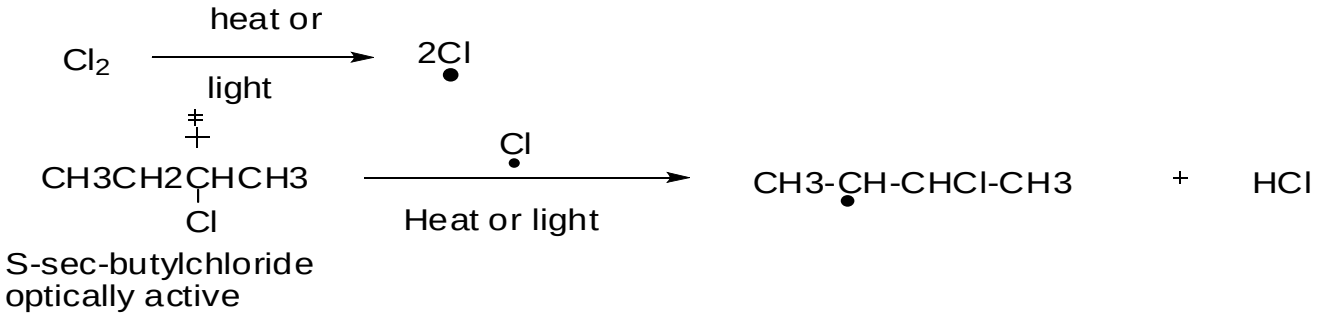


S-sec-butylchloride
optically active

2,3-dichlorobutane
separation from other
product by Fractional distillation

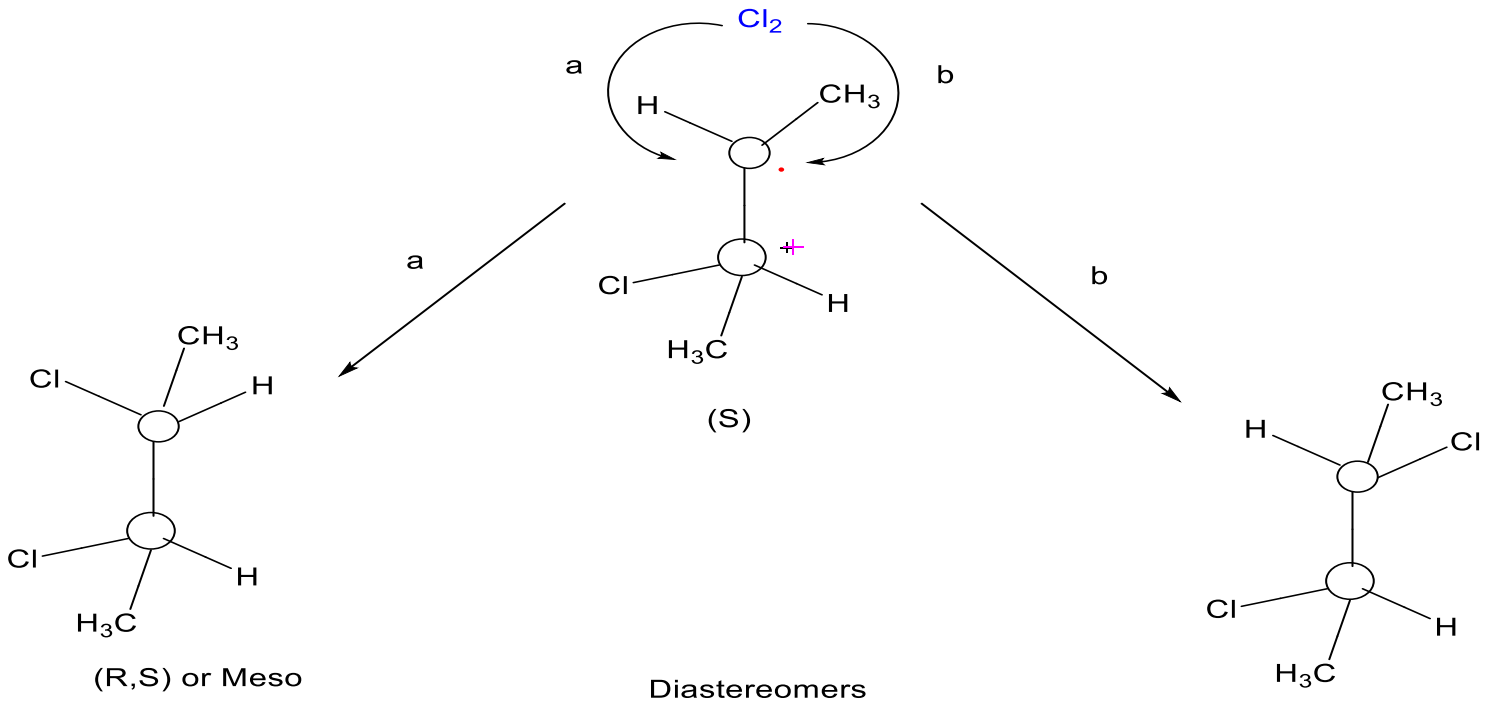
Note:- Configuration of original chiral center 2 will retained, since no bond to it was broken

Q) Is the product optically active or inactive?



S-sec-butylchloride
optically active

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



Formed in unequal amount
The configuration at the original chiral center is unchanged

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

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

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

In this case attachment at (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 ($CH_3CHOHCOOH$) is Formed in the ***contraction of muscles***.

Only (-) malic acid ($HOOCCH_2CHOHCOOH$) 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 Racimic mixture is ***converted*** by an optically active reagent into a mixture of salts (***diastereomers)***which can then be separated.

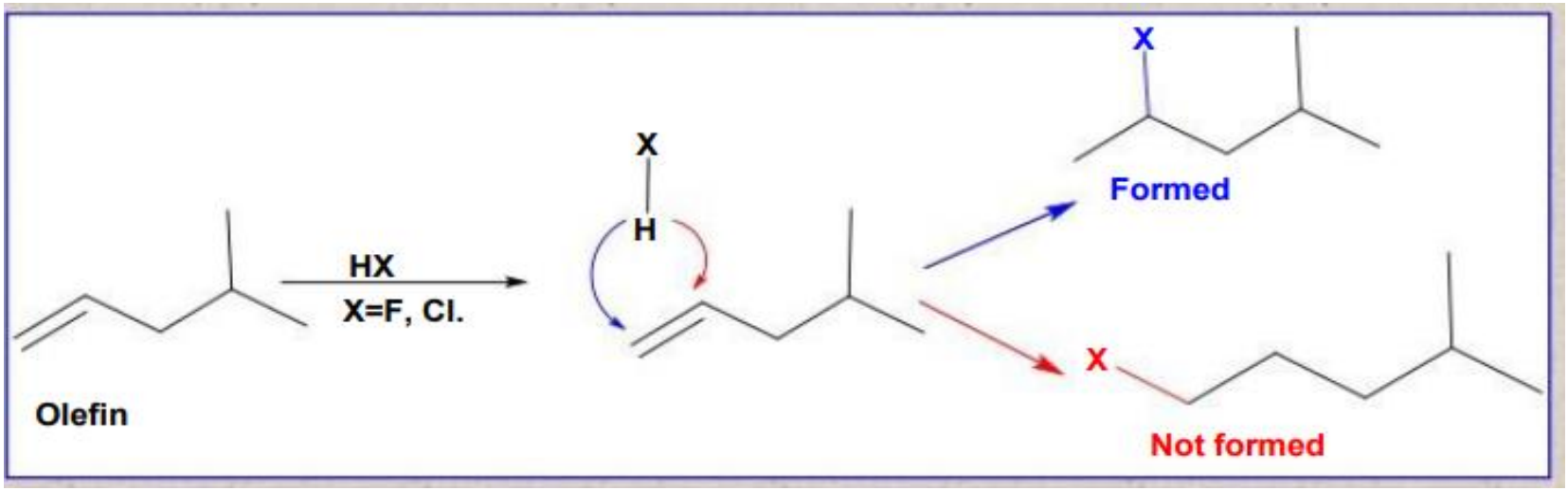
Stereochemistry of Addition Reactions:

