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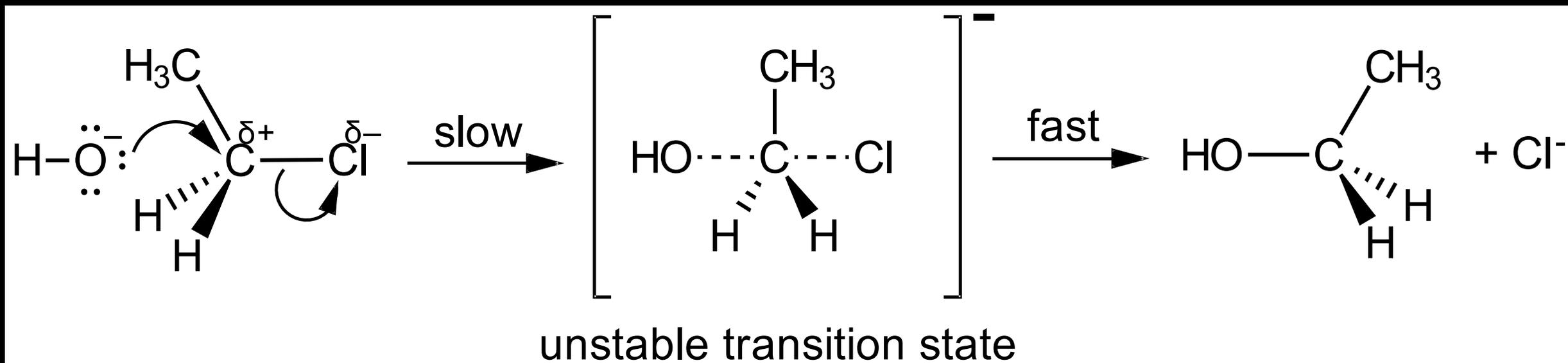
Tutorials for IB Chemistry

S_N2 mechanism

Nucleophilic substitution reactions

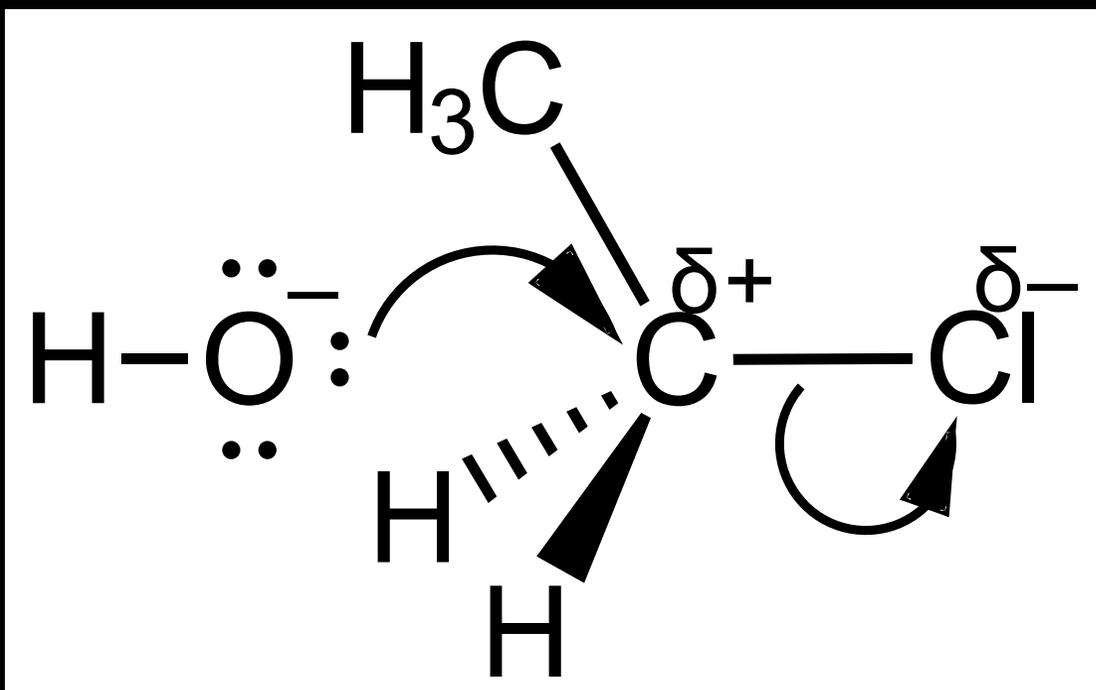
S_N2 - nucleophilic bimolecular substitution reaction.
It is a one-step reaction that involves the formation of an unstable transition state.

Primary halogenoalkanes undergo S_N2 reactions.



Nucleophilic substitution reactions

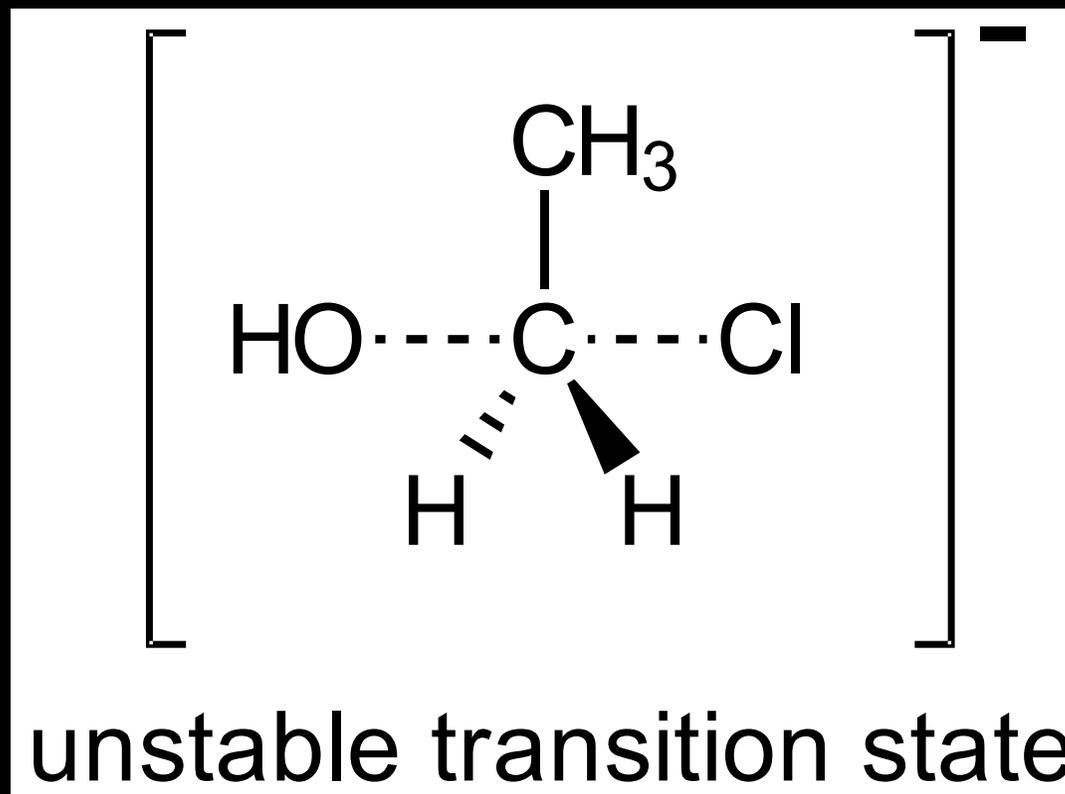
nucleophile
(OH⁻)



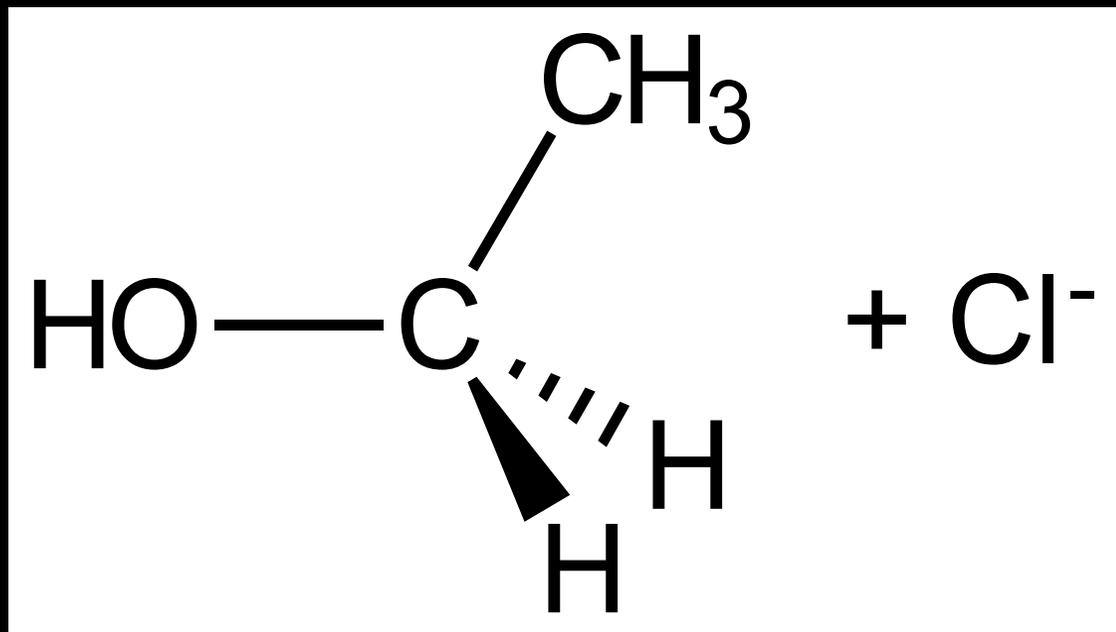
leaving
group (Cl⁻)

The nucleophile attacks on the opposite side of the leaving group (backside attack).

Nucleophilic substitution reactions

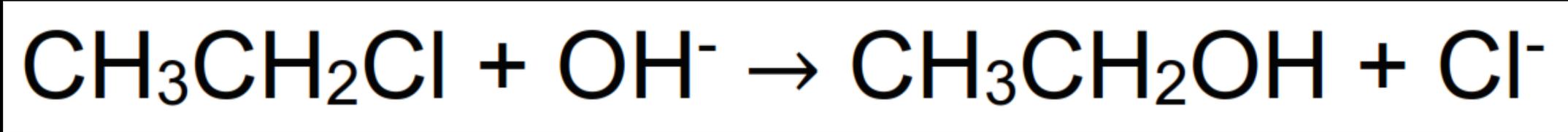
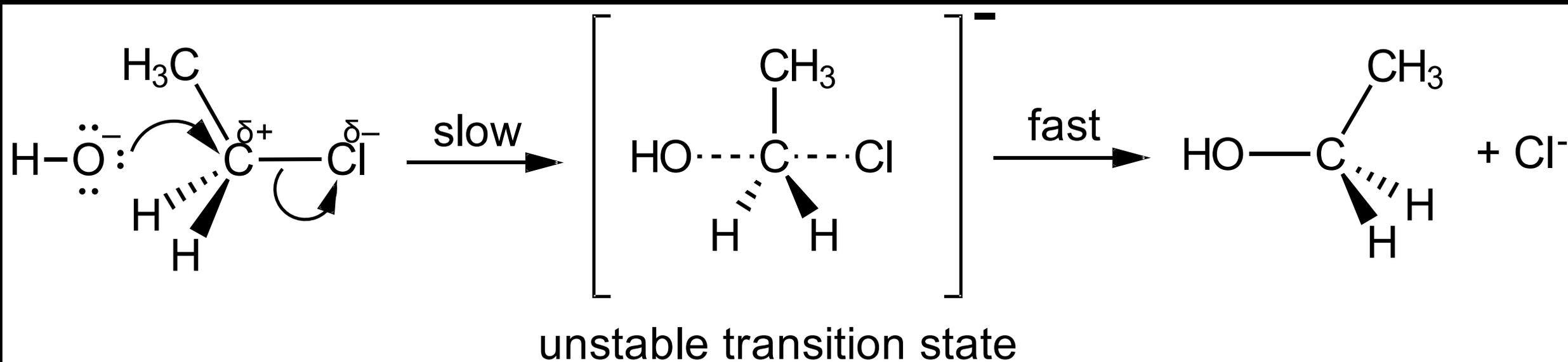


An unstable transition state is formed in which the carbon is weakly bonded to both the halogen and the nucleophile.



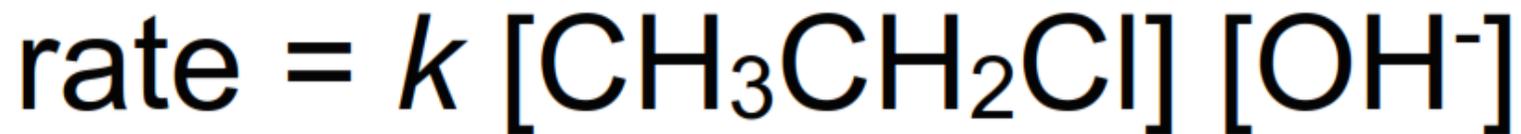
The carbon to halogen bond breaks heterolytically. The backside attack by the nucleophile causes inversion of the atoms around the carbon atom (S_N2 reaction is stereospecific).

Nucleophilic substitution reactions



The reaction conditions are warm with aqueous NaOH

The S_N2 reaction is bimolecular; the rate-determining step (slow step) depends on both the concentration of the halogenoalkane and the nucleophile.



The S_N2 mechanism is favoured by polar, aprotic solvents.

Aprotic solvents are not able to form hydrogen bonds as they lack O-H or N-H bonds.

Suitable solvents include propanone $(CH_3)_2CO$ and ethanenitrile (CH_3CN) .

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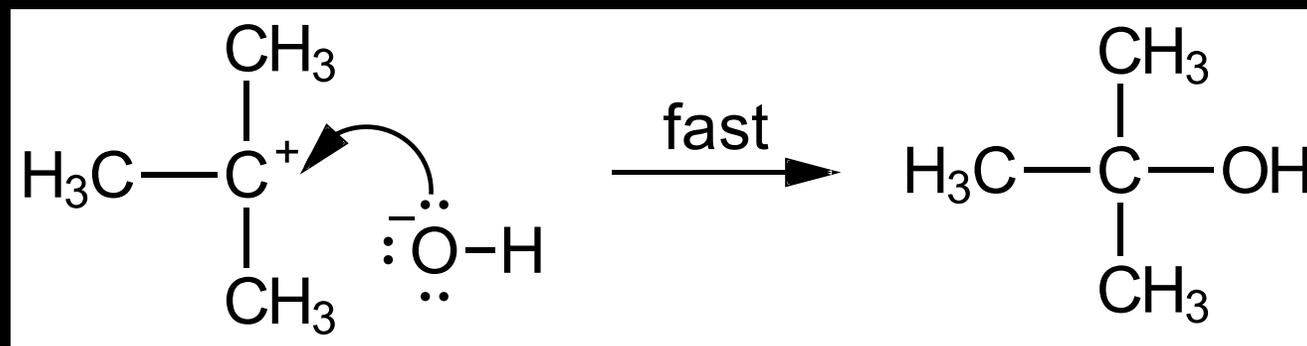
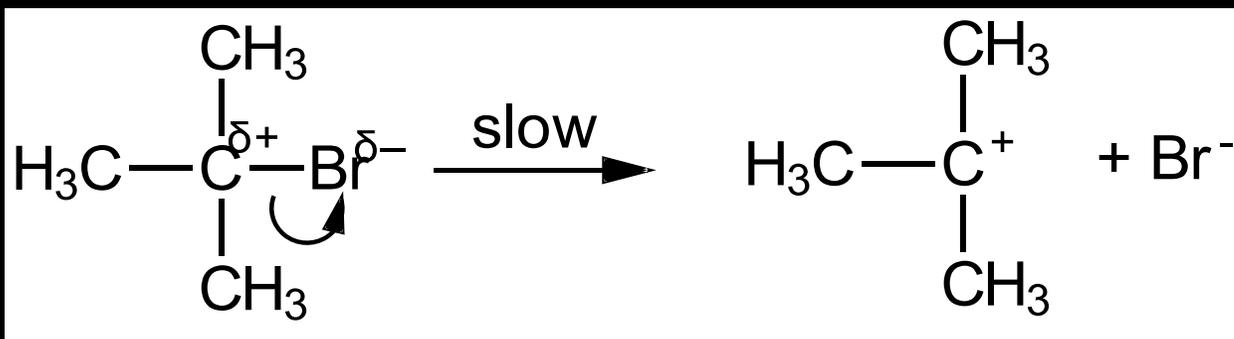
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S_N1 mechanism

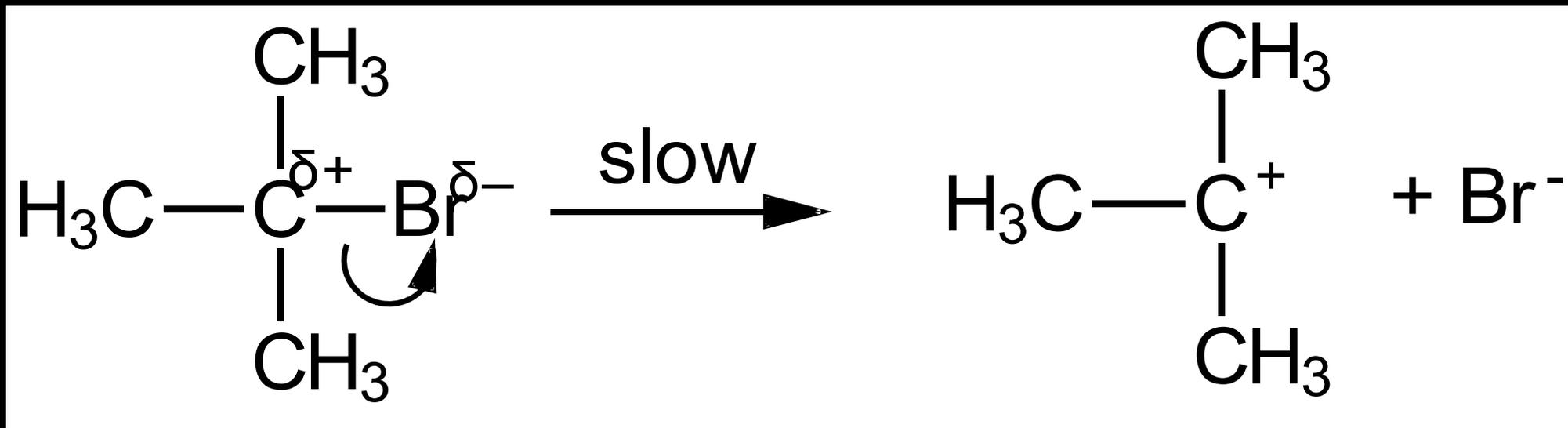
Nucleophilic substitution reactions

S_N1 - nucleophilic unimolecular substitution reaction.
It is a two-step reaction that involves the formation of a carbocation intermediate.

Tertiary halogenoalkanes undergo S_N1 reactions.



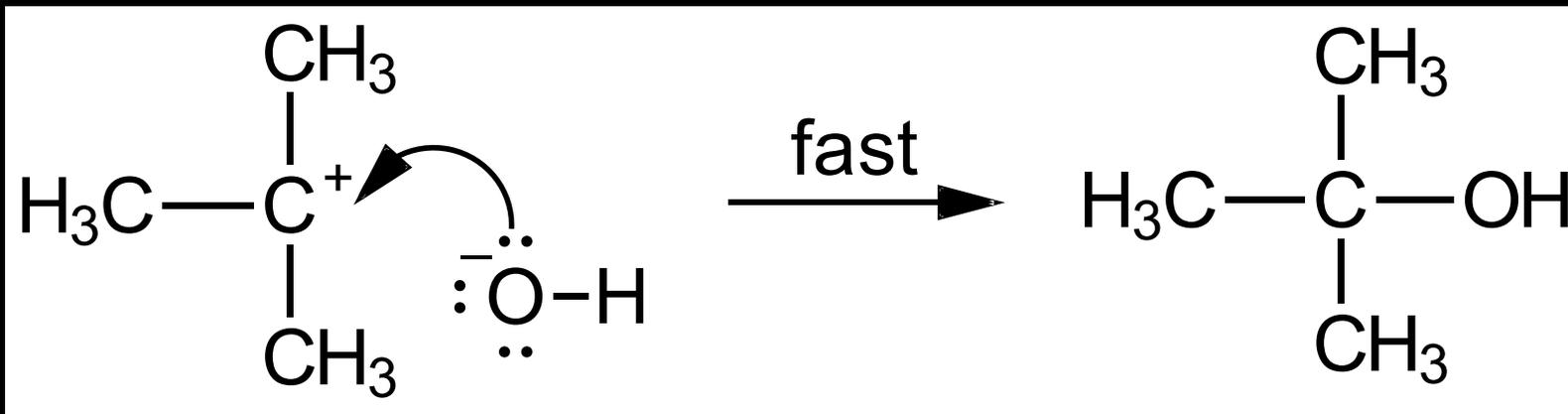
Nucleophilic substitution reactions



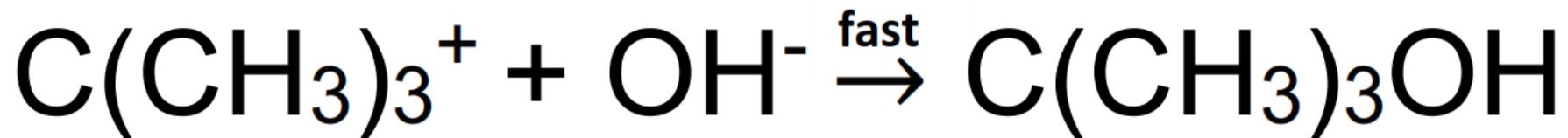
The presence of the 3 alkyl groups around the carbon – halogen bond make it difficult for an incoming group to attack this carbon (steric hindrance).

The C-Br bond breaks heterolytically forming a carbocation intermediate.

Nucleophilic substitution reactions



In the second step, the nucleophile attacks the carbocation, forming a tertiary alcohol.



The reaction is unimolecular; the rate-determining step (slow step) depends on the concentration of the halogenoalkane only.



The S_N1 mechanism is favoured by polar, protic solvents.

Protic solvents are able to form hydrogen bonds as they have O-H or N-H bonds.

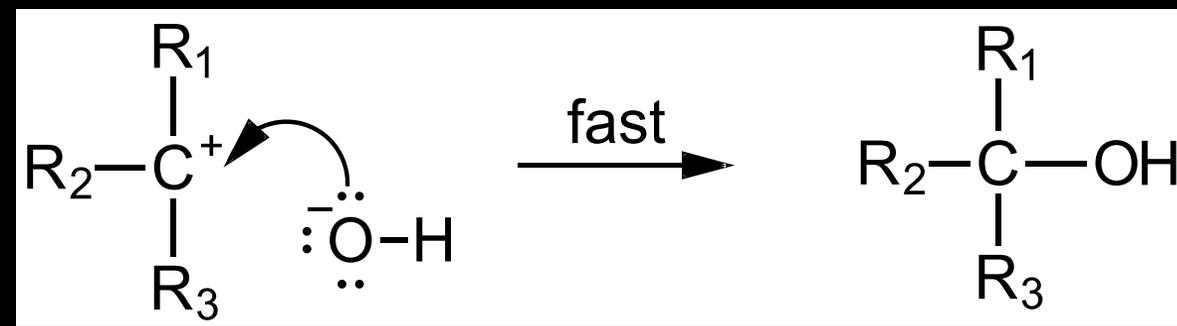
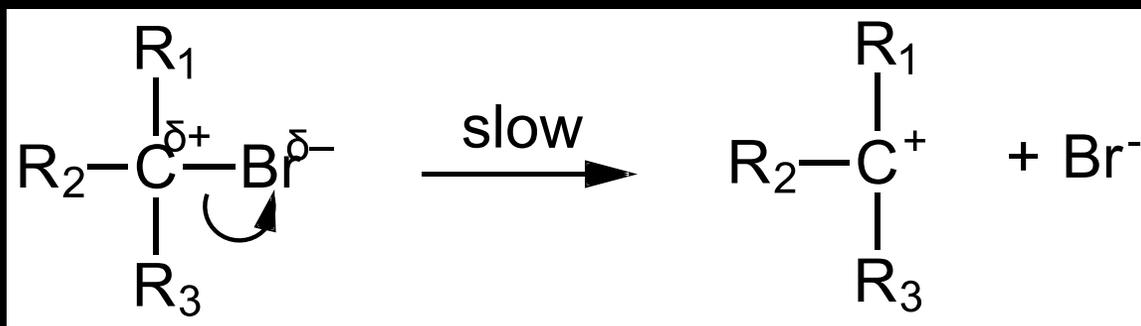
Suitable solvents include water, alcohols and carboxylic acids.

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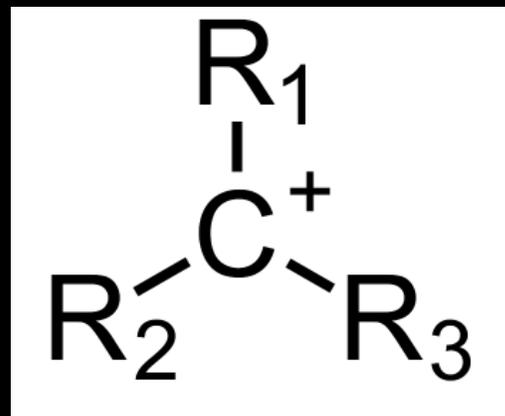
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**Stereochemistry of S_N
reactions**

The S_N1 mechanism involves the formation of a carbocation intermediate.

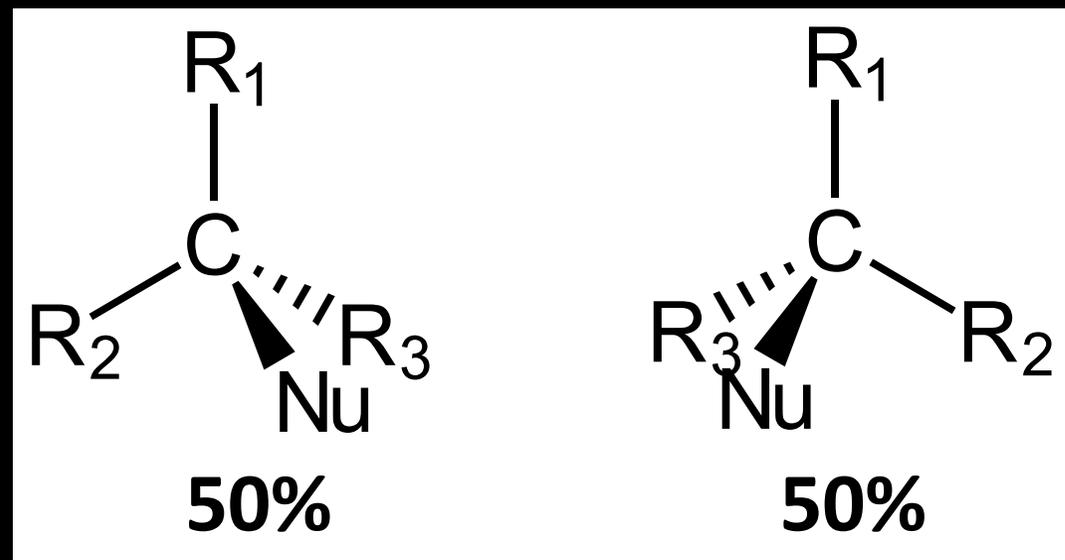
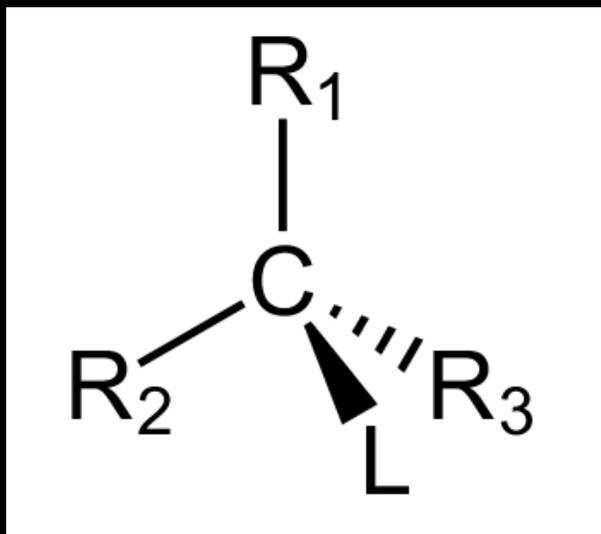
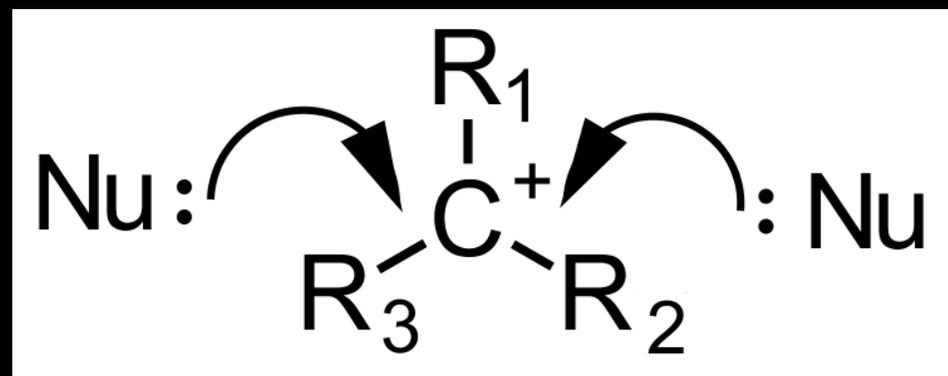


The carbocation formed is sp² hybridised with a trigonal planar geometry.



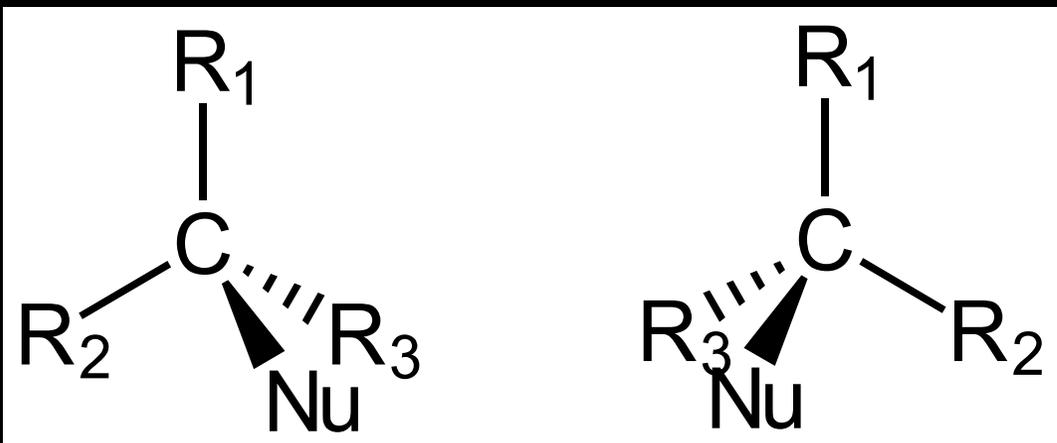
Stereochemistry of S_N reactions

The nucleophile can attack on either side of the carbocation intermediate.



The product can have the same stereochemical configuration as the reactant (retention) or opposite configuration (inversion).

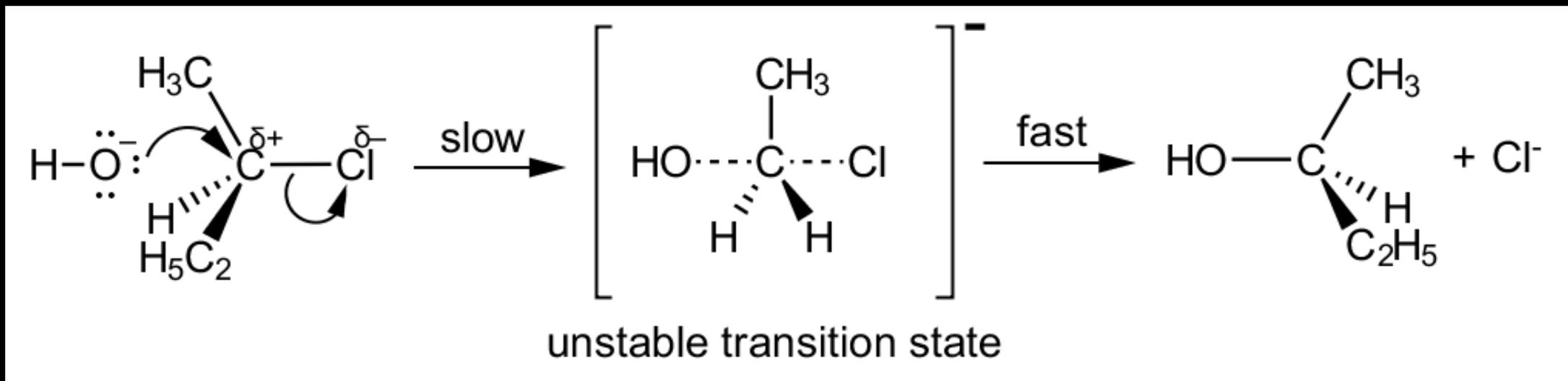
Retention



Inversion

This produces a racemic mixture with equal amounts of both enantiomer (optically inactive).

The S_N2 mechanism is stereospecific – the backside attack by the nucleophile produces inversion of the configuration.



The inversion of the configuration produces only one enantiomer (optically active).

The S_N1 reaction produces a racemic mixture of the two enantiomers which is optically inactive. It has no effect on the plane of plane-polarised light.

The S_N2 reaction is stereospecific with inversion of the configuration – the product is optically active.

It will rotate the plane of plane-polarised light.

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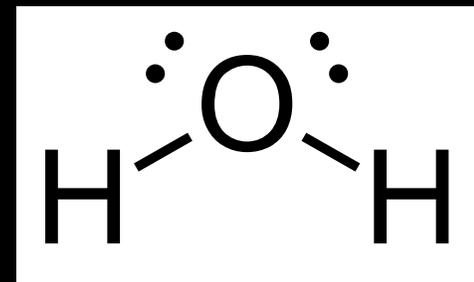
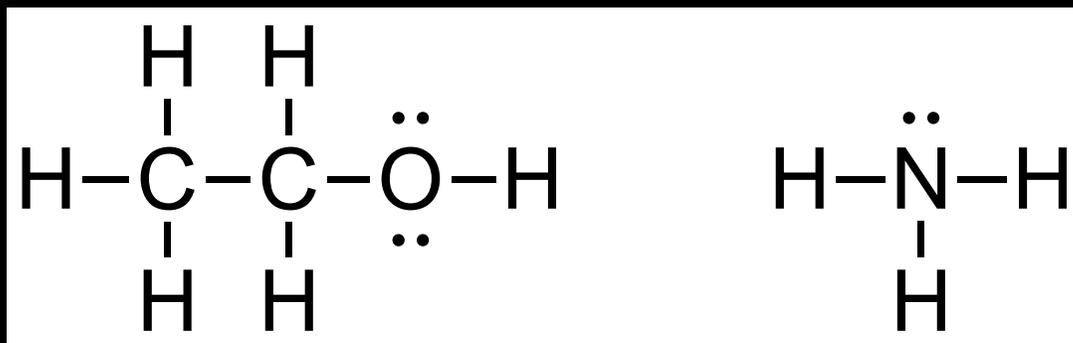
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Choice of solvent for

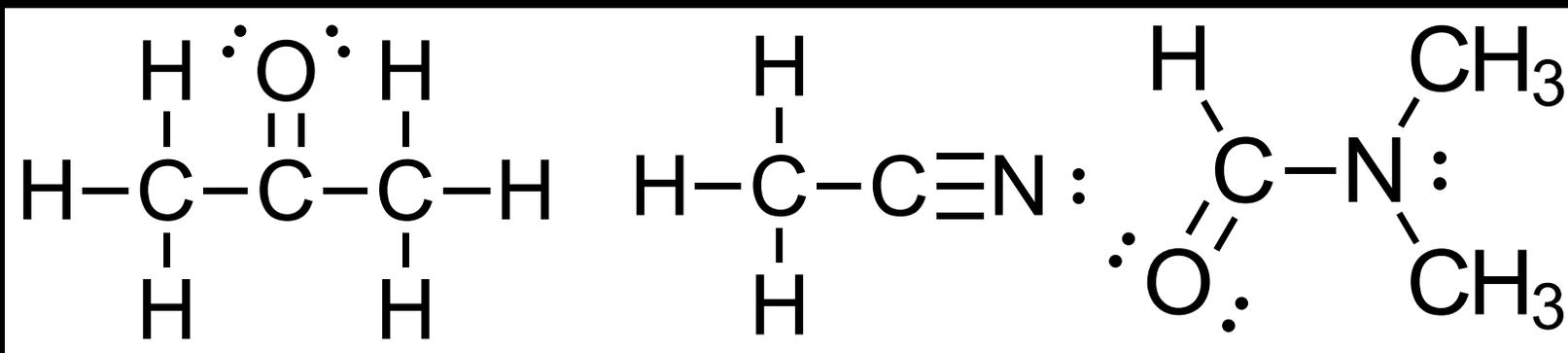
S_N1/S_N2

S_N1 / S_N2 choice of solvent

Polar protic solvents contain O-H or N-H bonds and are able to form hydrogen bonds.

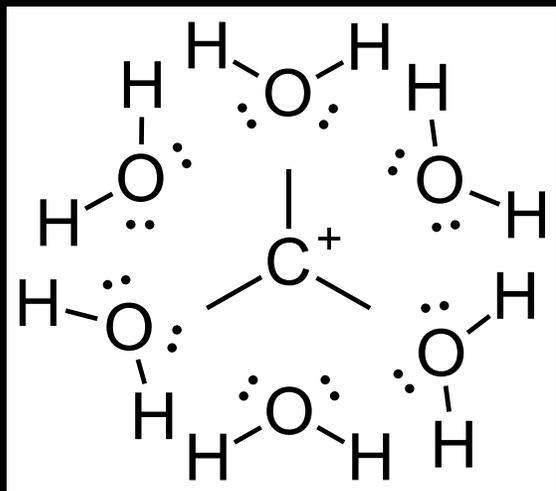


Polar aprotic solvents do not contain O-H or N-H bonds and are unable to form hydrogen bonds.

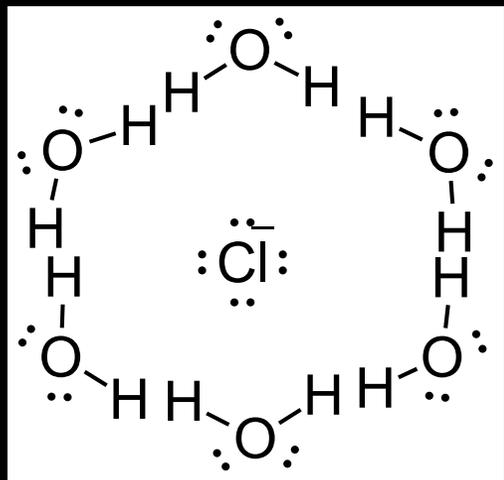


S_N1 / S_N2 choice of solvent

S_N1 reactions are favoured by the use of polar protic solvents.



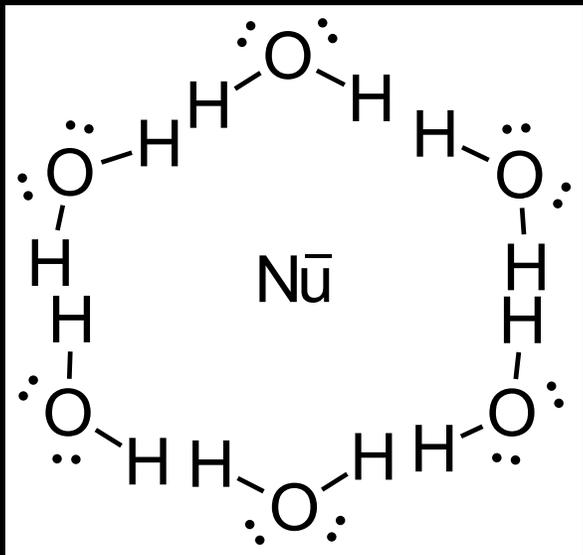
The solvent molecules solvate the carbocation intermediate through ion-dipole interactions. This has the effect of stabilising the carbocation intermediate.