Stereochemistry of Addition Reactions: Addition of halogen to Alkenes

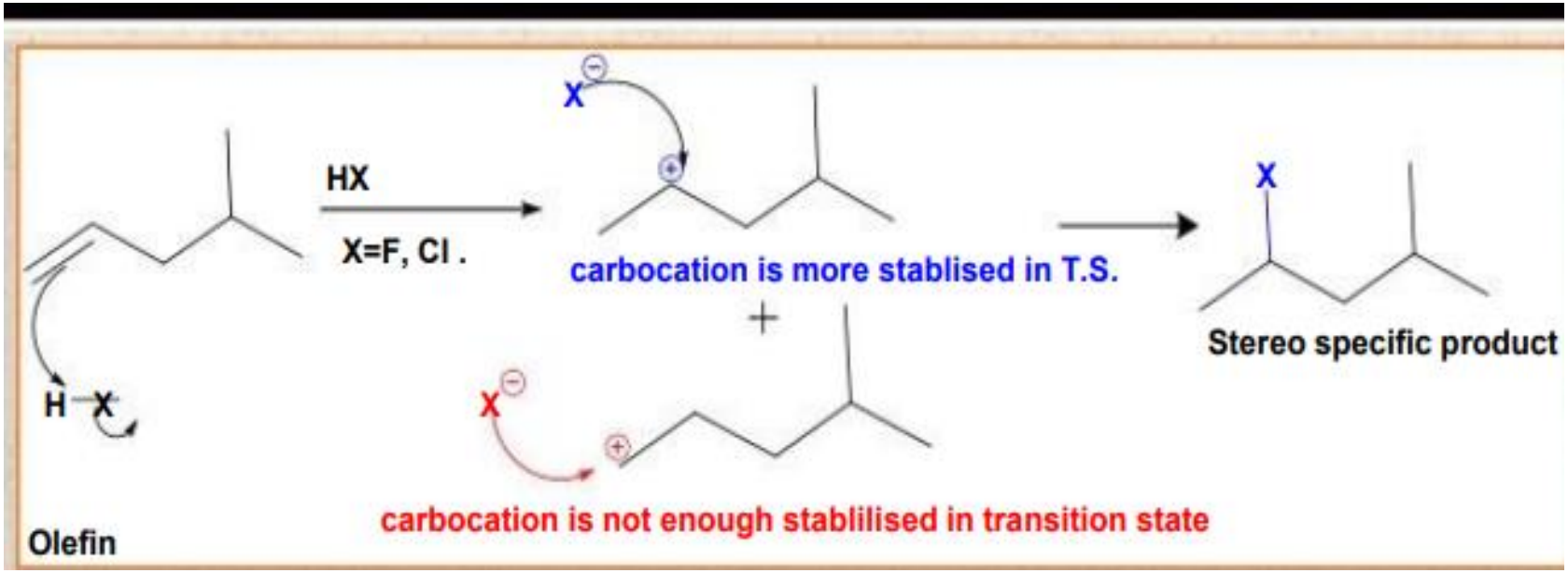
markovnikov’ additions Rules

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**.


X
X
H
HX
X=F, Cl.
Formed
X
Olefin
Not formed

Origin


X
HX
X=F, Cl .
carbocation is more stablised in T.S.
X
Stereo specific product
H X
X
carbocation is not enough stablilised in transition state
Olefin