The solvent also stabilises the anion (the leaving group) by forming hydrogen bonds, which also favours S_N1 reactions.

S_N1 / S_N2 choice of solvent

S_N2 reactions are favoured by the use of polar aprotic solvents.



Polar protic solvents solvate the nucleophile (due to hydrogen bonding), reducing its reactivity.

Polar aprotic solvents do not solvate the nucleophile, maintaining its reactivity – this favours the S_N2 reaction.

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**Comparison of S_N1
and S_N2 reactions**

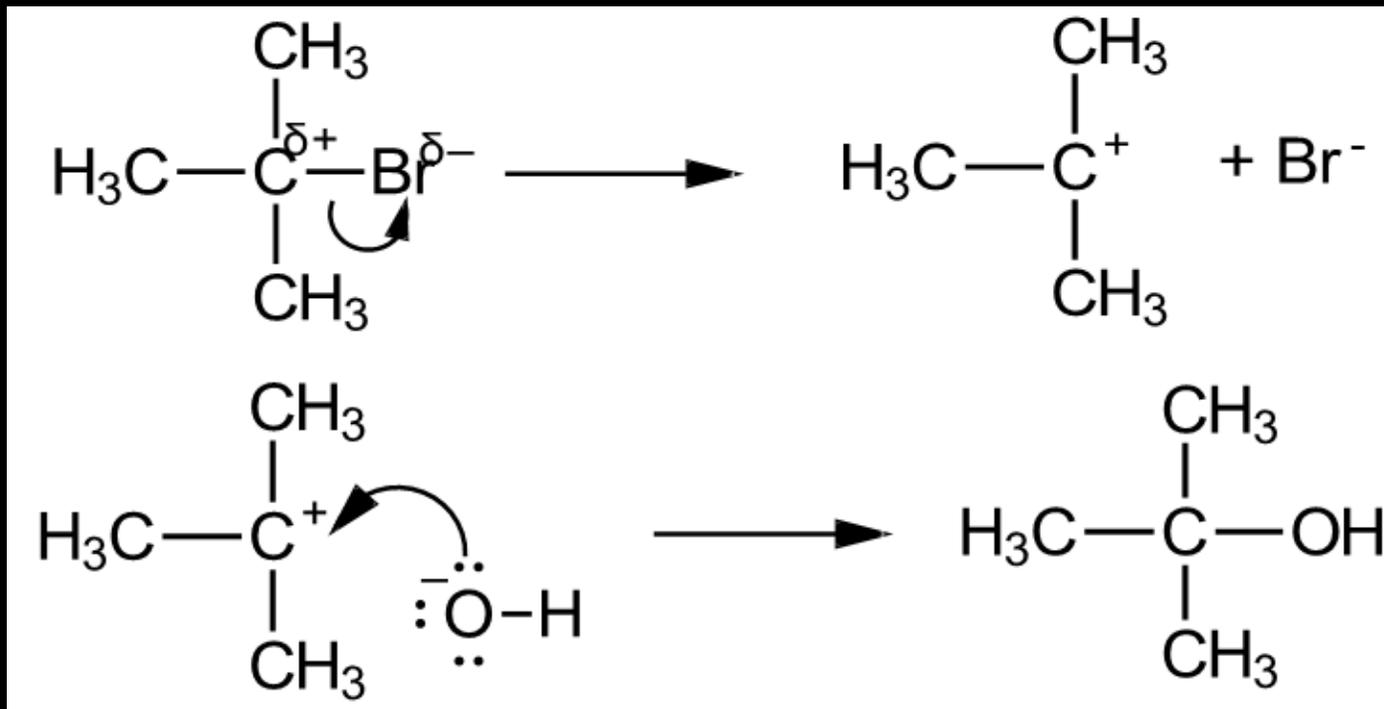
	S_N1	S_N2
Class of halogenoalkane	Tertiary	Primary
Number of steps	Two-step	One-step
Transition state or reaction intermediate	Carbocation intermediate	Transition state
Type of solvent	Polar protic	Polar aprotic
Type of bond fission	Heterolytic	Heterolytic

Nucleophilic substitution reactions

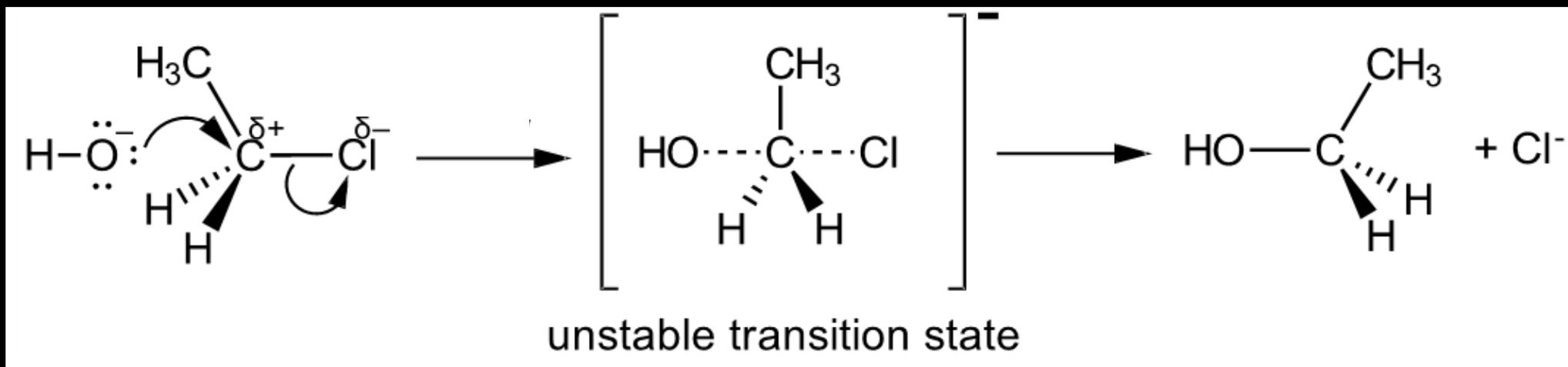
	S_N1	S_N2
Molecularity	Unimolecular	Bimolecular
Example rate expression	$\text{rate} = k[(\text{CH}_3)_3\text{CBr}]$	$\text{rate} = k[\text{CH}_3\text{CH}_2\text{Br}][\text{OH}^-]$
Relative rate of reaction	$3^\circ > 2^\circ > 1^\circ$	$1^\circ > 2^\circ > 3^\circ$
Change in stereochemistry	50/50 mix of enantiomers (racemic mixture - optically inactive)	Inversion of configuration (optically active)

Nucleophilic substitution reactions

S_N1



S_N2



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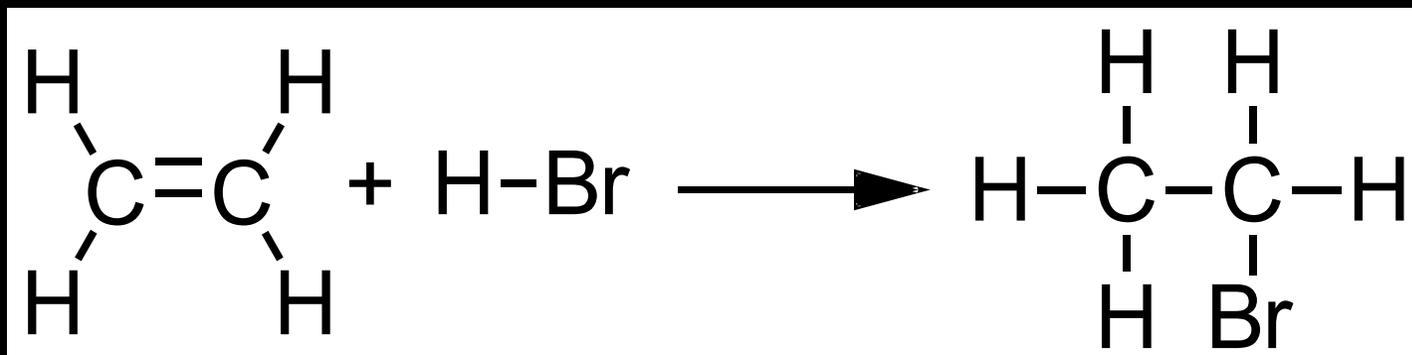
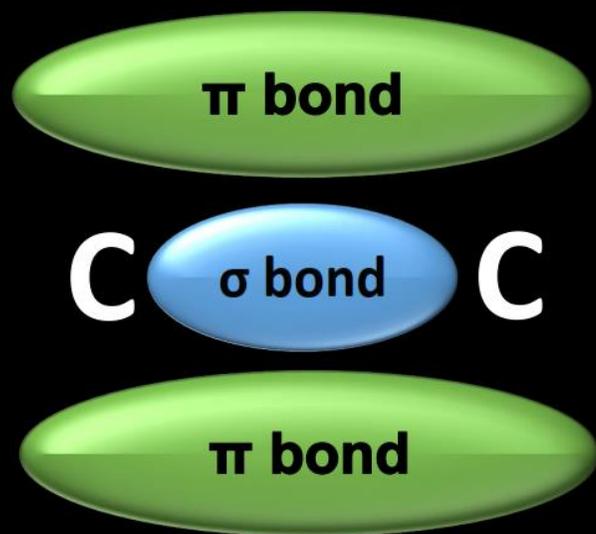
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**Electrophilic addition
reactions**

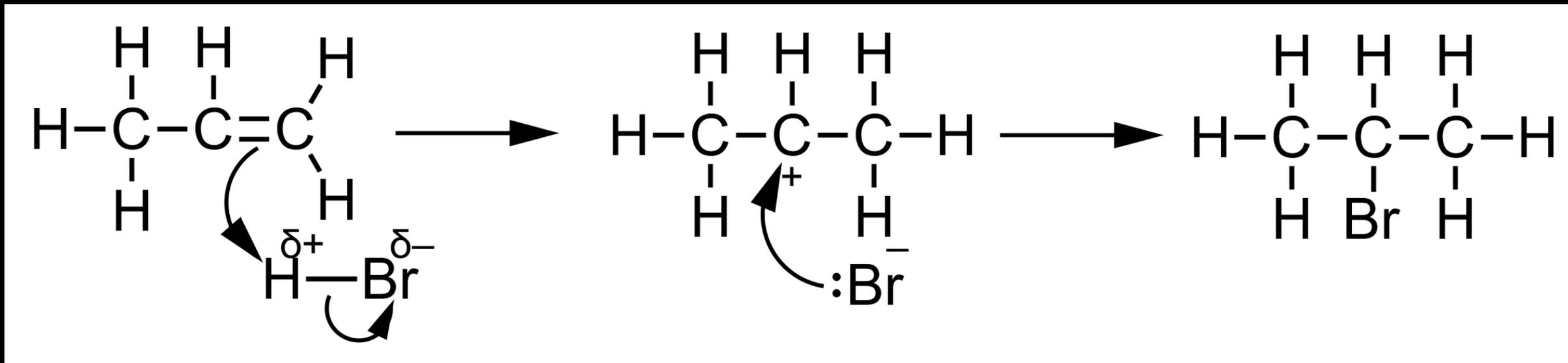
Electrophilic addition reactions

The carbon to carbon double bond in an alkene has a region of high electron density above and below the plane of the molecule.

Because of this high electron density, the π bond is attractive to electrophiles (species that are electron deficient).



Electrophilic addition reactions

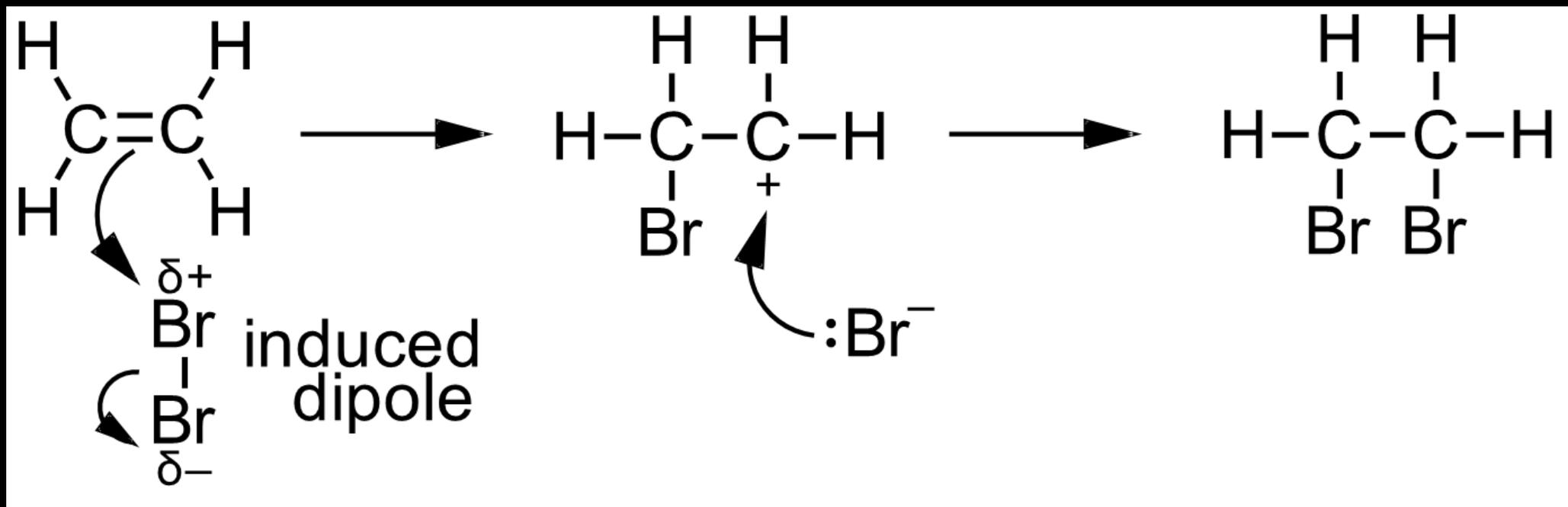


H-Br is a polar molecule; the hydrogen atom is attracted to the C=C double bond.

The H-Br bond breaks heterolytically forming a bromide ion. At the same time, the H atom bonds to one of the C atoms forming a carbocation.

The carbocation then combines with the Br^- ion forming bromoethane.

Electrophilic addition reactions

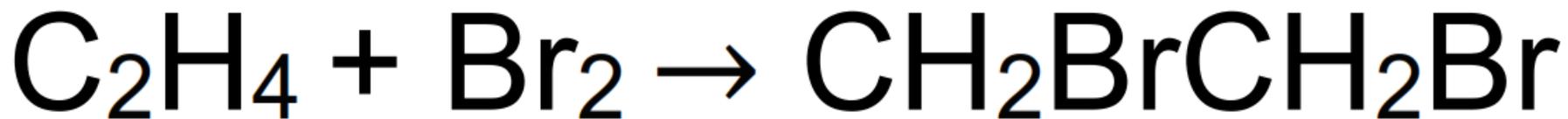
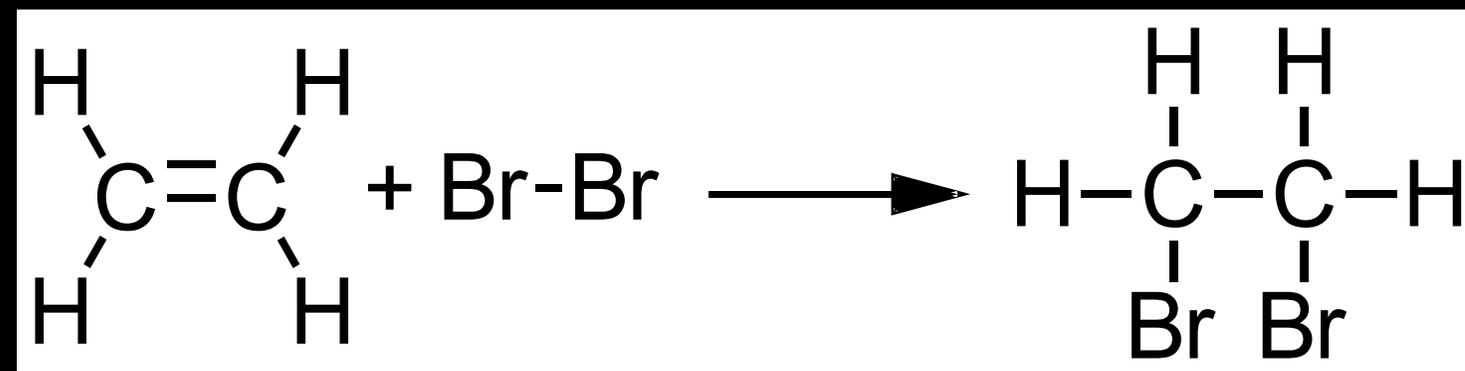
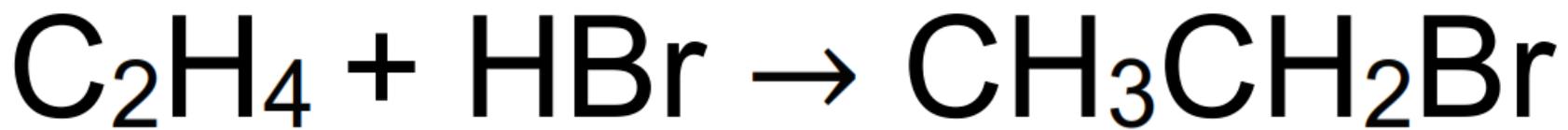
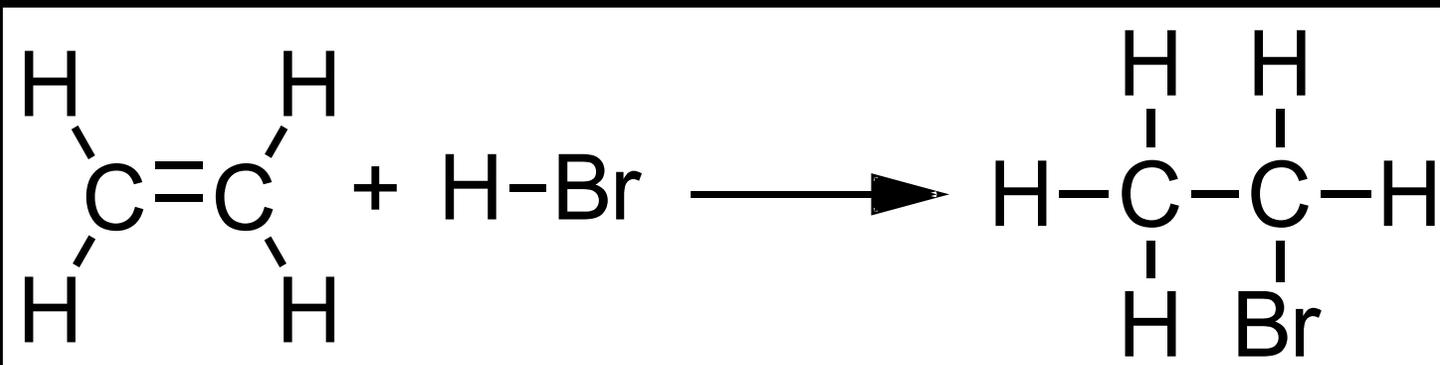


The Br atom nearest the double bond has a positive (induced) dipole.

The bromine molecule breaks heterolytically forming Br^+ and Br^- . The Br^+ bonds to the one of the C atoms forming a carbocation intermediate.

The carbocation then combines with the Br^- forming 1,2-dibromoethane.

Electrophilic addition reactions



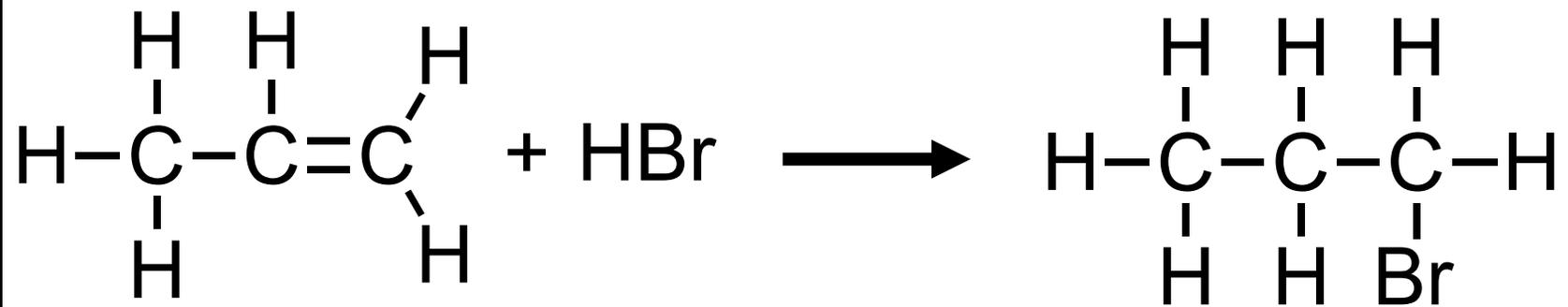
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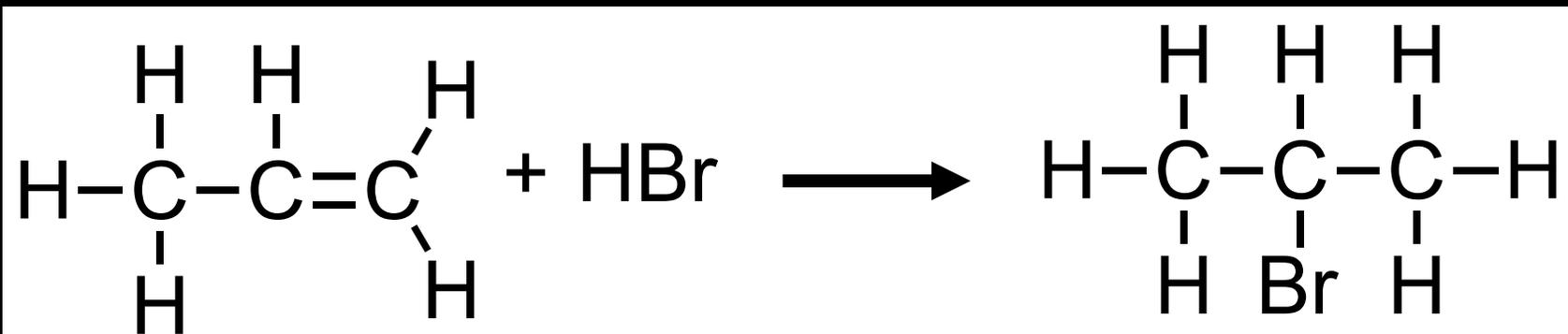
Markovnikov's rule

Markovnikov's rule

When propene (an asymmetrical alkene) reacts with hydrogen bromide, there are two possible products:



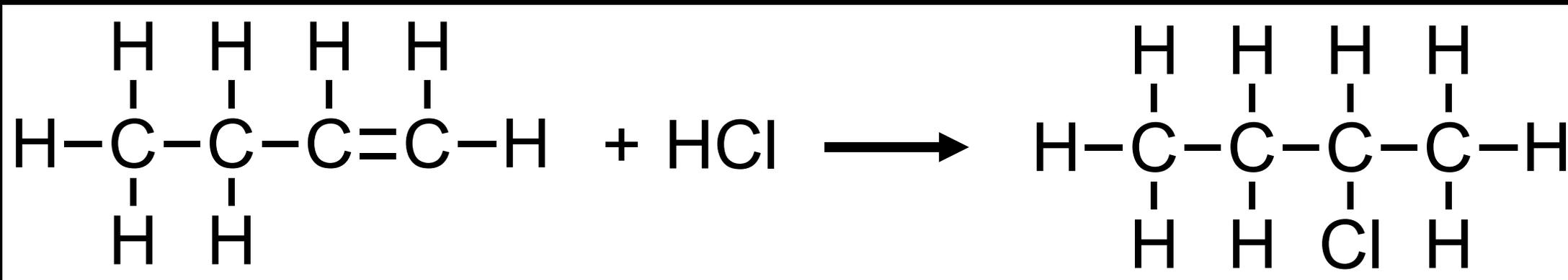
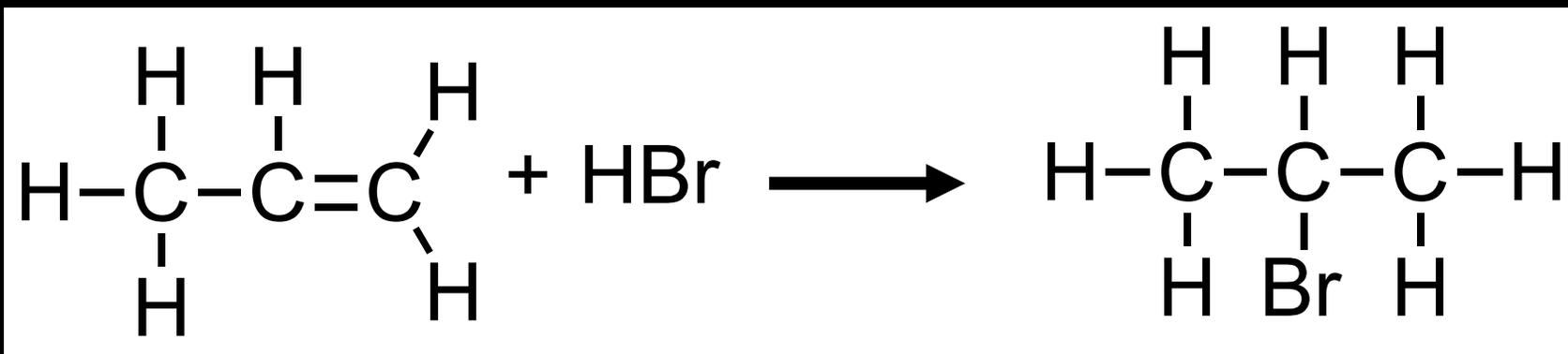
1-bromopropane



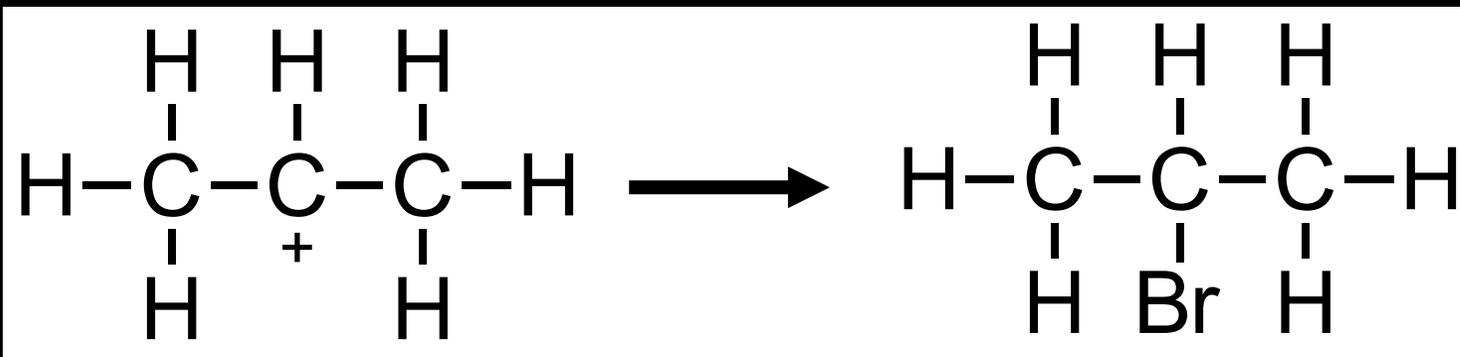
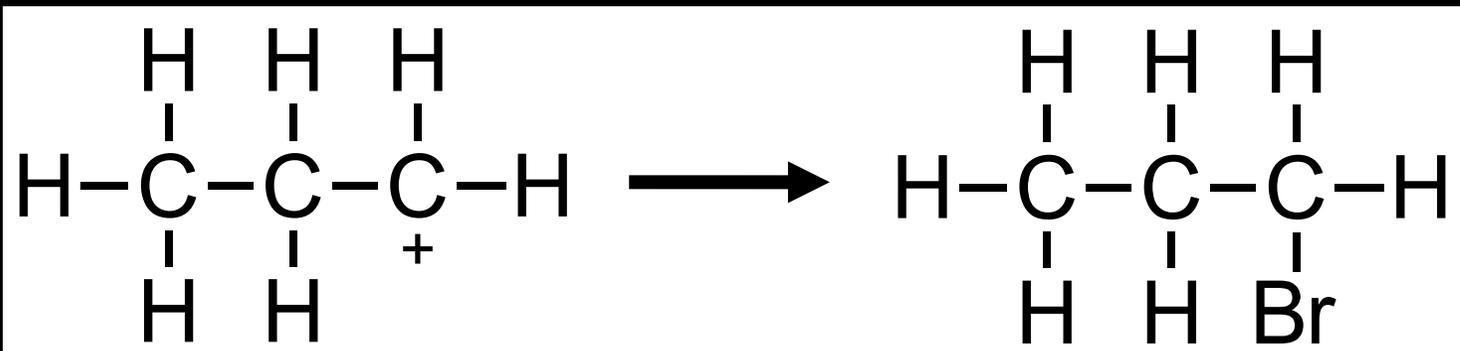
2-bromopropane

Markovnikov's rule

When an asymmetrical alkene reacts with a hydrogen halide, the hydrogen adds to the carbon atom that is already bonded to the greatest number of hydrogens.



Markovnikov's rule

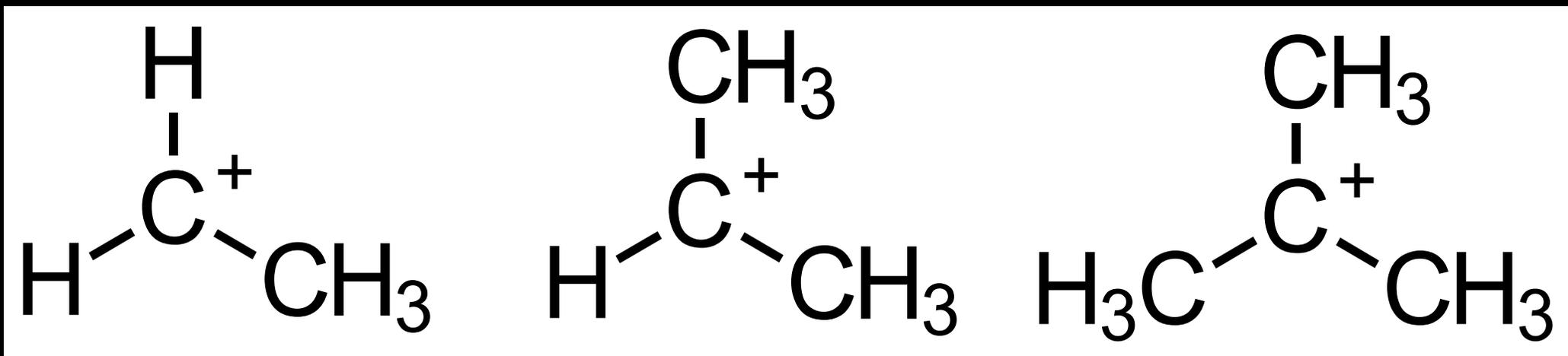


The primary carbocation is less stable than the secondary carbocation.

The order of stability is:
 $1^\circ < 2^\circ < 3^\circ$

The major product will be 2-bromopropane because of the greater stability of the secondary carbocation.

Markovnikov's rule



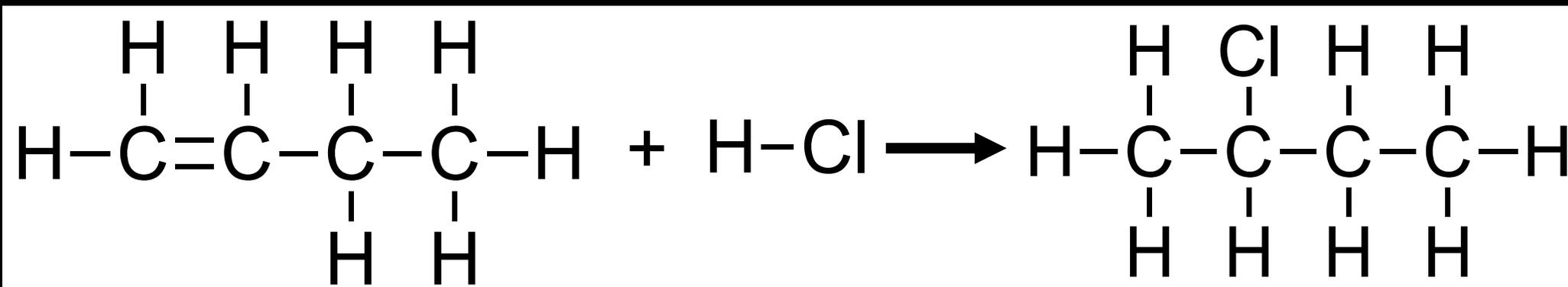
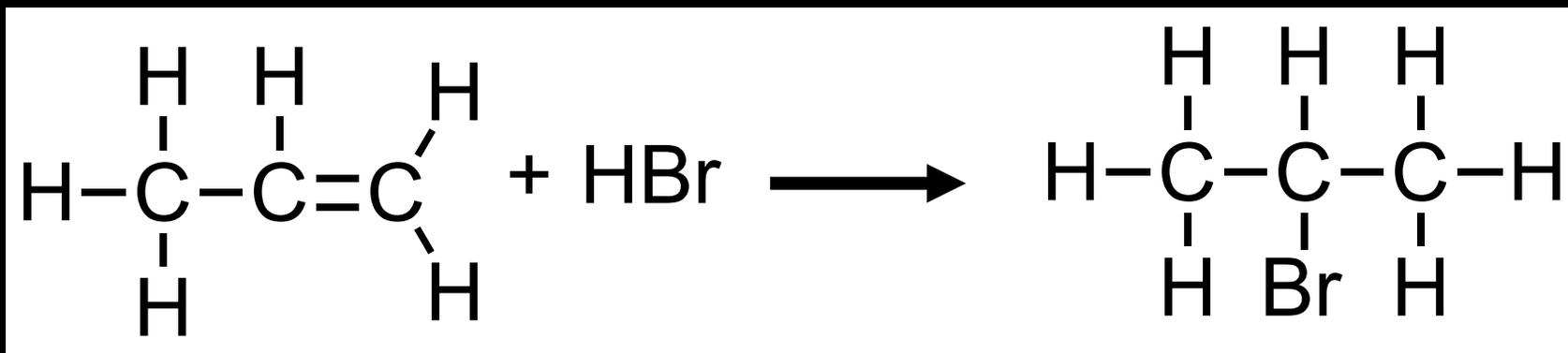
Increasing stability 

Carbocations are stabilised by electron-donating alkyl groups (positive inductive effect).

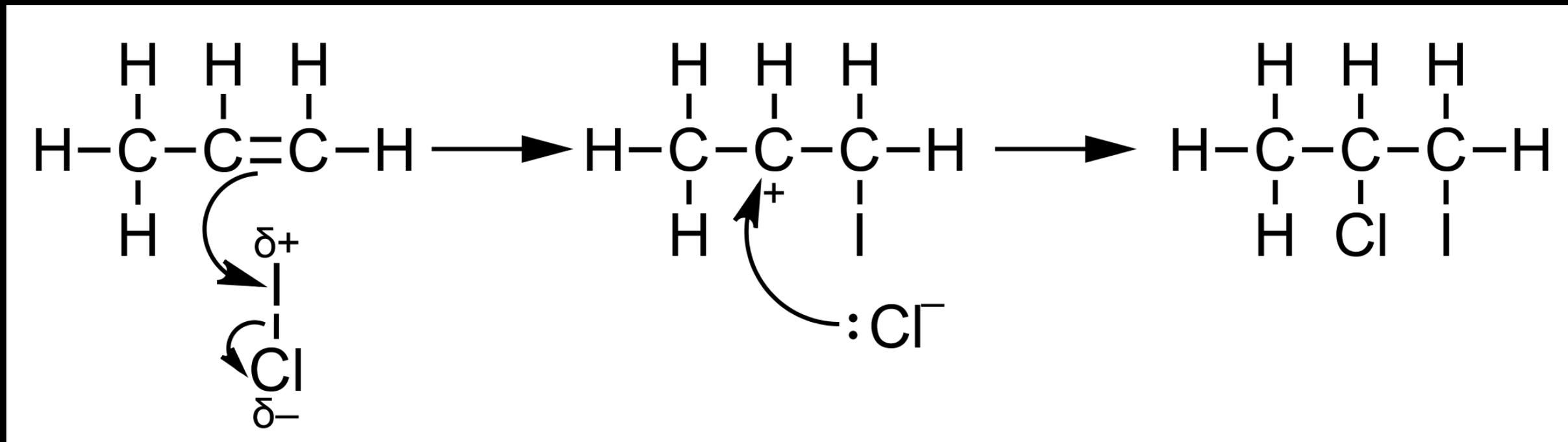
The more substituted the carbocation, the greater the stability.

Markovnikov's rule

When an asymmetrical alkene reacts with a hydrogen halide, the hydrogen adds to the carbon that is already bonded to the greatest number of hydrogens.



Markovnikov's rule



When an unsymmetrical alkene reacts with an interhalogen (I-Cl), the electrophilic portion of the molecule bonds to the carbon that is bonded to the greatest number of hydrogens.

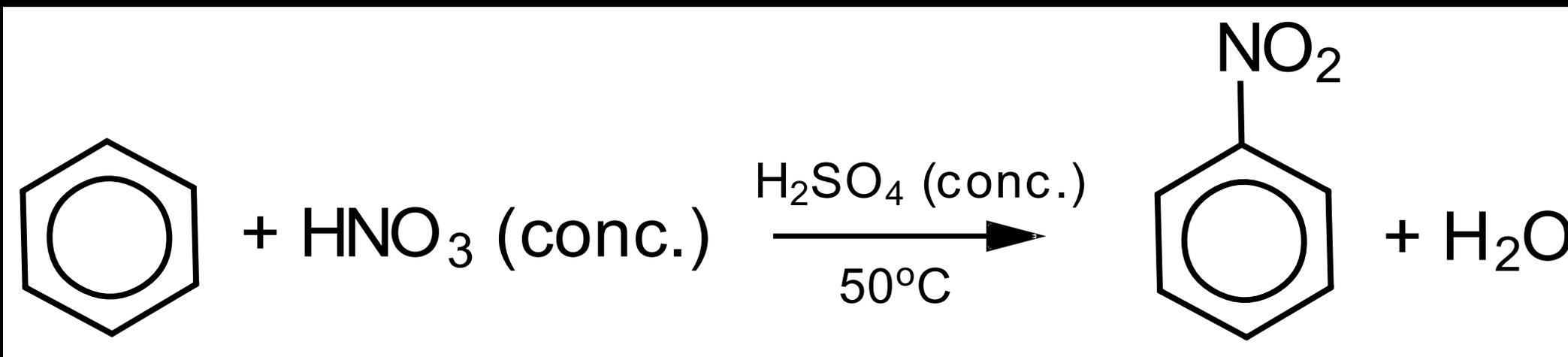
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Nitration of benzene

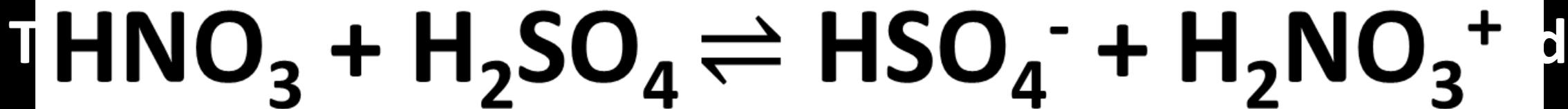
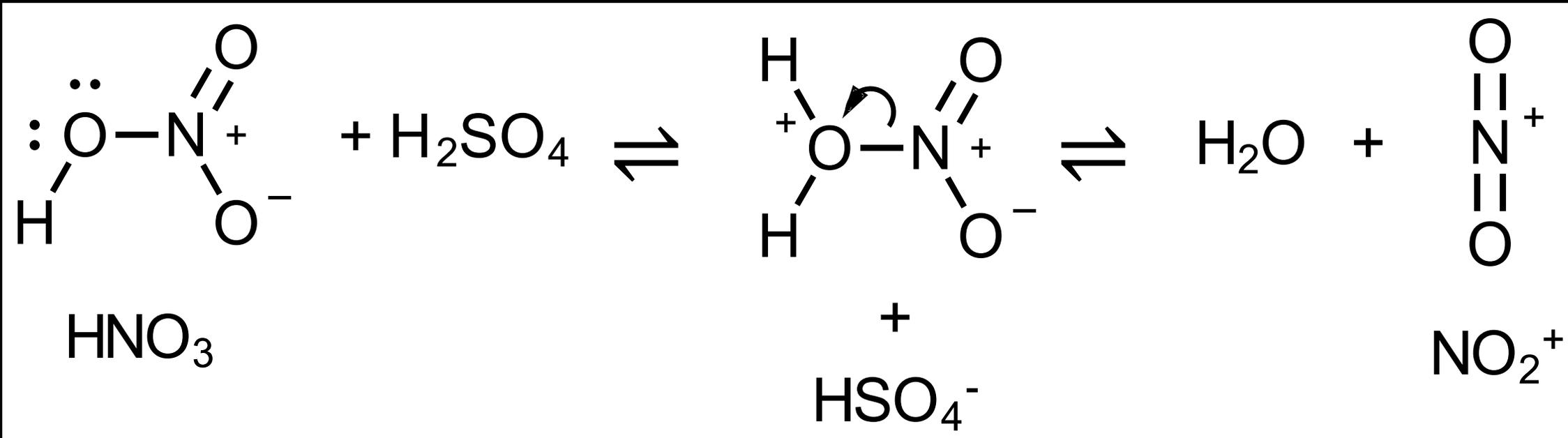
Nitration of benzene

Benzene reacts with a mixture of concentrated nitric acid (HNO_3) and concentrated sulfuric acid (H_2SO_4) to form nitrobenzene ($\text{C}_6\text{H}_5\text{NO}_2$) and water.