Stereochemistry of Addition Reactions: Addition of halogen to Alkenes

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

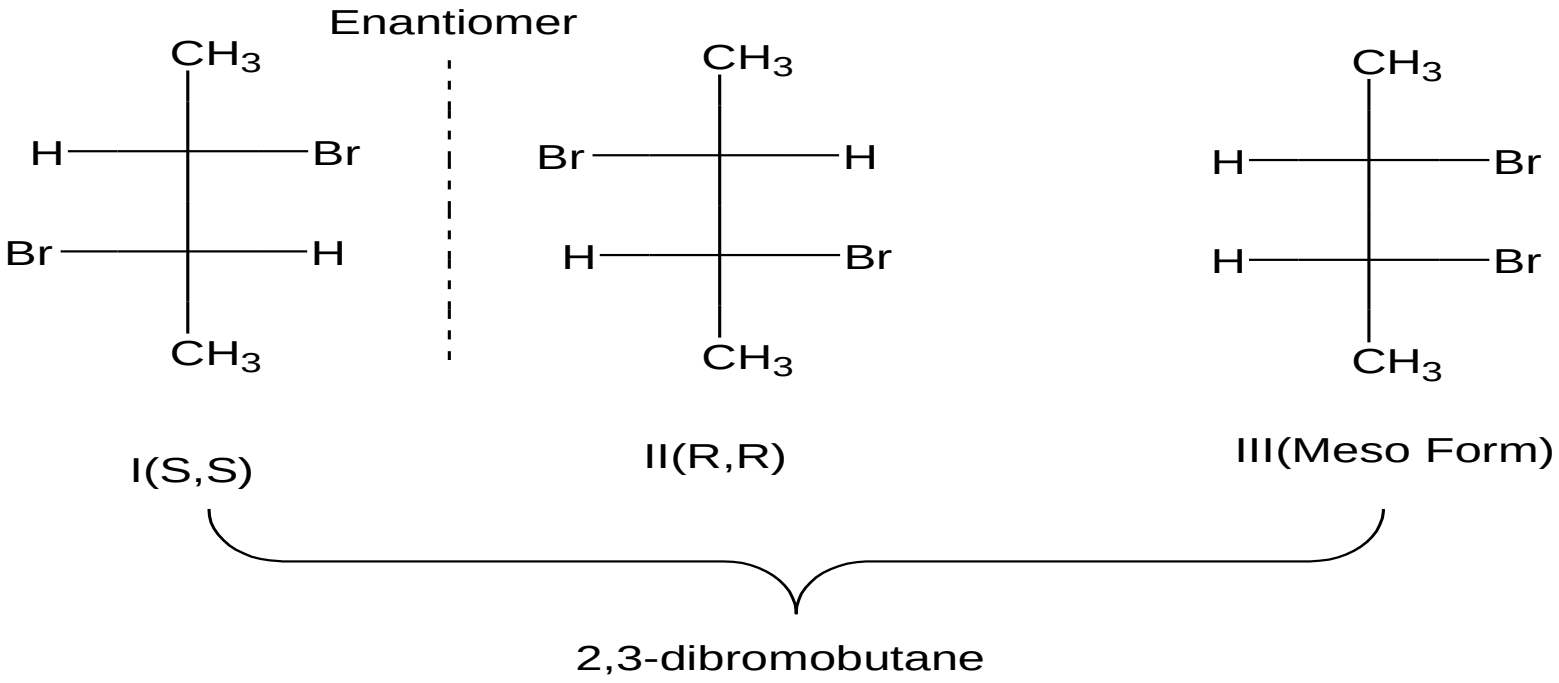
achiral molecule

chiral molecule
optically inactive

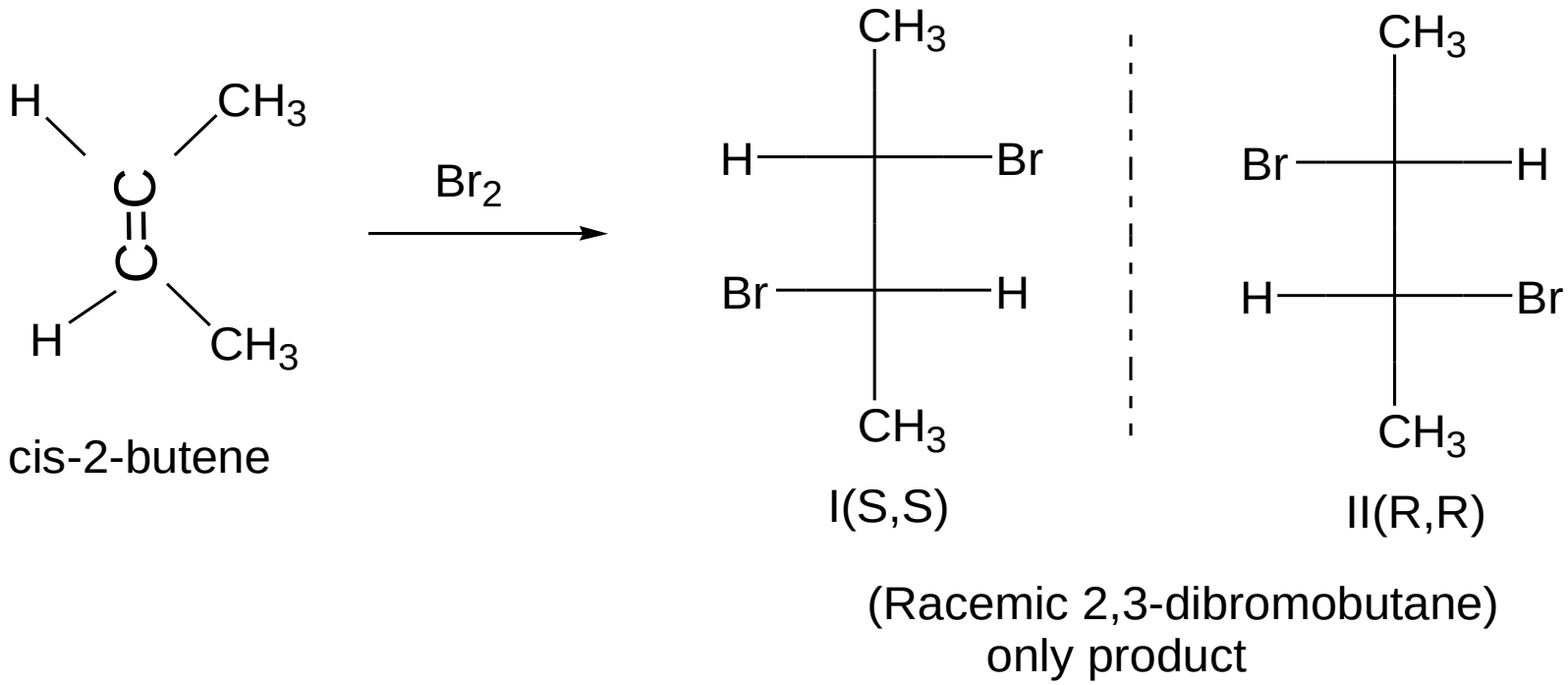
$CH_3CH=CHCH_3 + Br_2$ —addition reaction→ CH_3-CHBr-CHBr-CH_3

2,3-dibromobutane

exist as a pair of
geometric isomer
cis and trans



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

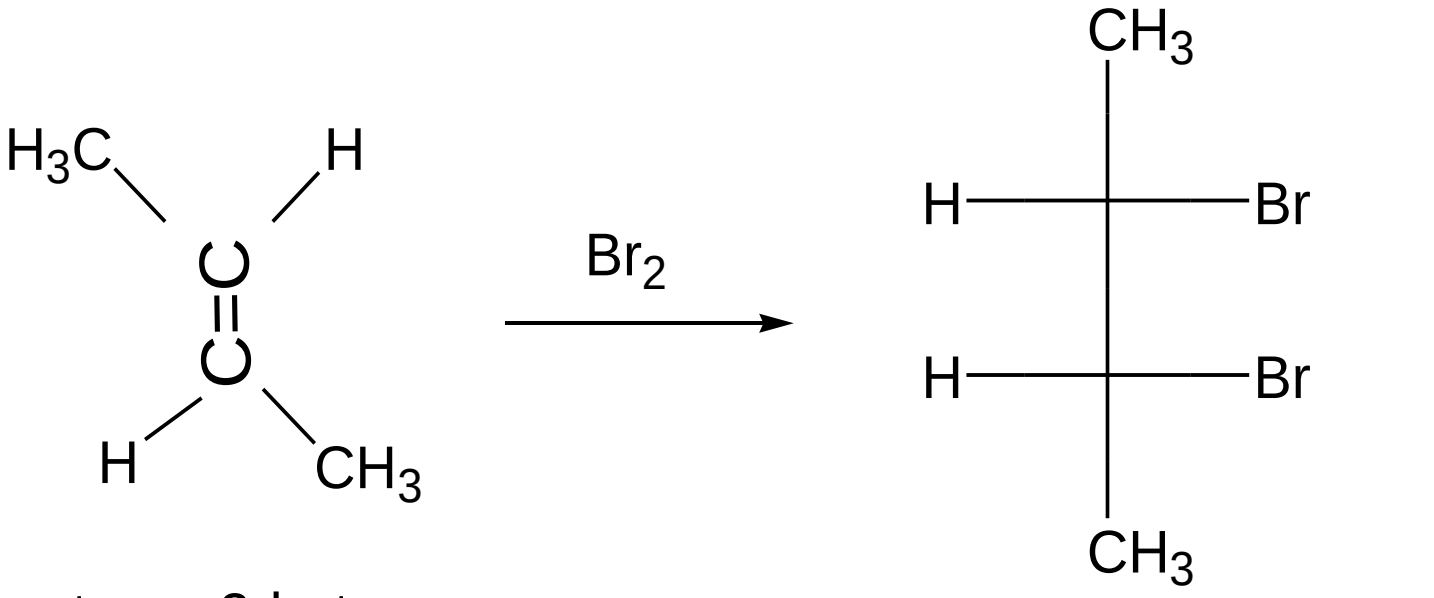


A reaction that yields mainly ***one stereoisomer*** (or one pair of enantiomers) of several possible diastereomers is called a **stereoselective reaction**.

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

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

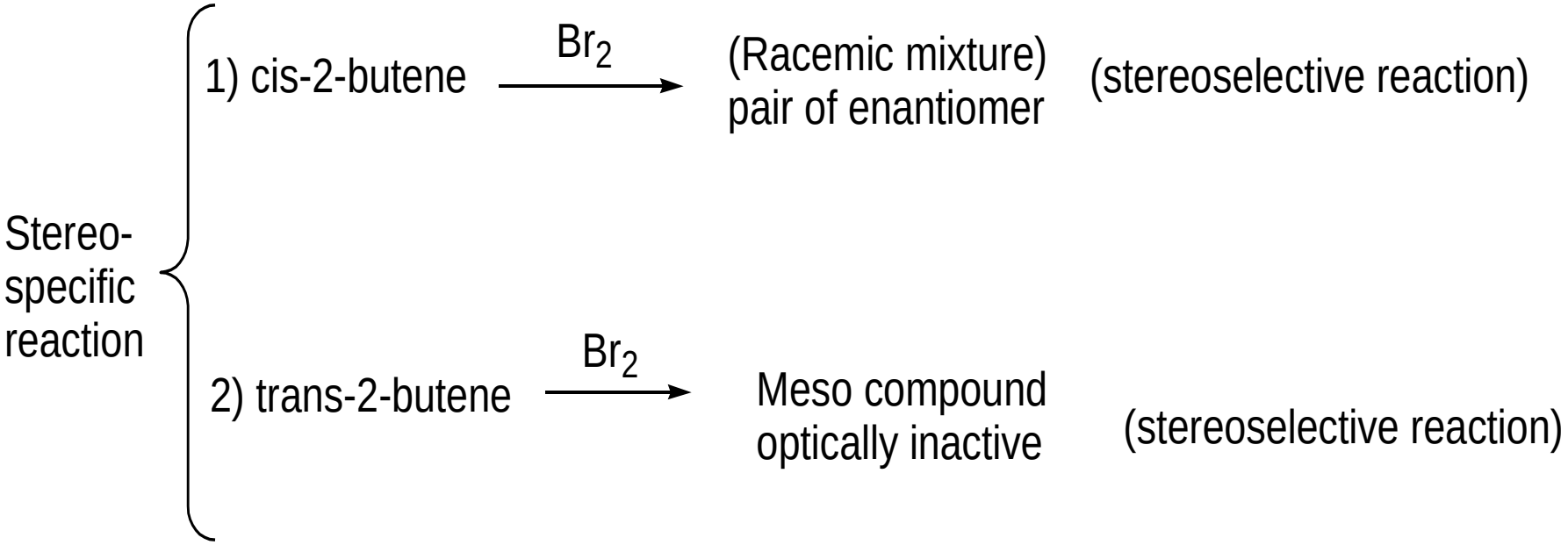
- The trans alkene yields only ***Meso-2,3-dibromo butane***.



trans-2-butene

Meso-2,3-dibromobutane
only product

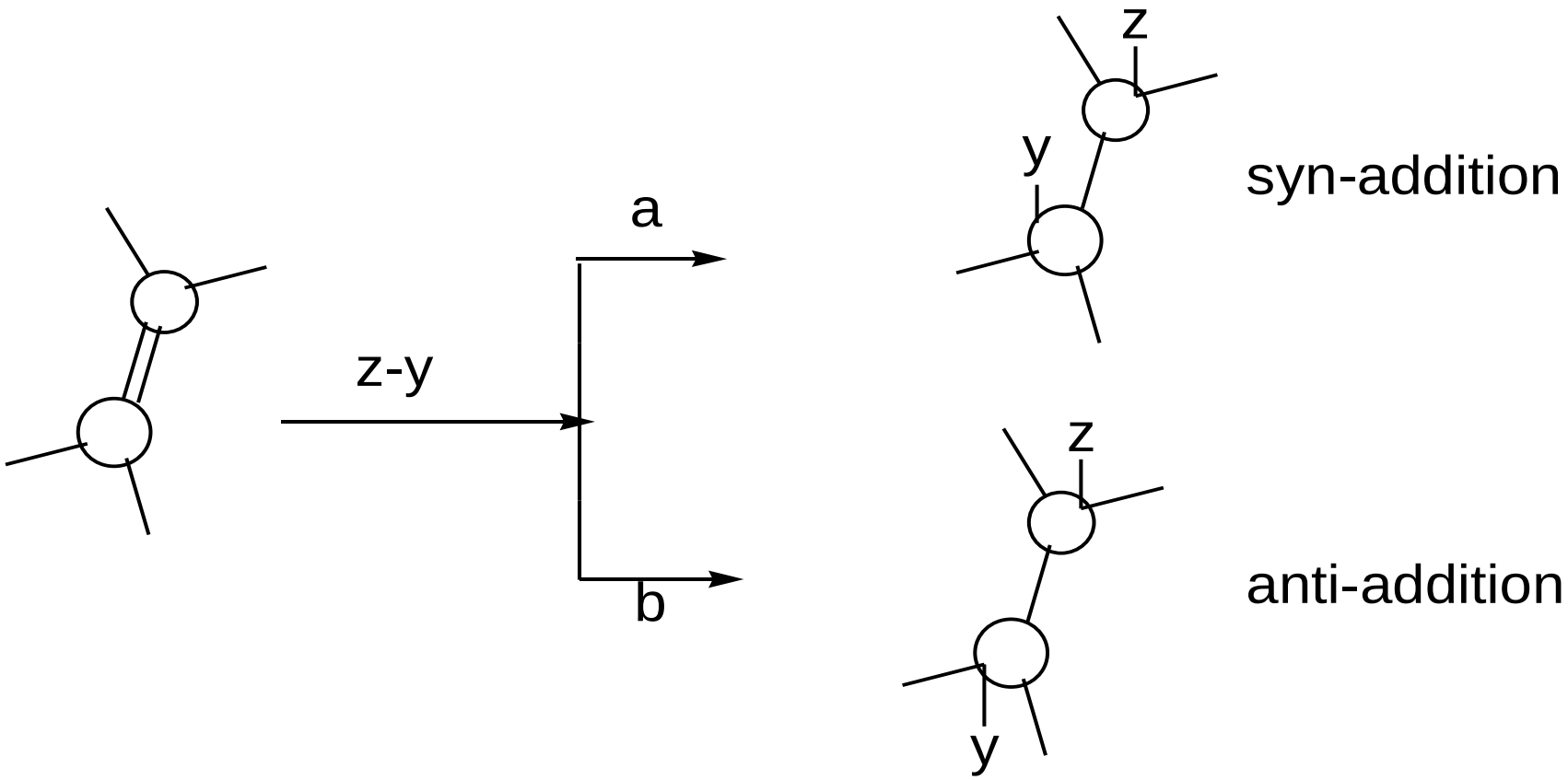
Just which product we obtain depends upon which stereoisomer we start with



Stereo specific reaction:-

A reaction 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.

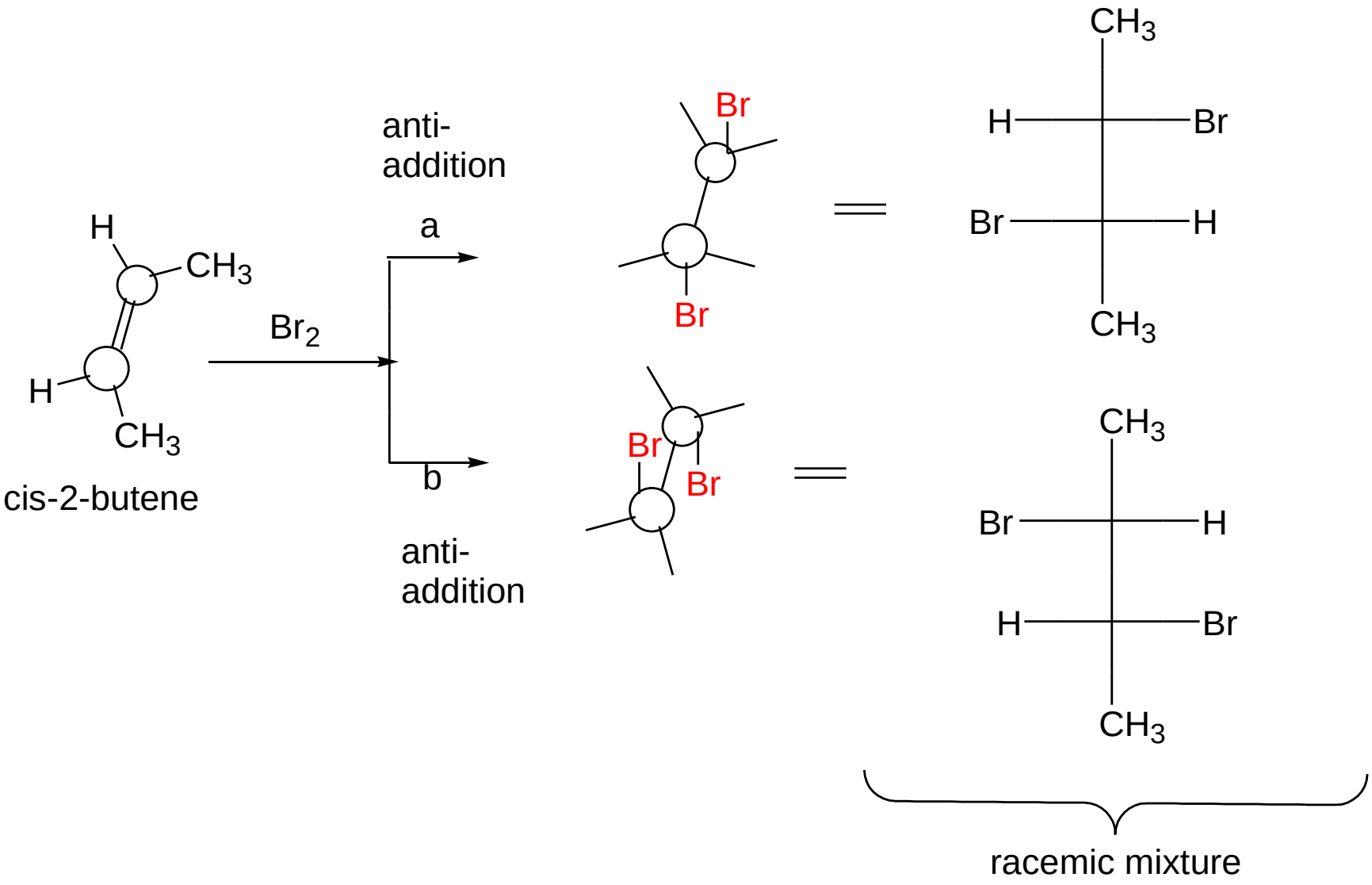


Syn-addition--→ means the added groups to the double bond is attached to the **same face**.