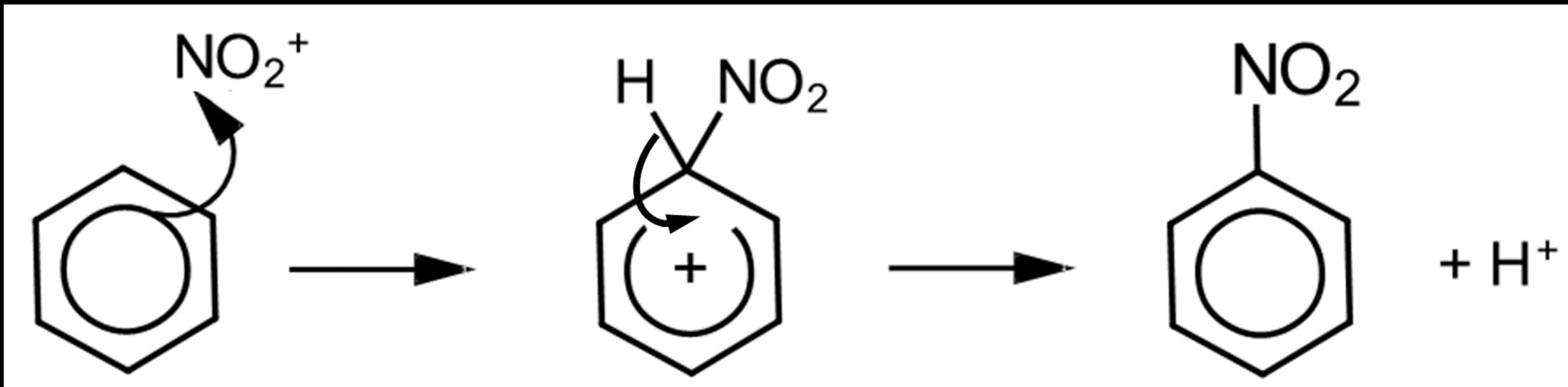
The concentrated H_2SO_4 acts as a catalyst.
This is an electrophilic substitution reaction.

Nitration of benzene



The sulfuric acid protonates the nitric acid, which then loses a molecule of water to form the nitronium ion (NO₂⁺).

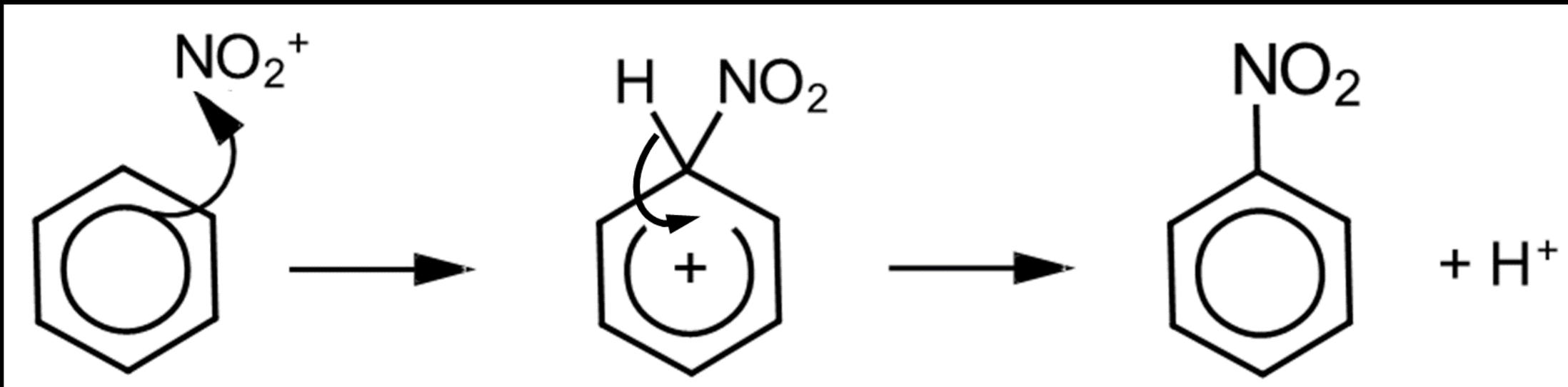
Nitration of benzene



NO_2^+ is a strong electrophile and is attracted to the delocalized π electron cloud in benzene. It then reacts with the π electrons to form a carbocation intermediate.

The loss of a hydrogen ion (proton) leads to the reformation of the arene ring in the nitrobenzene. The hydrogen ion released reacts with the HSO_4^- to reform the sulfuric acid catalyst.

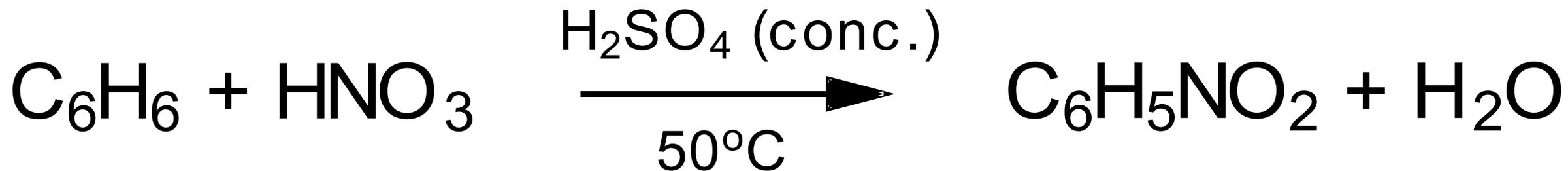
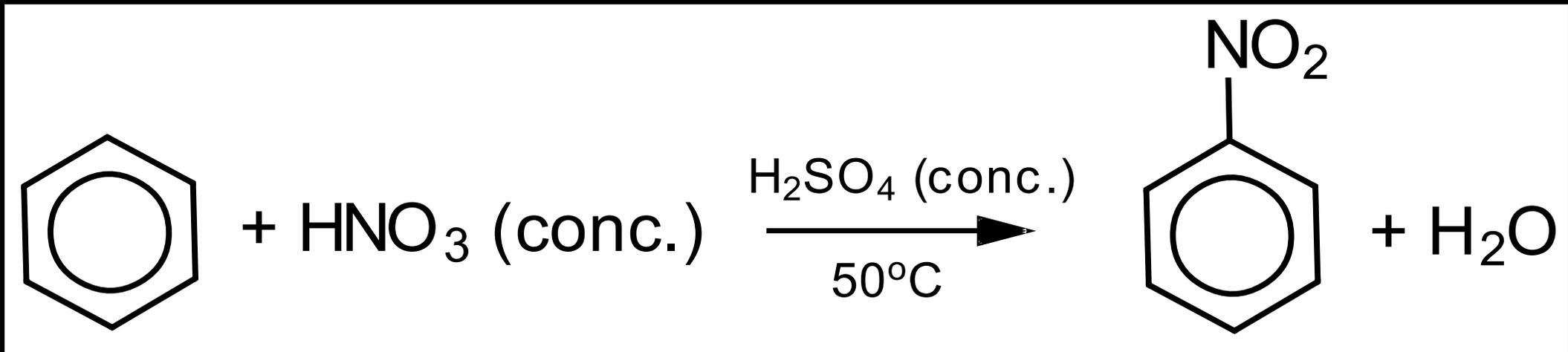
Nitration of benzene



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Nitration of benzene

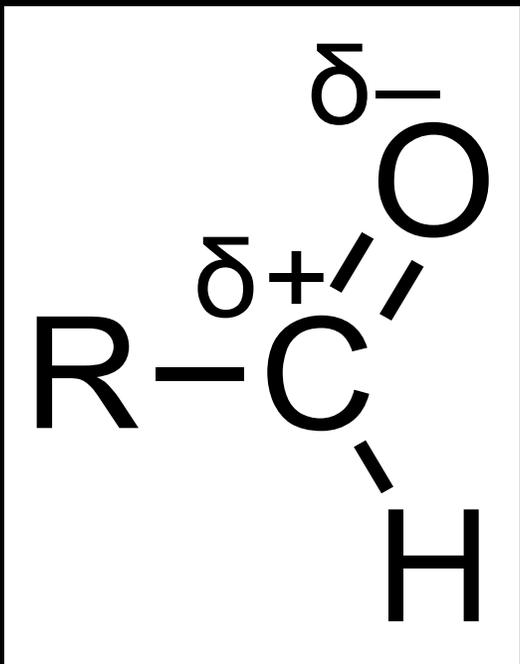


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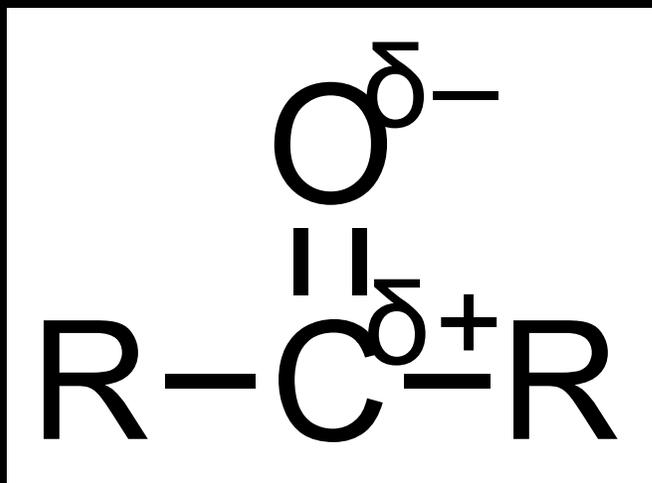
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**Reduction of carbonyl
compounds**

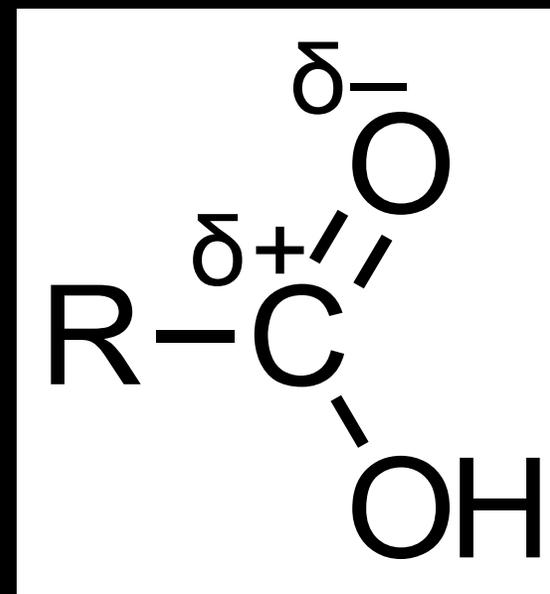
Reduction reactions



aldehydes



ketones

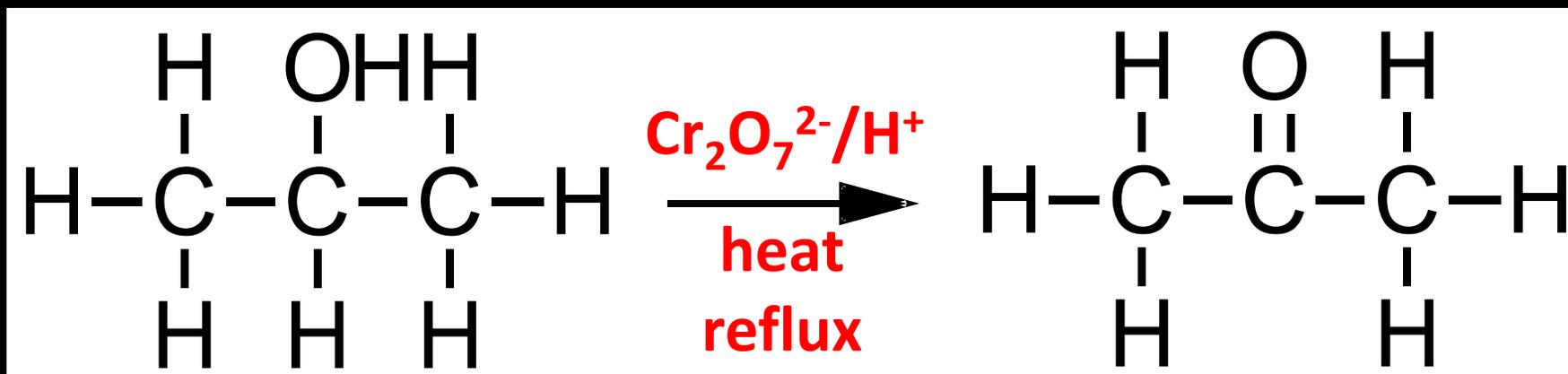
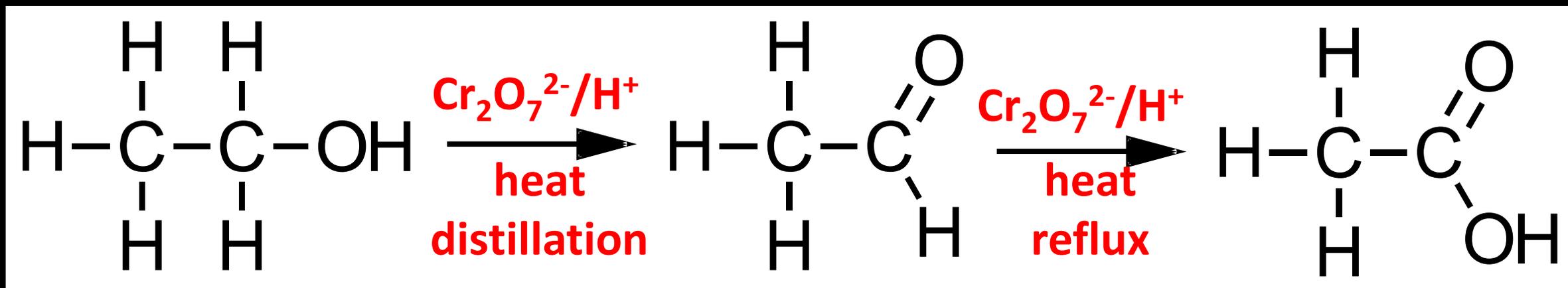


carboxylic acids

The carbon to oxygen bond is a polar bond because of the difference in electronegativity between carbon and oxygen.

Reduction reactions

Primary and secondary alcohols can be oxidized to aldehydes, ketones or carboxylic acids depending on the conditions.



Reduction reactions

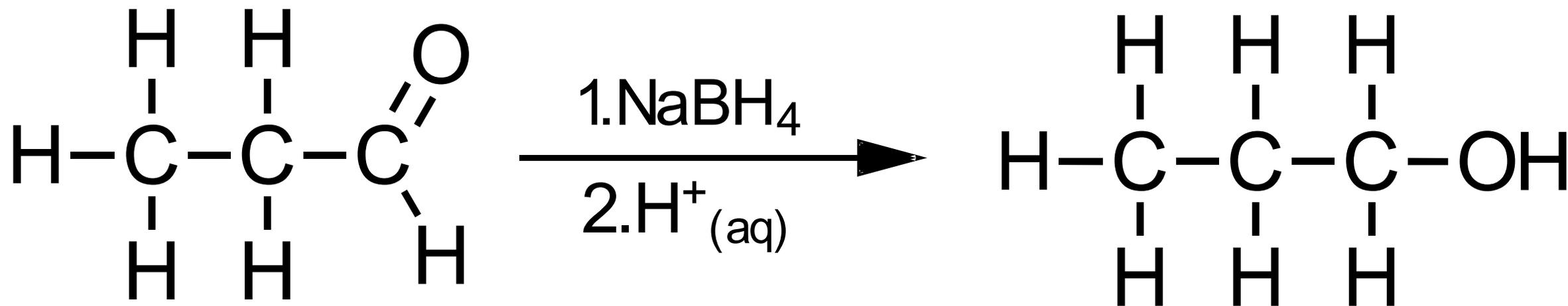
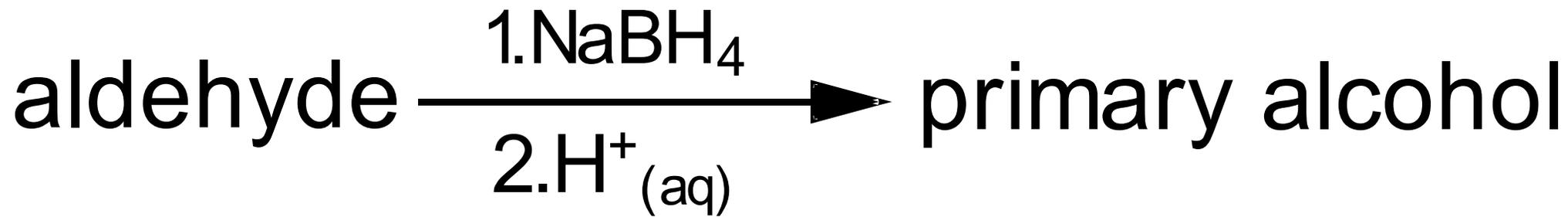
These oxidation reactions can be reversed by using a suitable reducing agent.

Sodium borohydride (NaBH_4), in aqueous or alcoholic solution (protic solvents).

Lithium aluminium hydride (LiAlH_4) in anhydrous conditions such as dry ether (aprotic solvent). The reaction is then acidified to obtain the product.

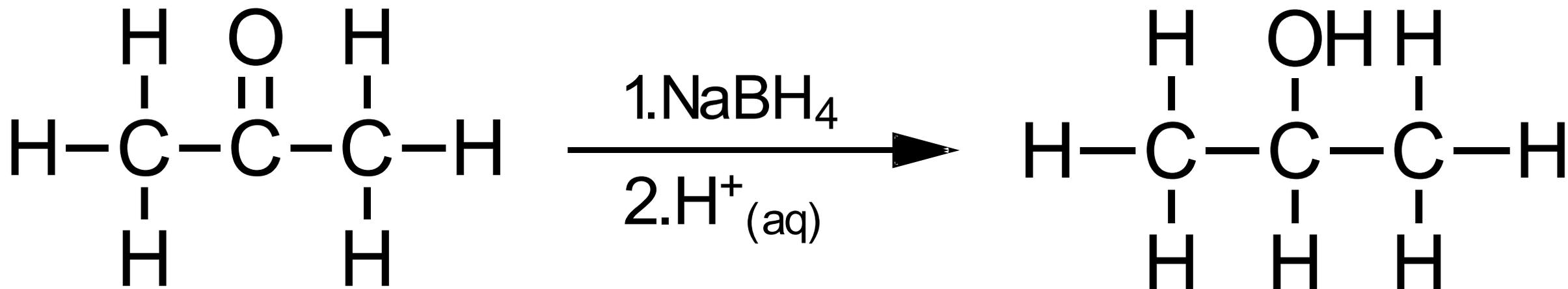
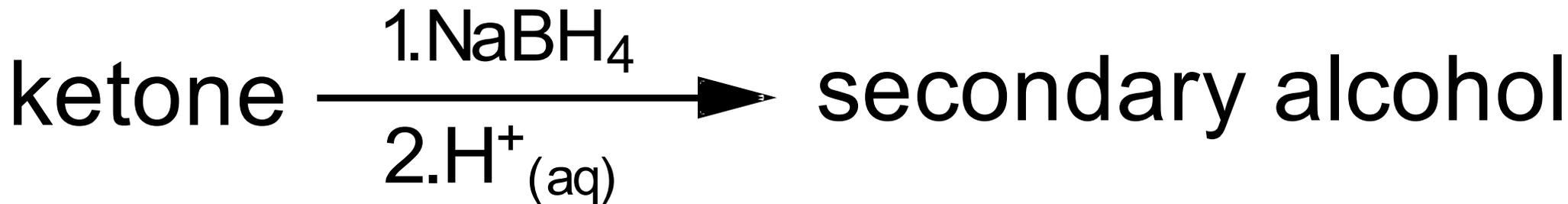
Both these reagents produce the hydride ion (H^-) which acts as a reducing agent undergoing a nucleophilic addition reaction with the electron deficient carbon atom of the carbonyl group.