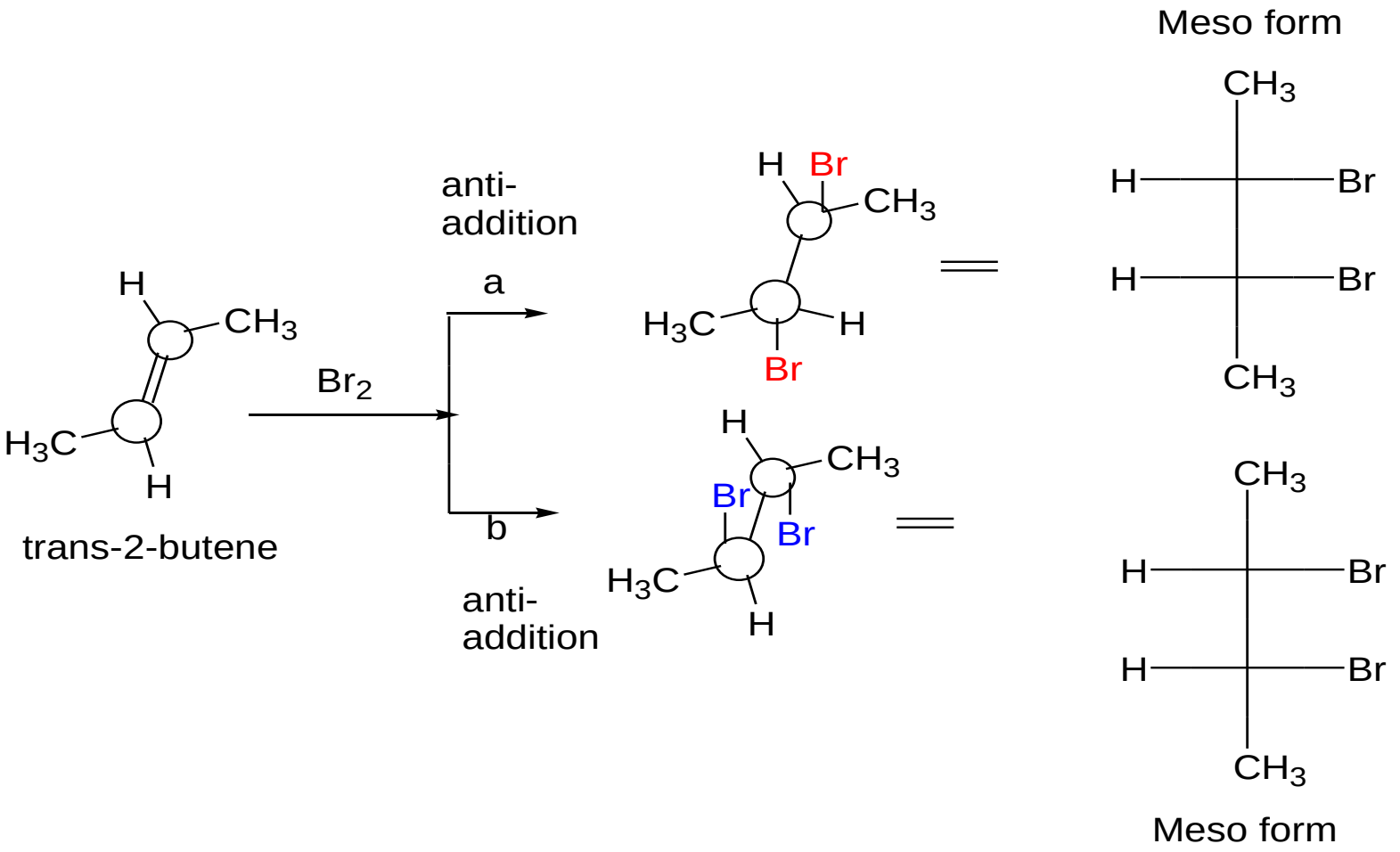
Anti- syn addition -→ means the added groups to the double bond is attached to **opposite face.**

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



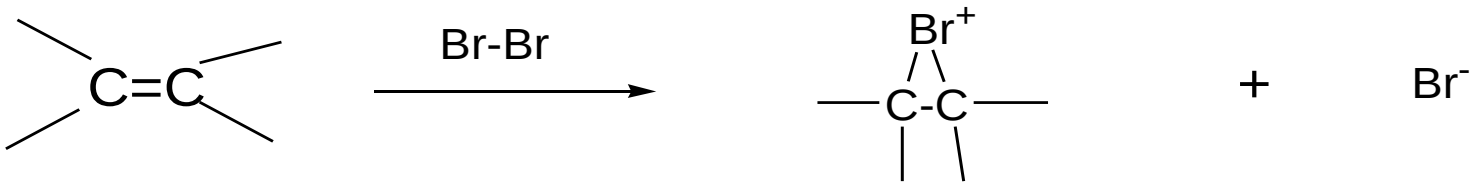
Both compound have a ***plane of symmetry*** and they are the same compound and it is **Meso form**