Reduction reactions



Conditions: heat with NaBH_4 , then acidify.

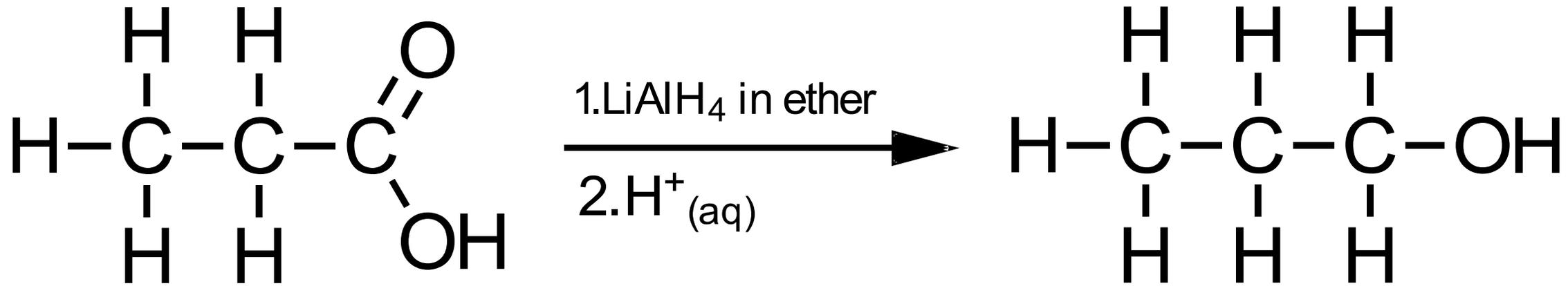
Reduction reactions



Conditions: heat with NaBH_4 , then acidify.

Reduction reactions

carboxylic acid $\xrightarrow[2. H^+ (aq)]{1. LiAlH_4 \text{ in ether}}$ primary alcohol



Conditions: heat with $LiAlH_4$ in dry ether, then acidify ($NaBH_4$ is not a strong enough reducing agent to reduce carboxylic acids).

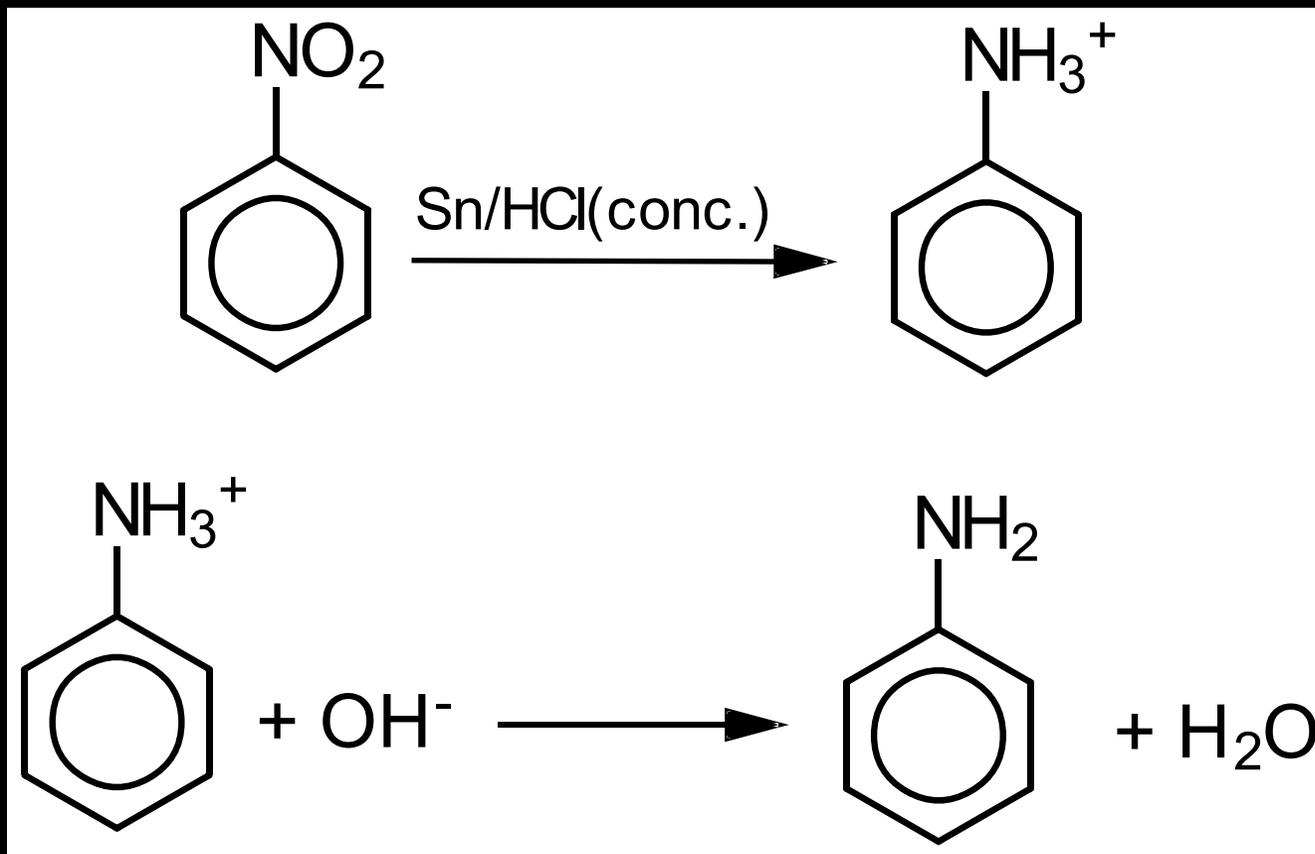
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**Reduction of
nitrobenzene**

Reduction of nitrobenzene

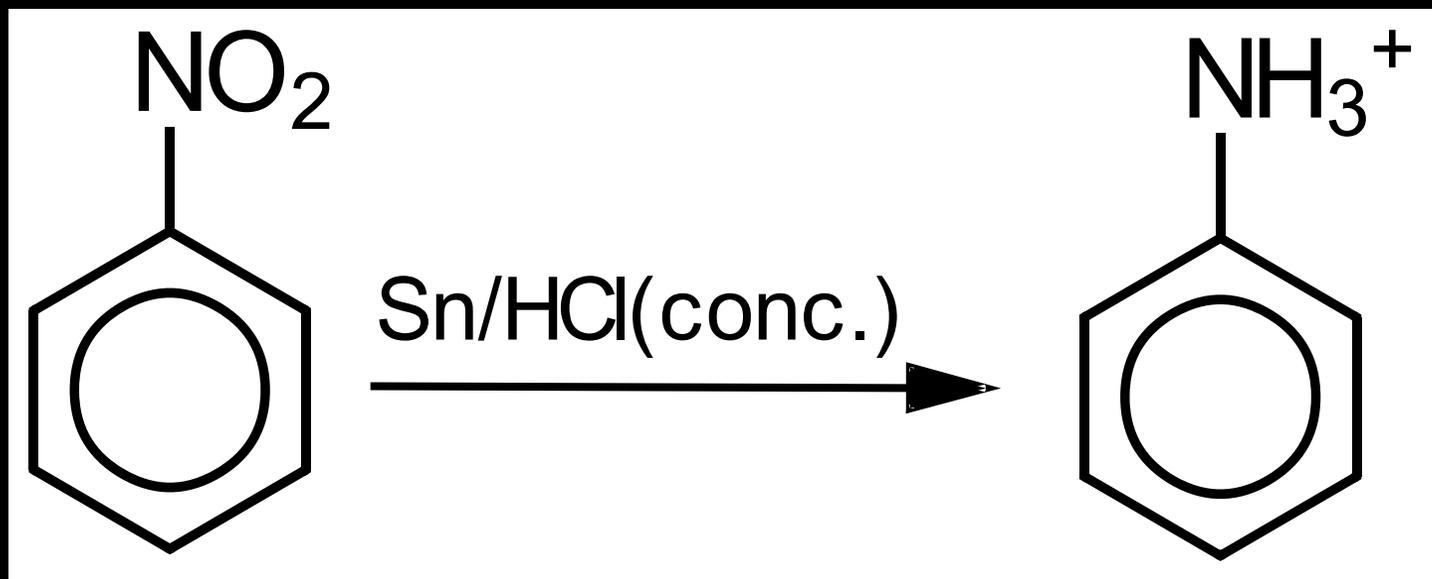
Nitrobenzene ($C_6H_5NO_2$) can be reduced to phenylamine (aniline), $C_6H_5NH_2$, in a two stage reaction.



Reduction of nitrobenzene

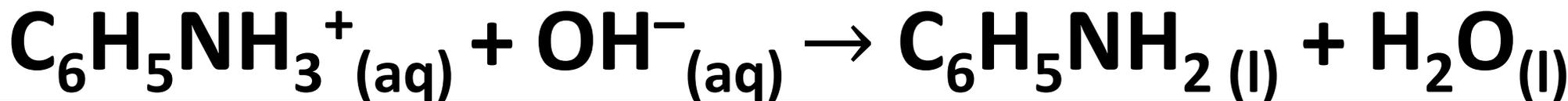
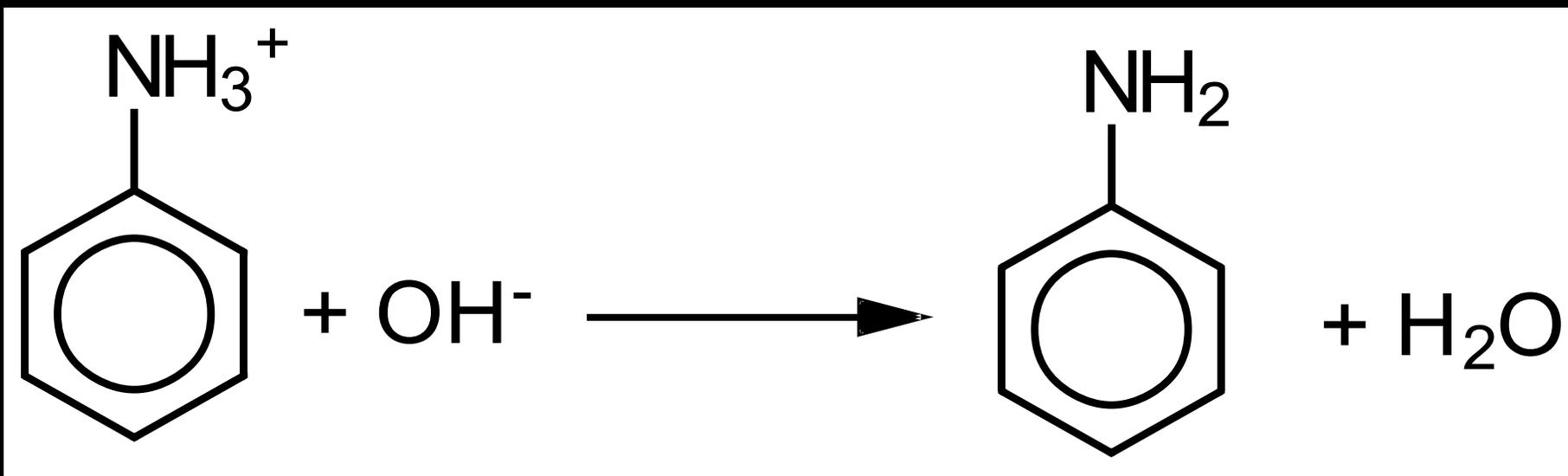
Stage 1 – $\text{C}_6\text{H}_5\text{NO}_2$ is reacted with Sn and conc. HCl (heat under reflux in a boiling water bath).

The product is the phenylammonium ion ($\text{C}_6\text{H}_5\text{NH}_3^+$)



Reduction of nitrobenzene

Stage 2 – $\text{C}_6\text{H}_5\text{NH}_3^+$ is reacted with NaOH to remove the hydrogen ion (H^+) and produce phenylamine ($\text{C}_6\text{H}_5\text{NH}_2$).

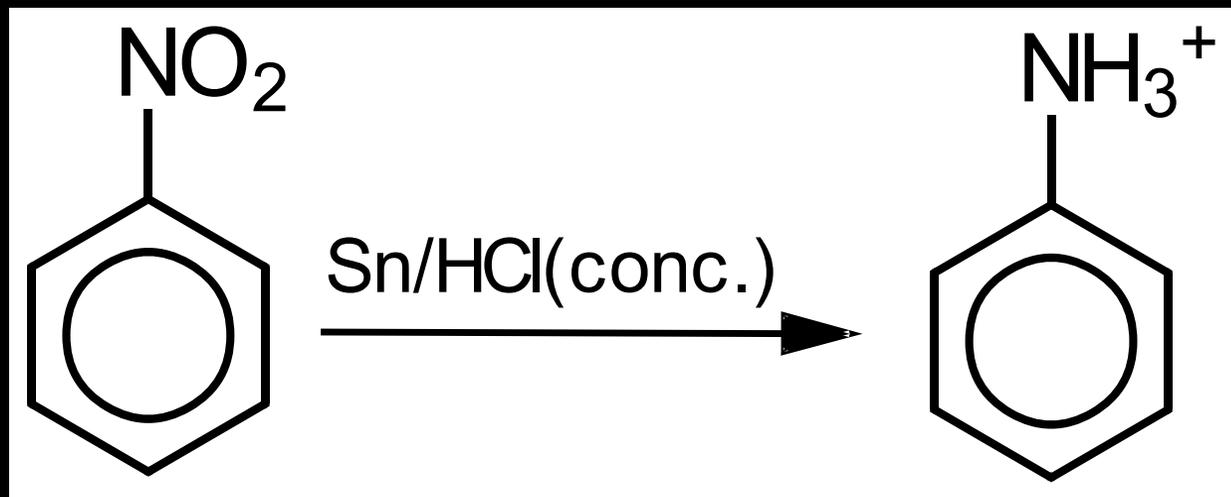


Reduction of nitrobenzene

Nitrobenzene ($C_6H_5NO_2$) can be reduced to phenylamine (aniline) ($C_6H_5NH_2$) in a two stage reaction.

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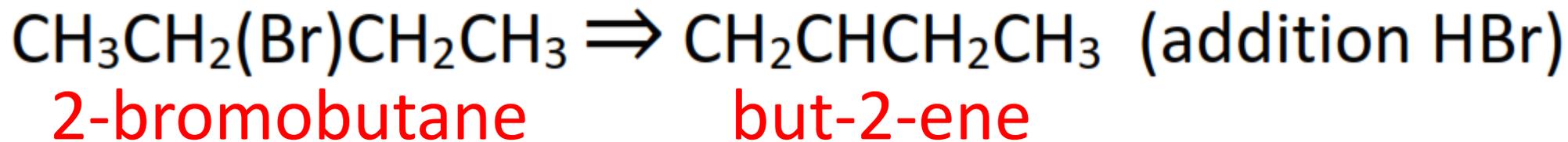
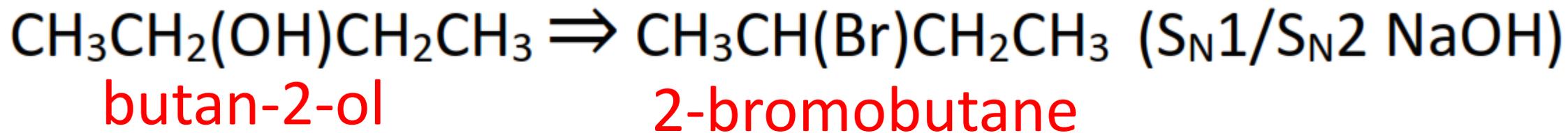
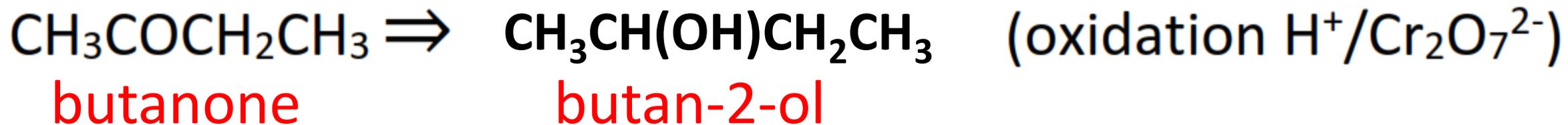
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Retro-synthesis

Retro-synthesis

Outline the steps involved in the retro-synthesis of butanone starting with an alkene.



Retro-synthesis

Retro-synthesis involves planning a synthesis backwards, by starting at the product, (the target molecule) and taking it back one step at a time to simple, available starting materials (precursors).