Mechanism of halogen addition

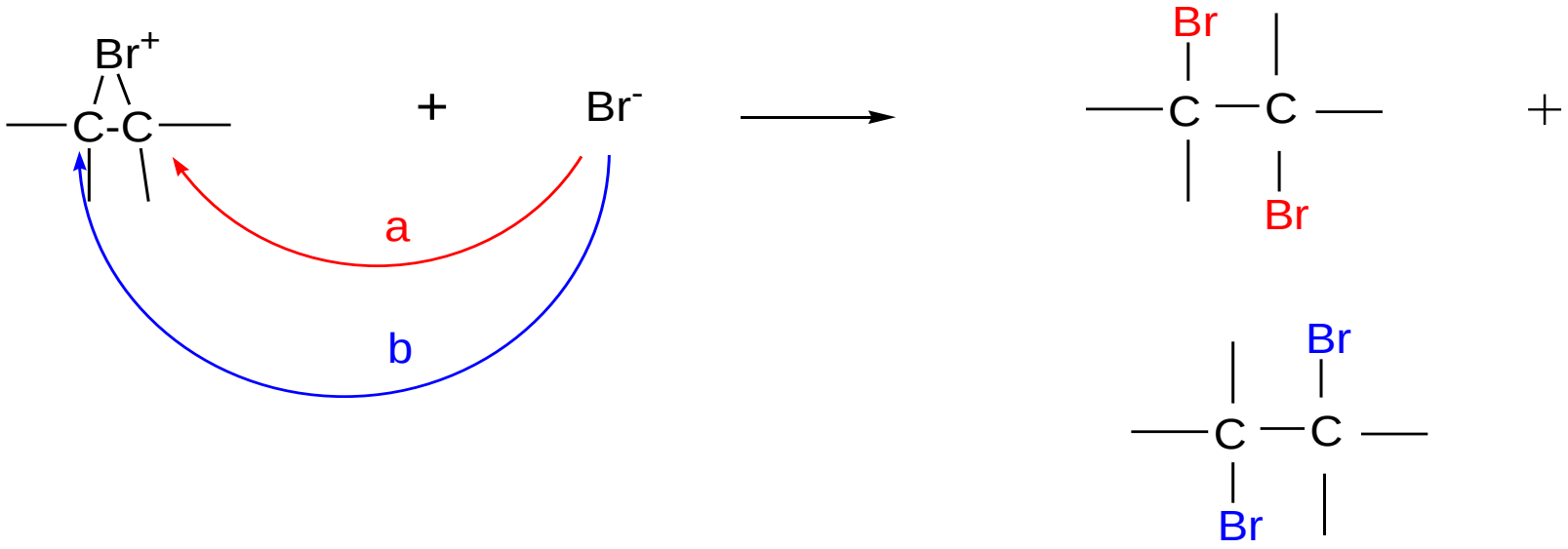
Bromonium ion mechanism

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

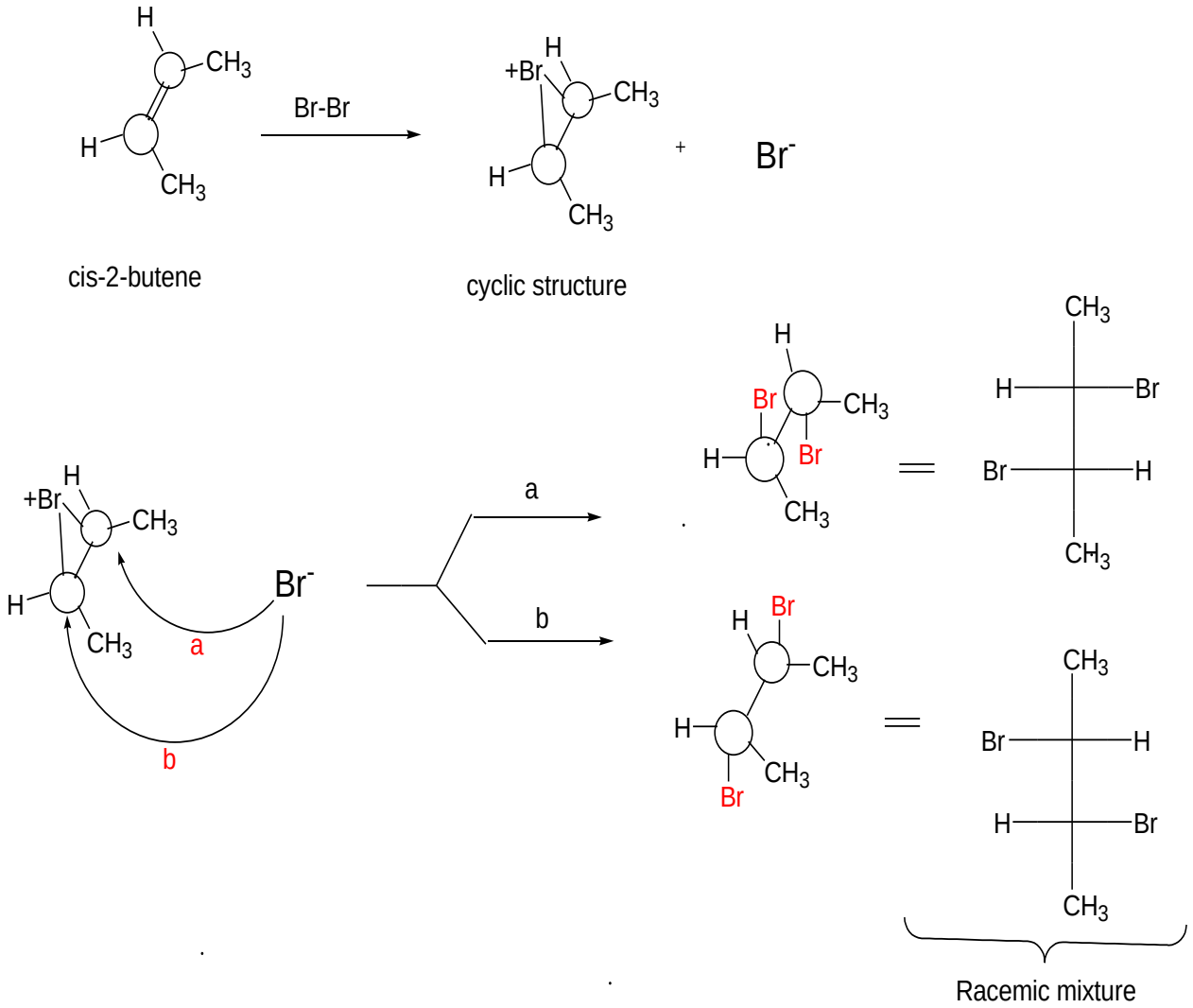
Bromonium ion mechanism



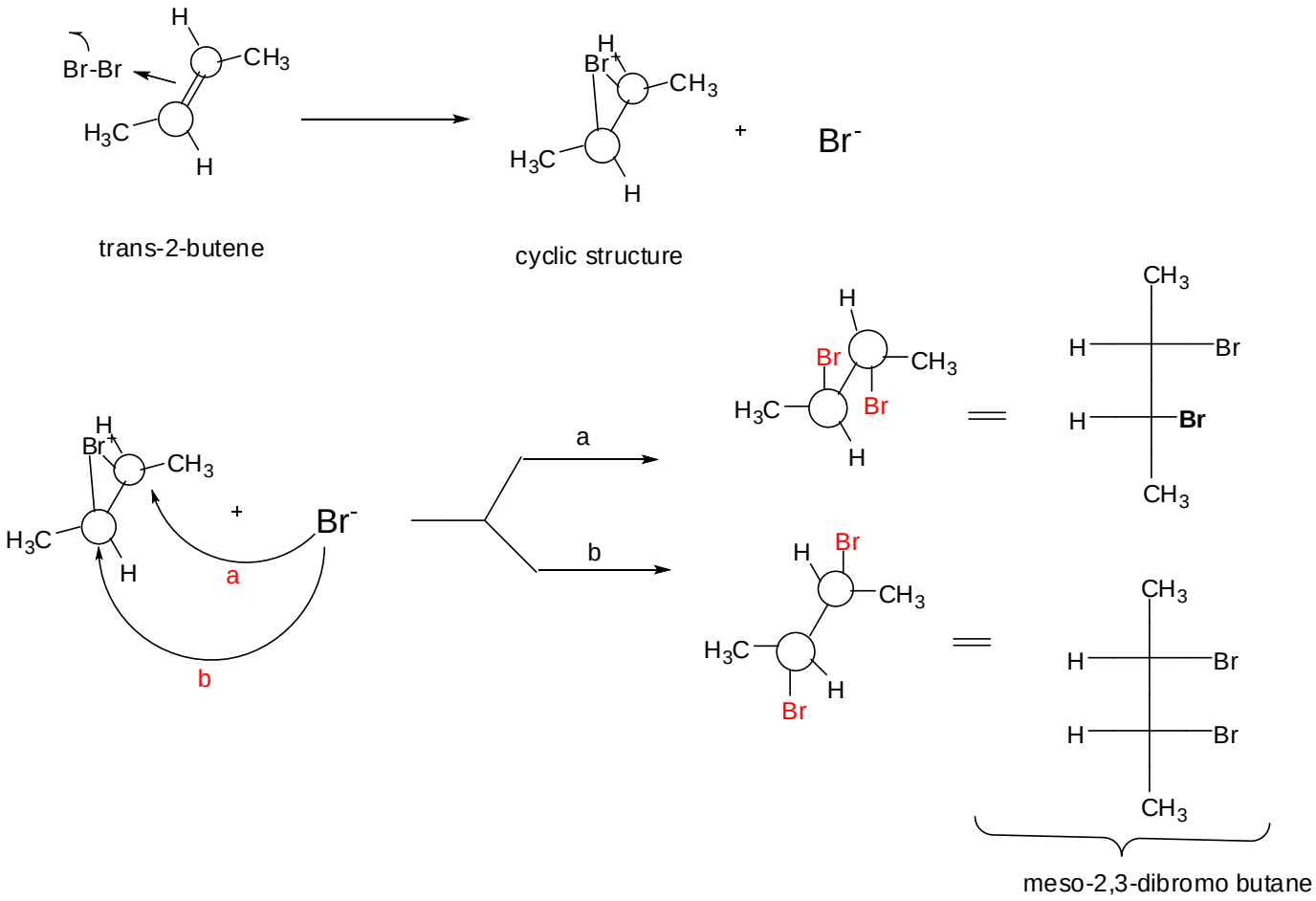
cyclic structure
prevent the free rotation



For applying the mechanism in stereochemistry



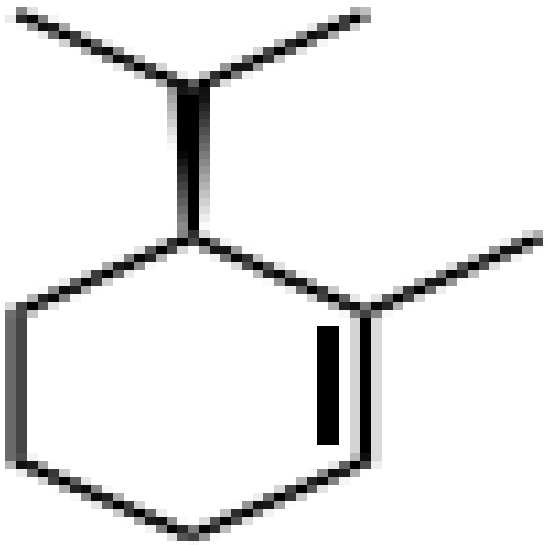
Now let us carry the same operation on trans-2-butene



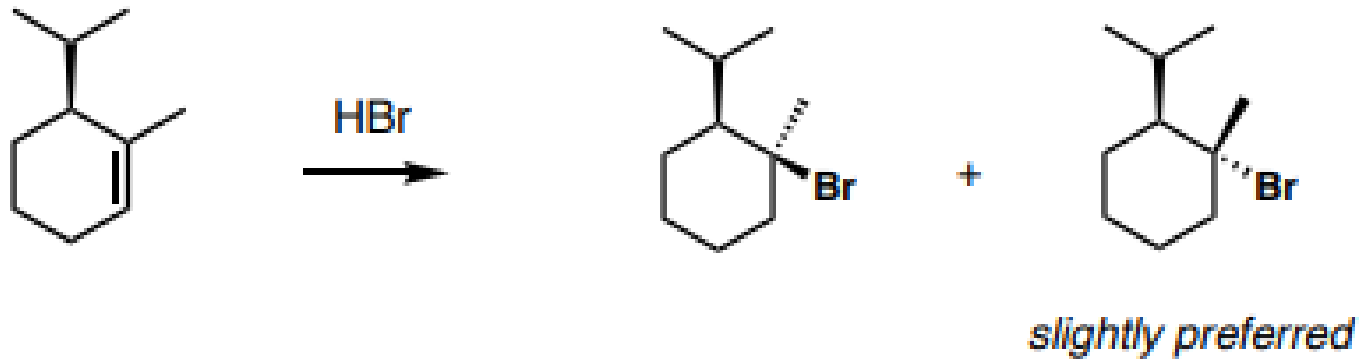
-Addition of bromine to trans-2-butene via a cyclic bromonium ion

- opposite-side attacks give the same product

Alkene with an asymmetric center



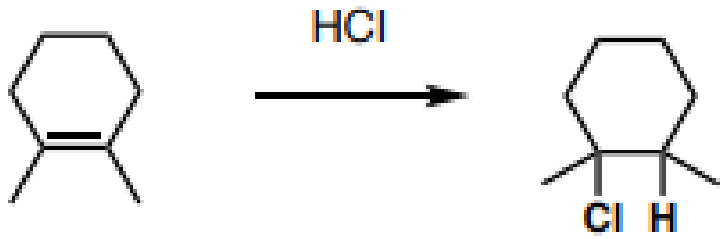
Alkene now has an asymmetric center



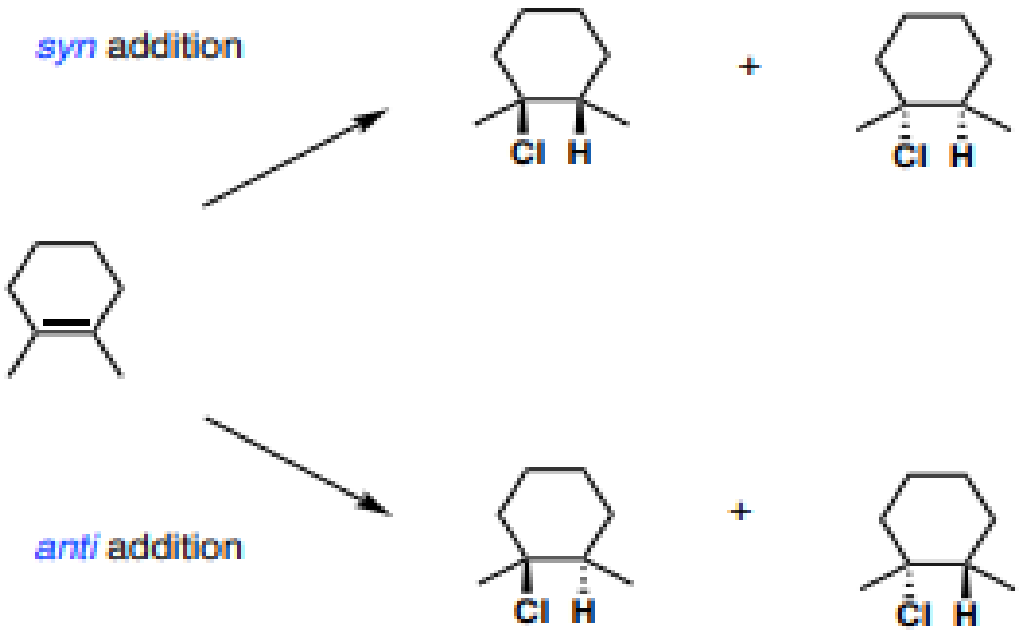
If the starting compound has an **asymmetric center** and the reaction forms a product with a new asymmetric center, **the product will be a pair of Diastereomers**

Example:

How many new Asymmetric Centers are formed?