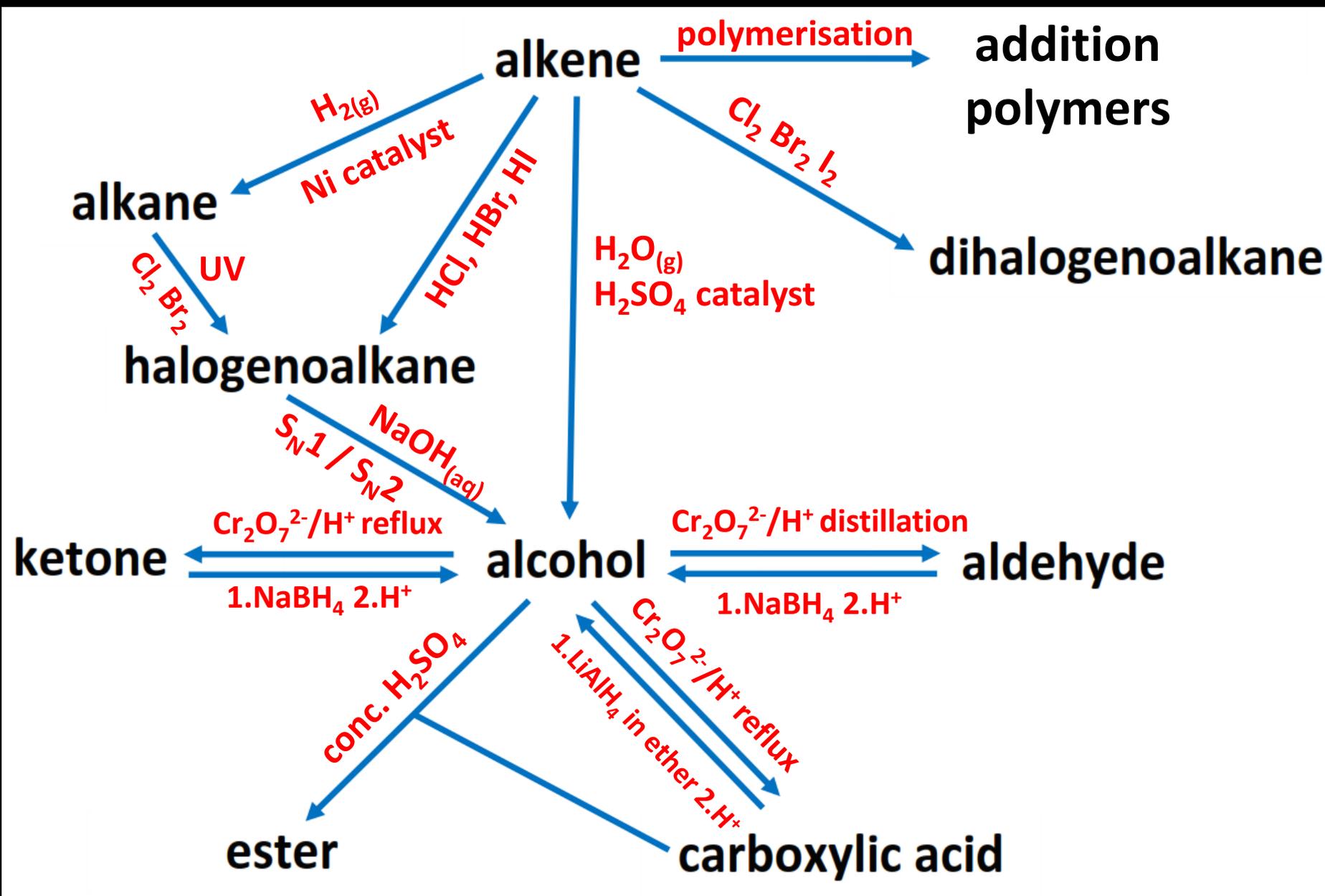
target molecule \Rightarrow precursor 1 \Rightarrow precursor 2 \Rightarrow starting material

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**Organic reaction
pathways**

Organic reaction pathways



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Isomerism

Isomerism

Isomerism – compounds with same molecular formula but different arrangement of atoms

Stereoisomerism –
different spatial
arrangement of atoms

Structural isomerism –
atoms and functional
groups attached in
different ways

Isomerism

Stereoisomerism

**Configurational
isomerism –
interconvert only by
breaking a bond**

**Conformational
isomerism –
interconvert by rotation
around a σ bond**

Isomerism

Configurational isomerism

```
graph TD; A[Configurational isomerism] --> B["cis-trans and E/Z isomerism – restricted rotation around atoms"]; A --> C["Optical isomerism – asymmetric or chiral carbon atom"]
```

cis-trans and *E/Z*
isomerism –
restricted rotation
around atoms

Optical isomerism –
asymmetric or chiral
carbon atom

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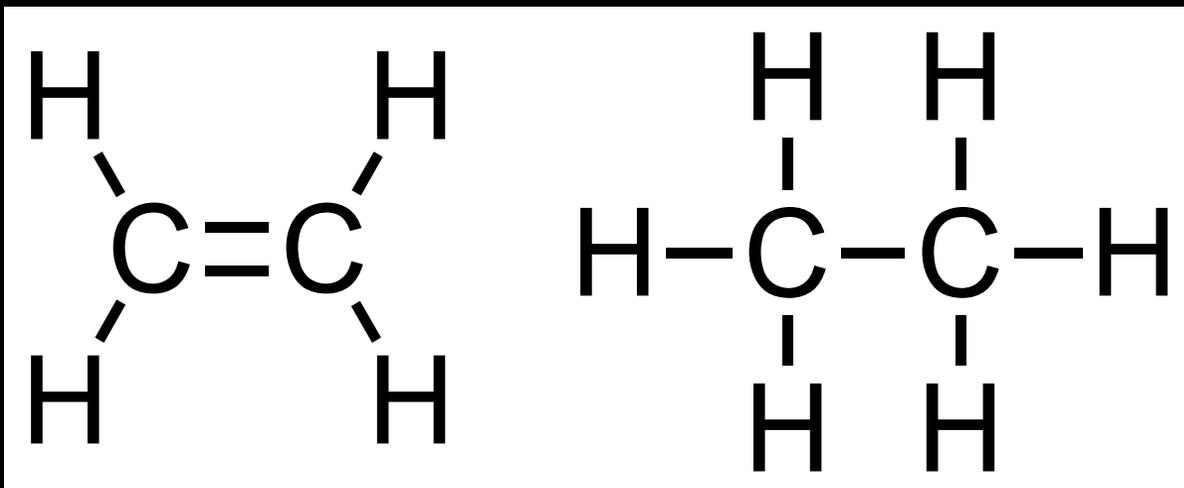
Tutorials for IB Chemistry

**Conformational
isomerism**

Conformational isomers

Conformational isomers (conformers) are stereoisomers produced by rotation about carbon-carbon single bonds.

C=C bond
made of 1 σ
and 1 π bond
(restricted
rotation)



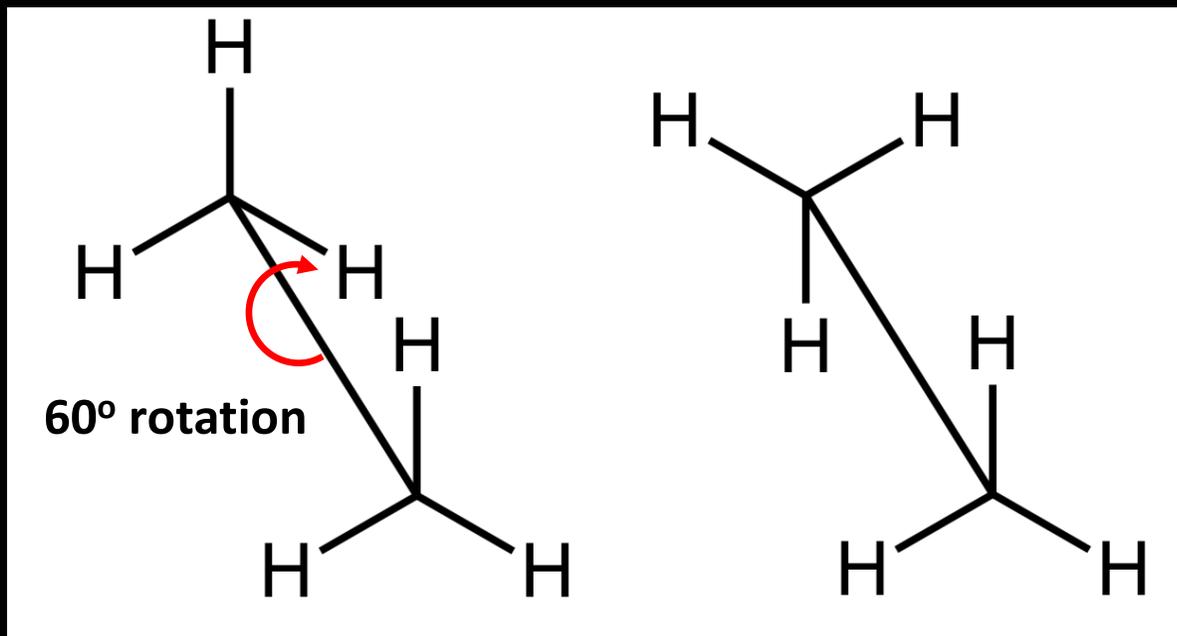
C-C bond
made of 1 σ
bond
(free rotation)

The two conformers can interconvert readily at room temperature.

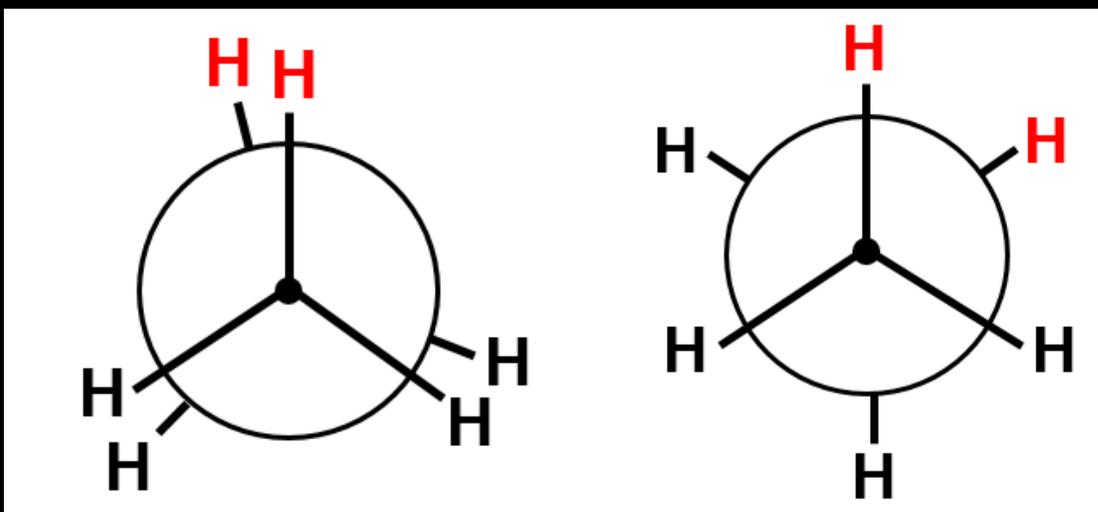
Conformational isomers



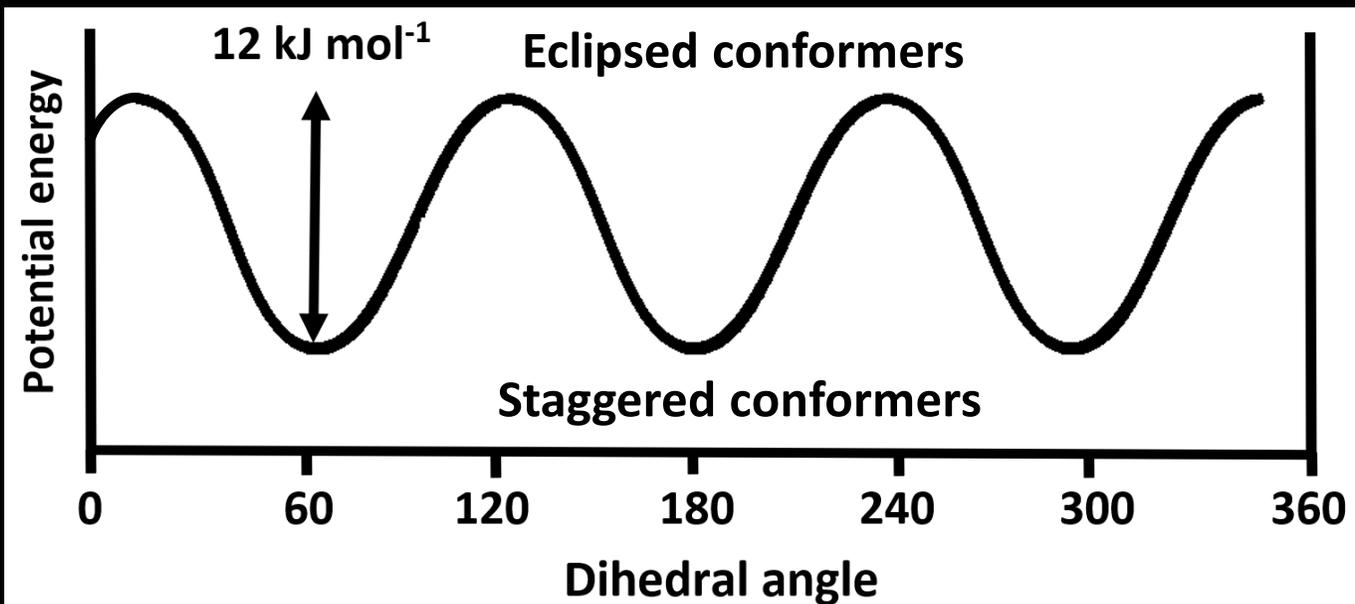
Eclipsed conformer



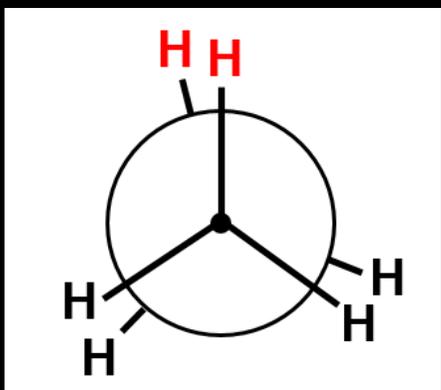
Staggered conformer



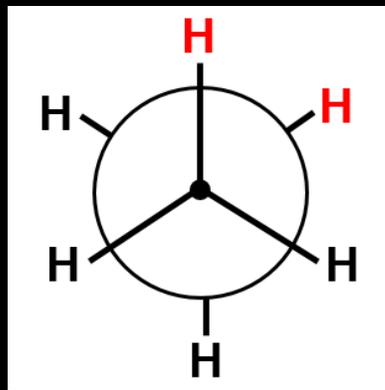
Conformational isomers



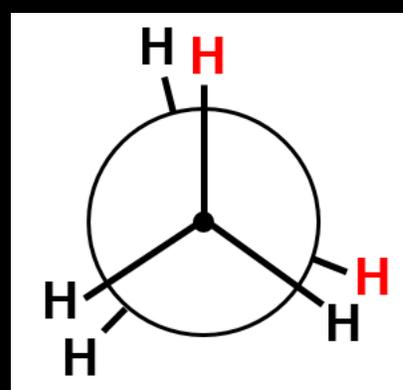
The staggered conformation is more stable by approximately 12 kJ mol⁻¹



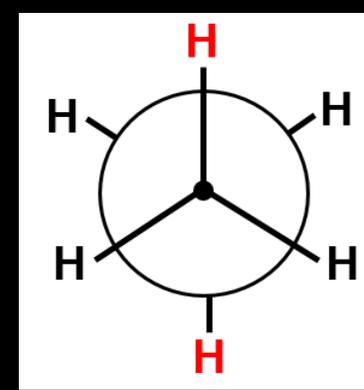
Dihedral angle = 0°



Dihedral angle = 60°



Dihedral angle = 120°



Dihedral angle = 180°

Conformational isomers

Conformational isomers occur because of the free rotation around a carbon-carbon single bond (composed of one σ bond).

The staggered conformers are more stable than the eclipsed conformers.

The two conformers interconvert rapidly at room temperature because of the small difference in energy between them.

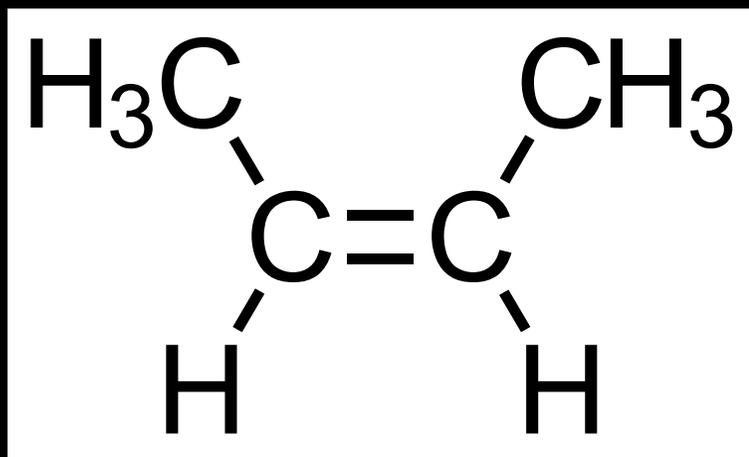
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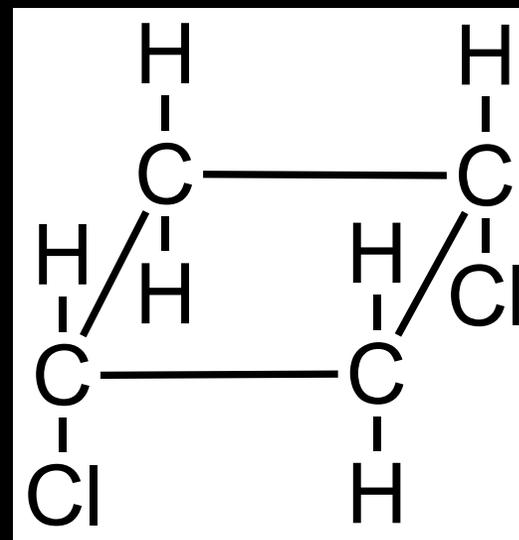
***cis-trans* isomerism**

cis-trans isomerism

cis-trans isomerism occurs where there is restricted rotation around a carbon to carbon bond.



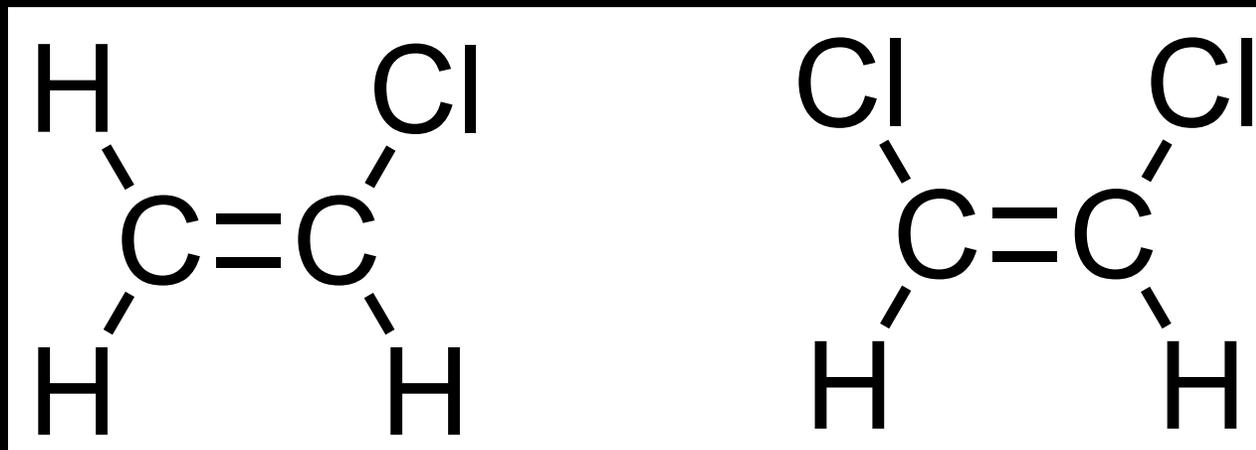
Restricted rotation
around a C=C bond



Restricted rotation in
a cyclic compound

cis-trans isomerism

For *cis-trans* isomerism to occur, there must be two different groups on each of the carbon atoms of the C=C bond.