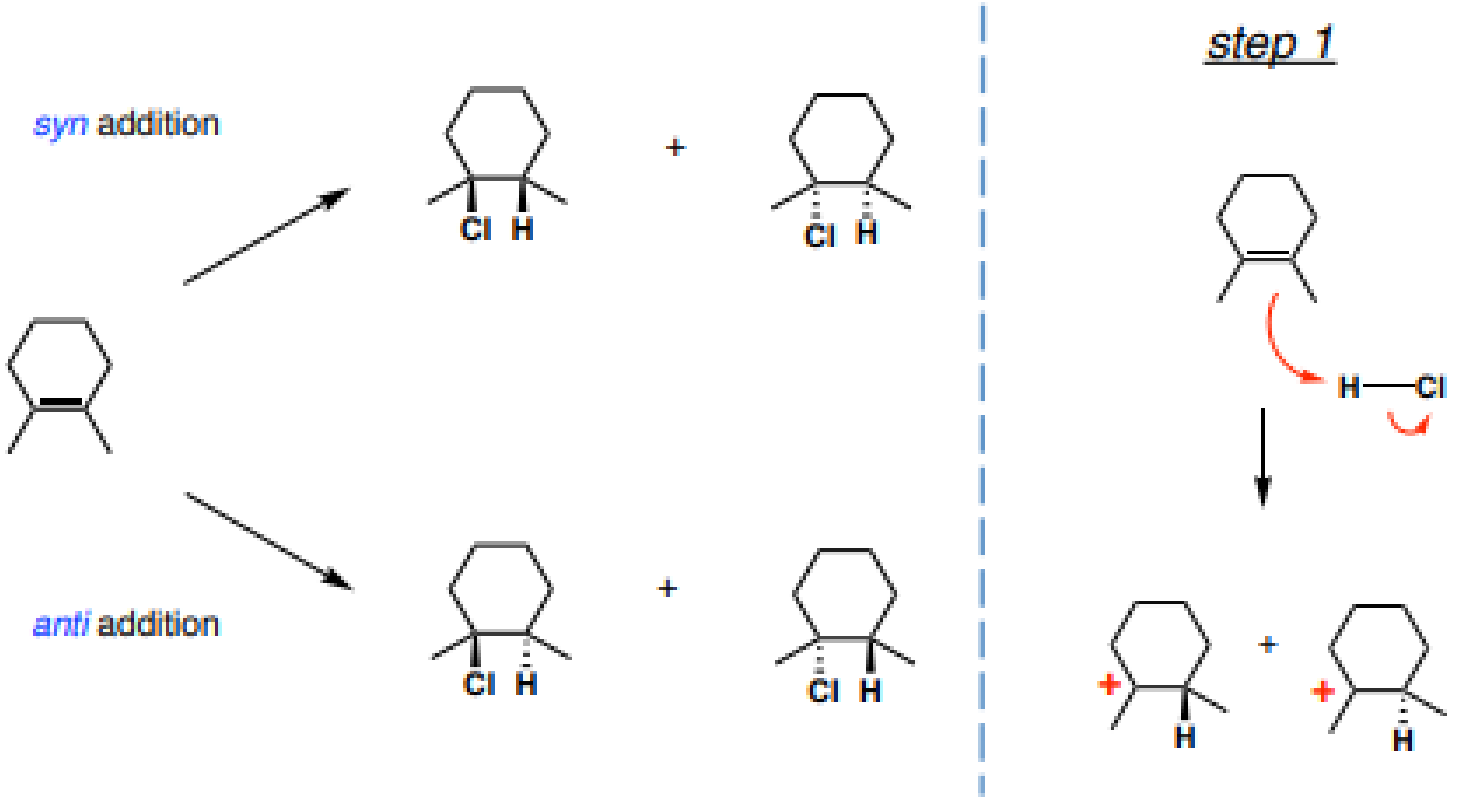


Syn and *Anti* Additions



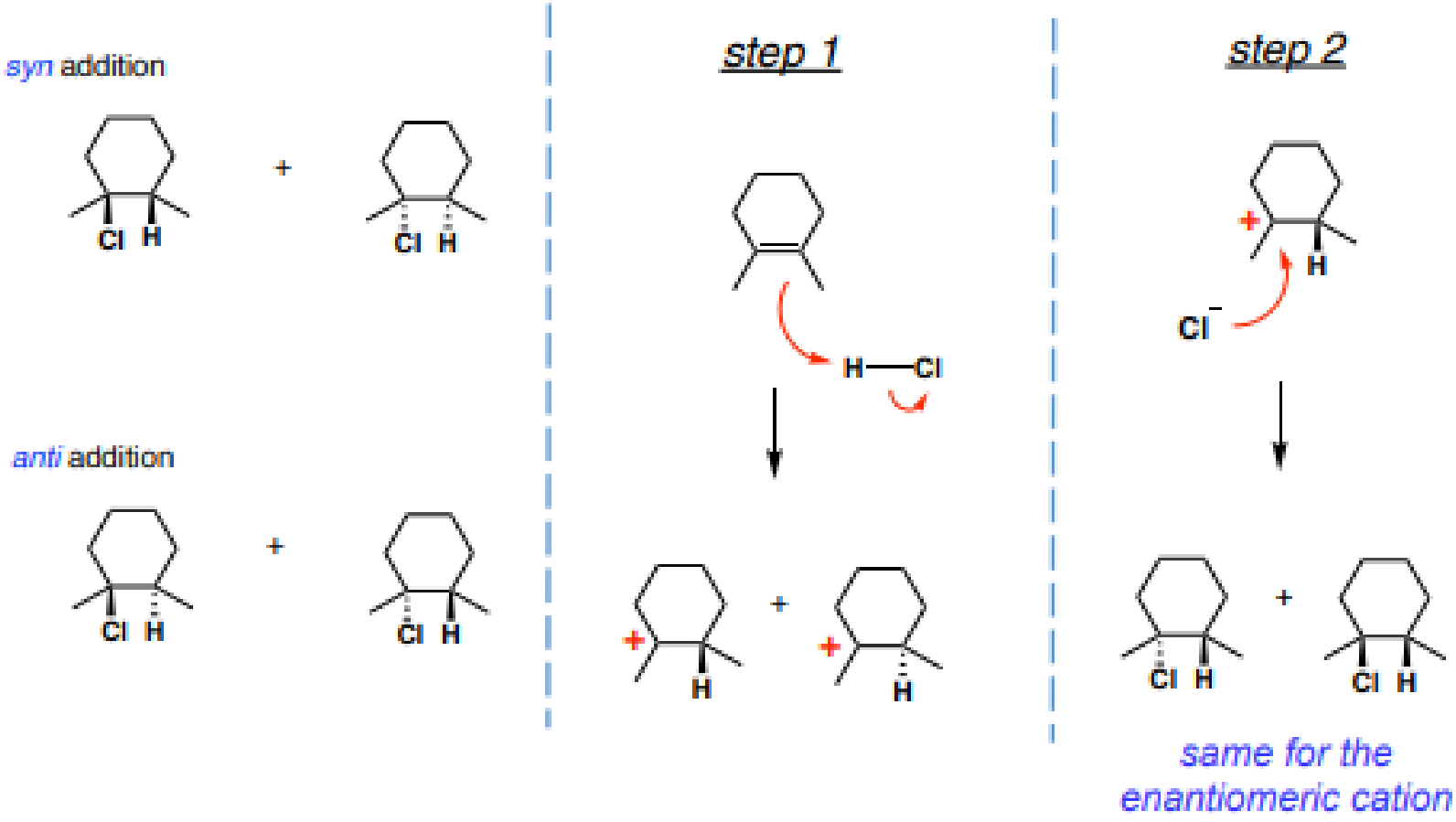
syn addition: new bonds on the same side of the double bond
anti additions: new bonds on the opposite side of the double bond

Four Stereoisomers are Obtained if the Reaction Forms a Carbocation Intermediate



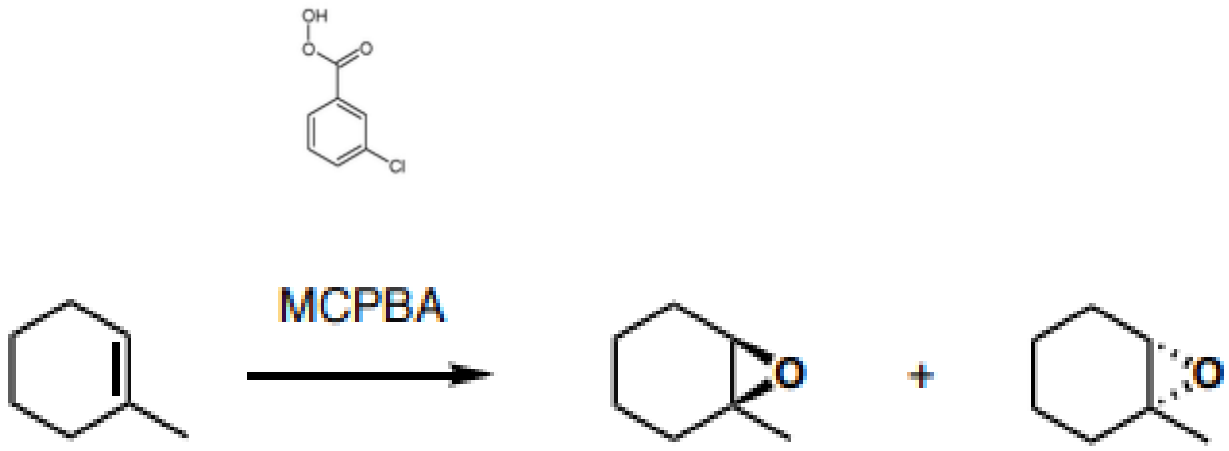
The stereoisomers obtained as products depend on the mechanism of the reaction.

Four Stereoisomers are Obtained if the Reaction Forms a Carbocation Intermediate



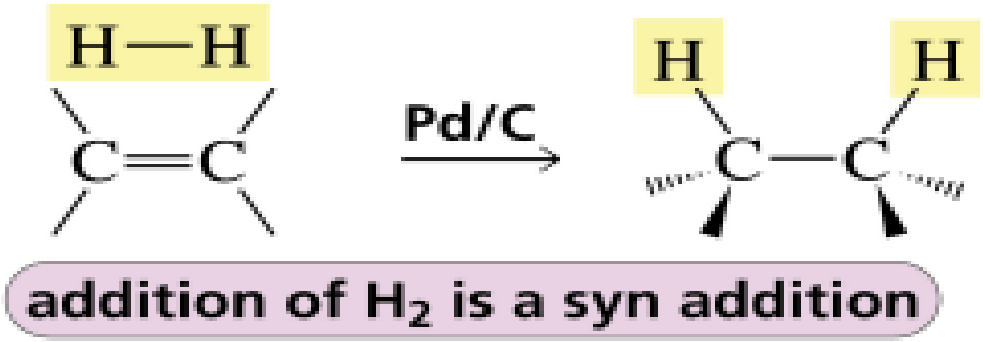
The stereoisomers obtained as products depend on the mechanism of the reaction.

Epoxidation: syn or anti addition?



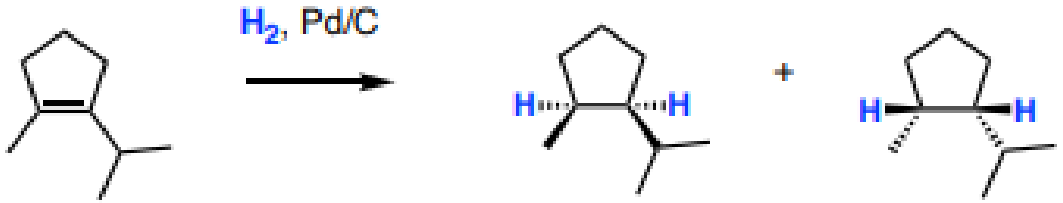
only syn addition

The Stereochemistry of Hydrogen Addition

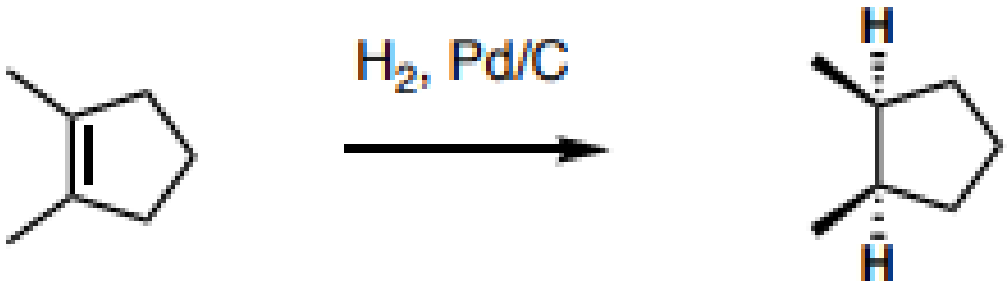


only syn addition

Syn H_2 Addition Forms Only the Cis Stereoisomers..



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



Thank you for your attention