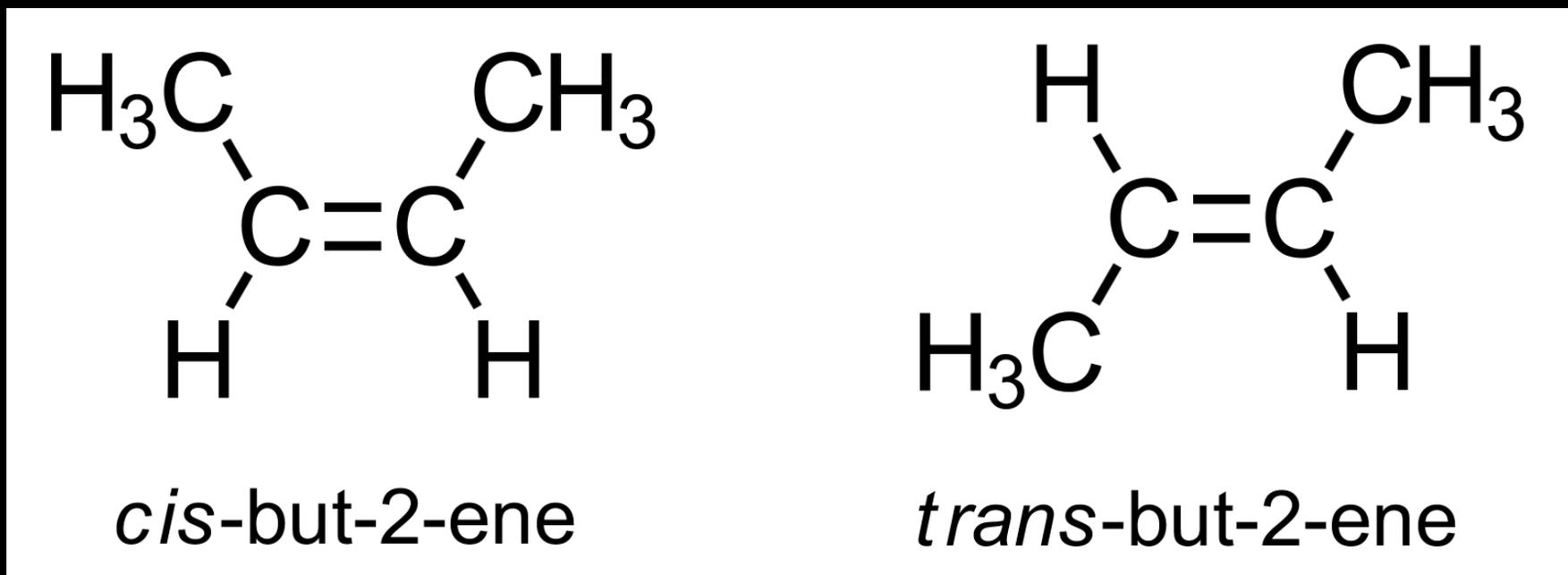


This molecule does not have *cis-trans* isomers

This molecule does have *cis-trans* isomers

cis-trans isomerism

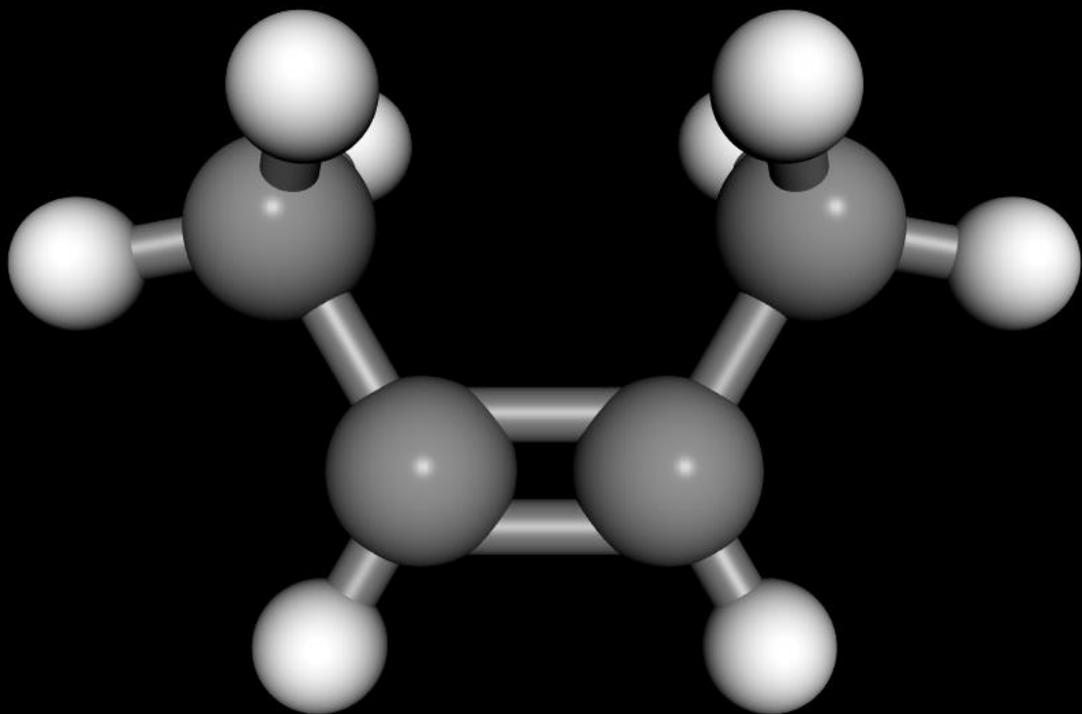
The π bond in the C=C bond restricts rotation, forming two different isomers.



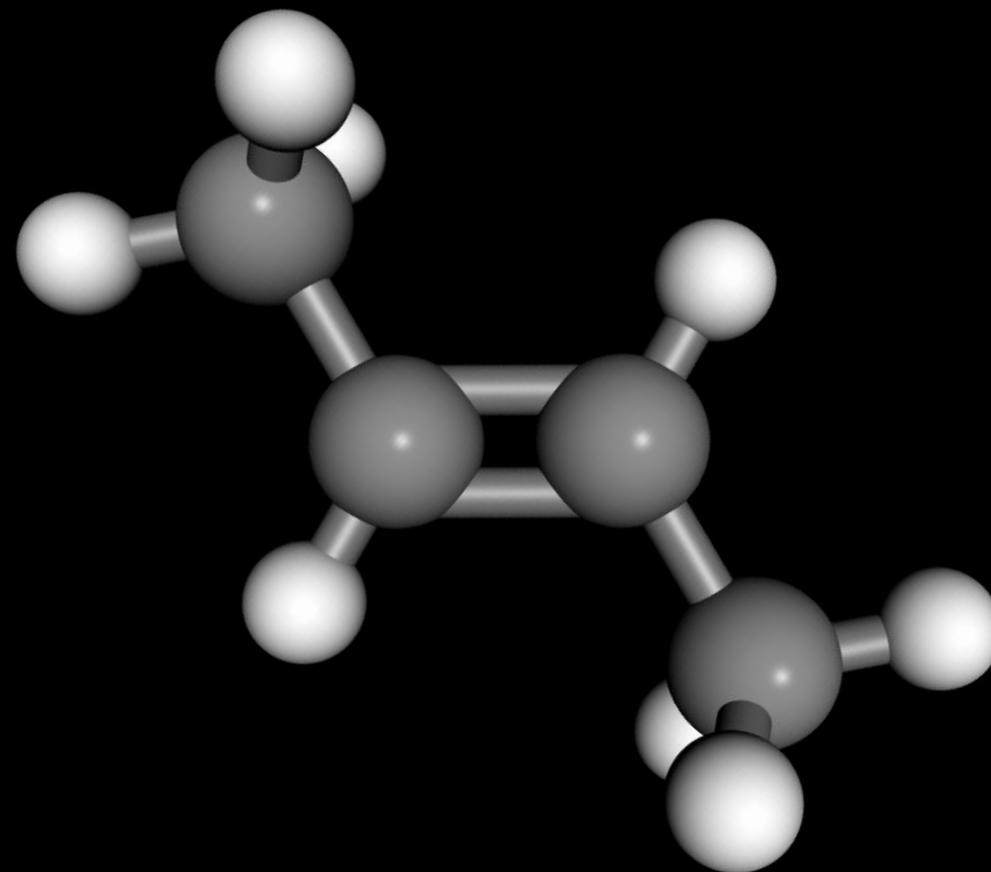
cis isomer – same groups on the same side of C=C bond.

trans isomer – same groups on opposite sides of C=C bond.

cis-trans isomerism



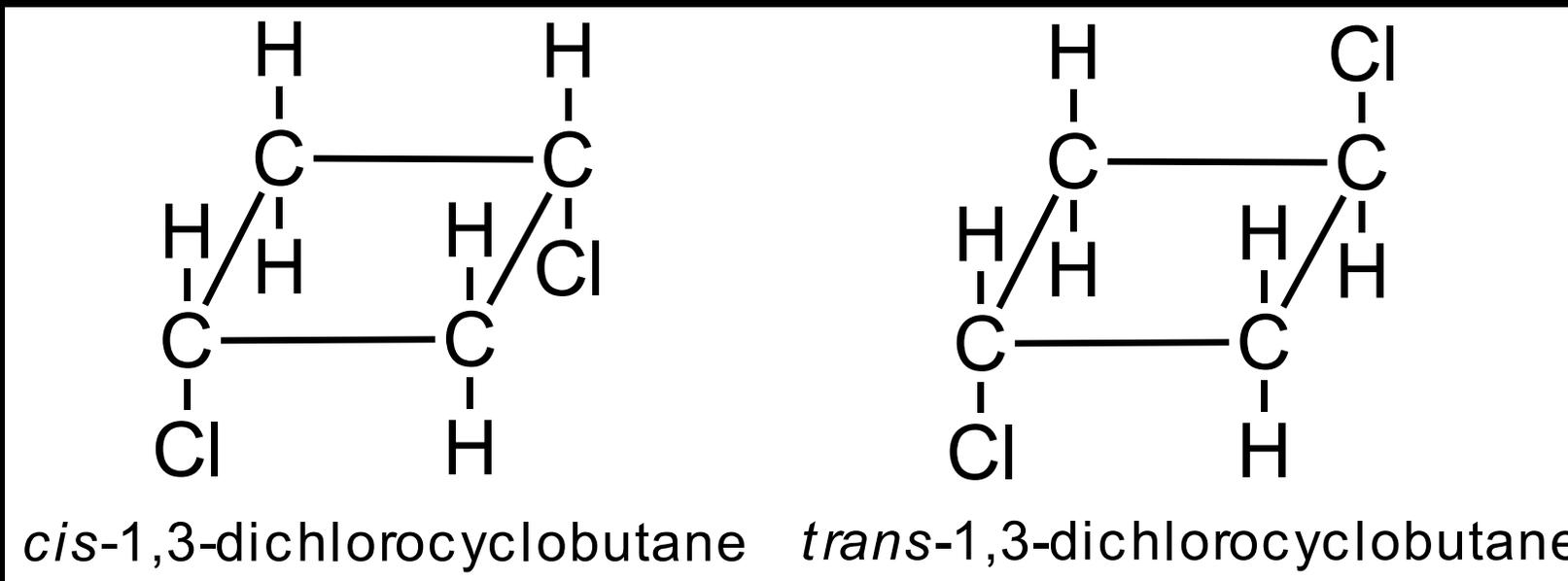
cis-but-2-ene



trans-but-2-ene

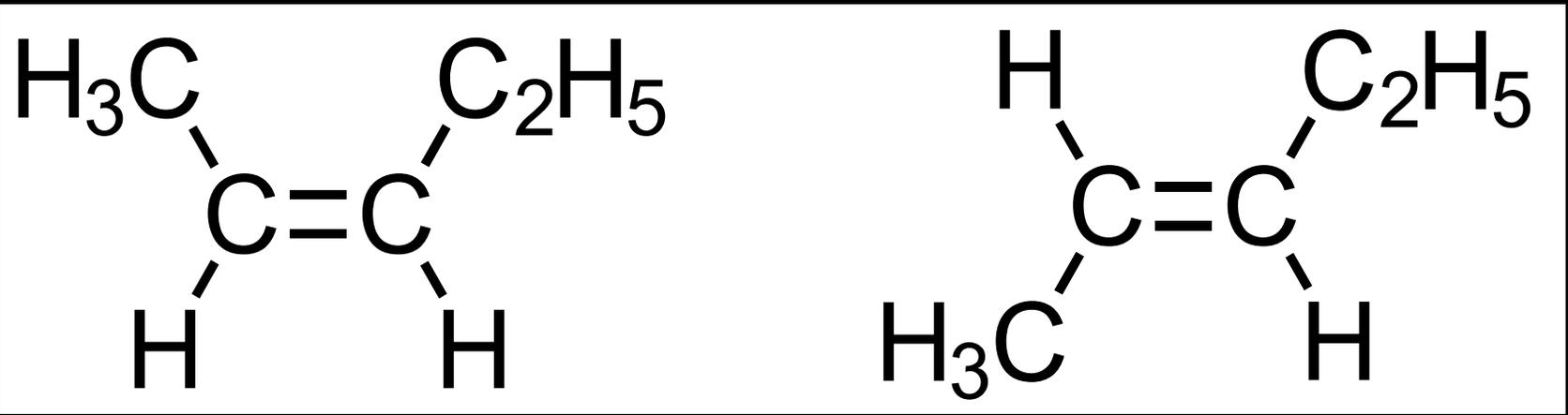
cis-trans isomerism

Cyclic compounds contain a ring structure that restricts rotation. When the molecule contains two or more different substituents attached to the ring, two different isomers are formed.



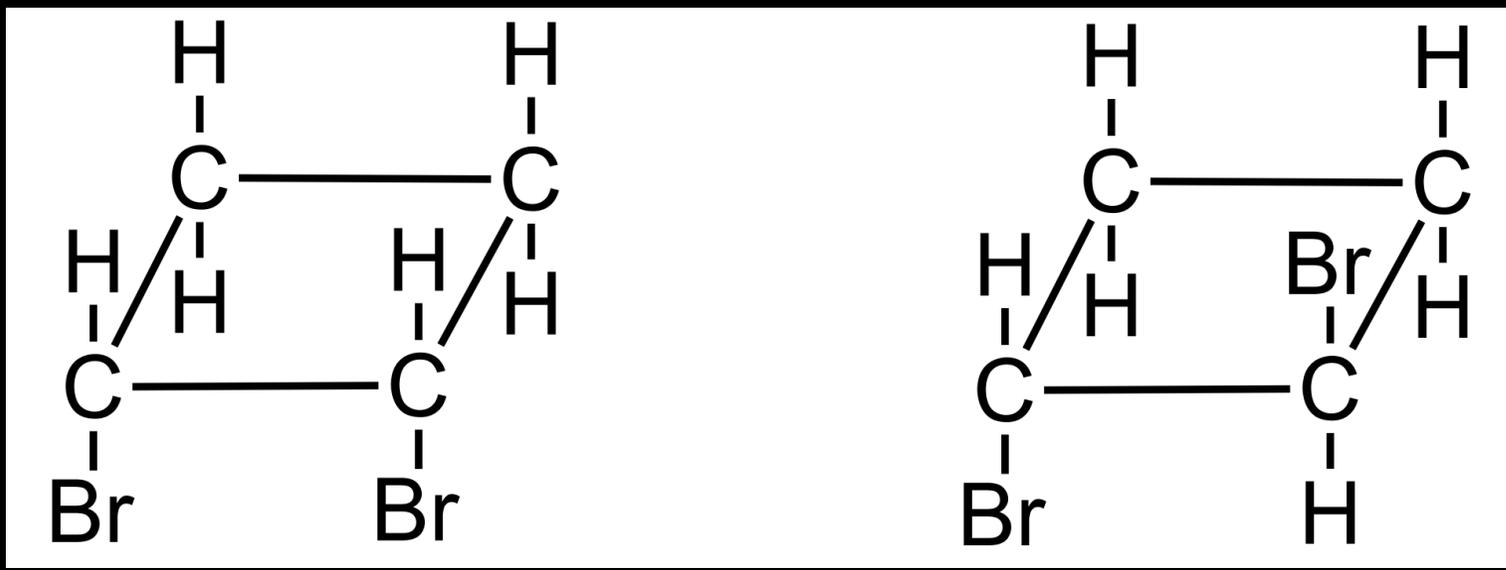
cis isomer has the substituents on the same side of the ring, *trans* isomer has the substituents on opposite sides of the ring.

cis-trans isomerism



cis-pent-2-ene

trans-pent-2-ene



cis-1,2-dibromocyclobutane

trans-1,2-dibromocyclobutane

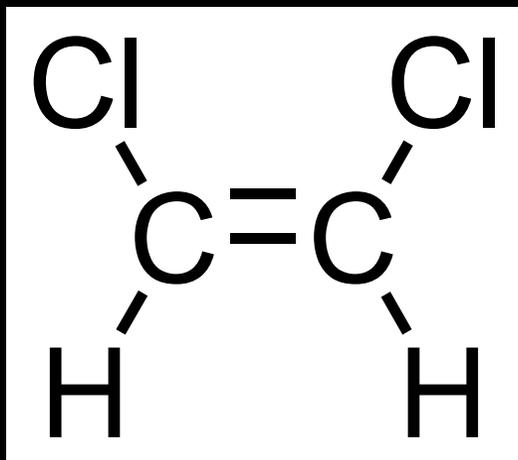
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**Physical properties of
cis-trans isomers**

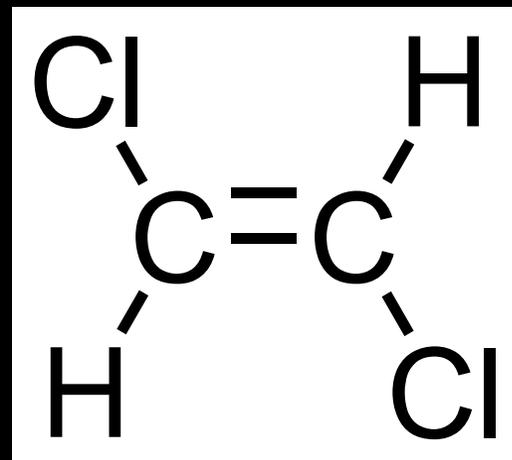
cis-1,2-dichloroethene

polar
molecule
B.P. 60°C
M.P. -80°C



trans-1,2-dichloroethene

non-polar
molecule
B.P. 48°C
M.P. -50°C

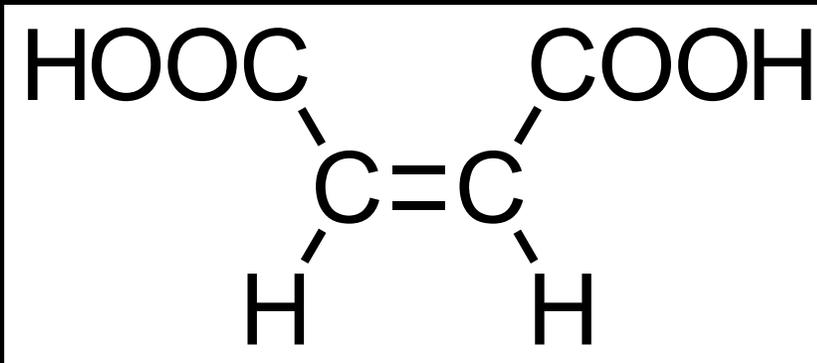


The polarity of the molecule influences the boiling point.

The symmetry of the molecule influences the melting point (closely packed molecules have stronger intermolecular forces).

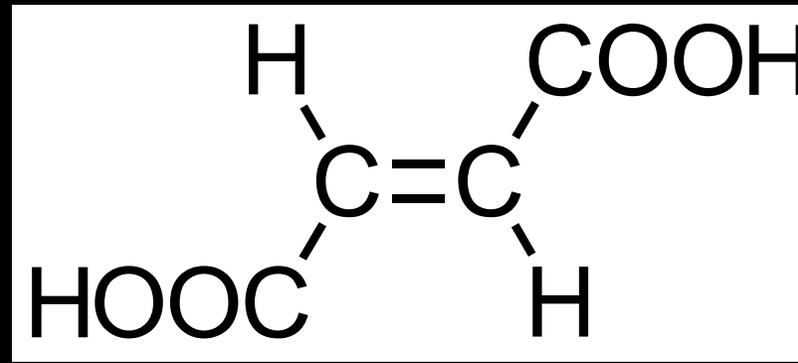
cis-butenedioic acid

M.P.
139 °C



trans-butenedioic acid

M.P.
287 °C



The **cis-isomer** forms intramolecular hydrogen bonds (within the molecule).

The **trans-isomer** forms intermolecular hydrogen bonds (between molecules).

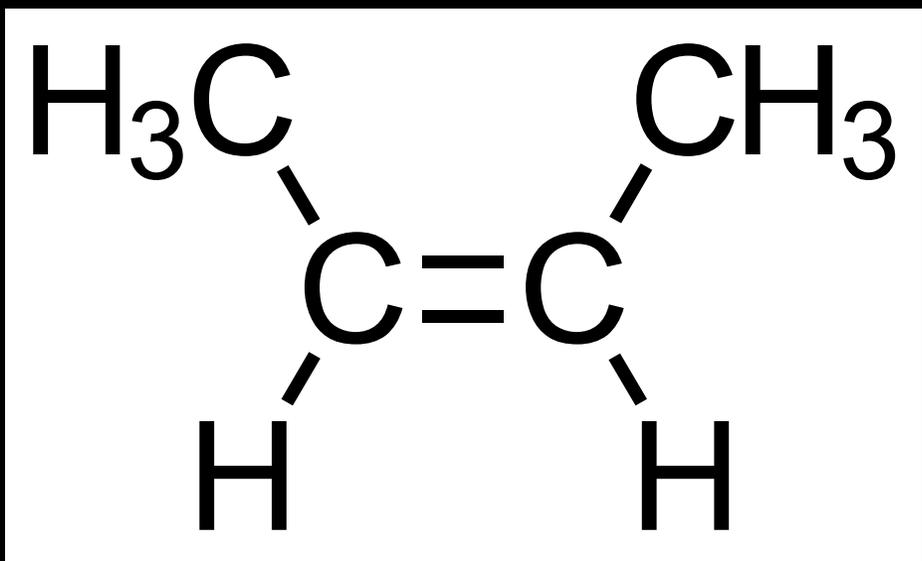
MSJChem

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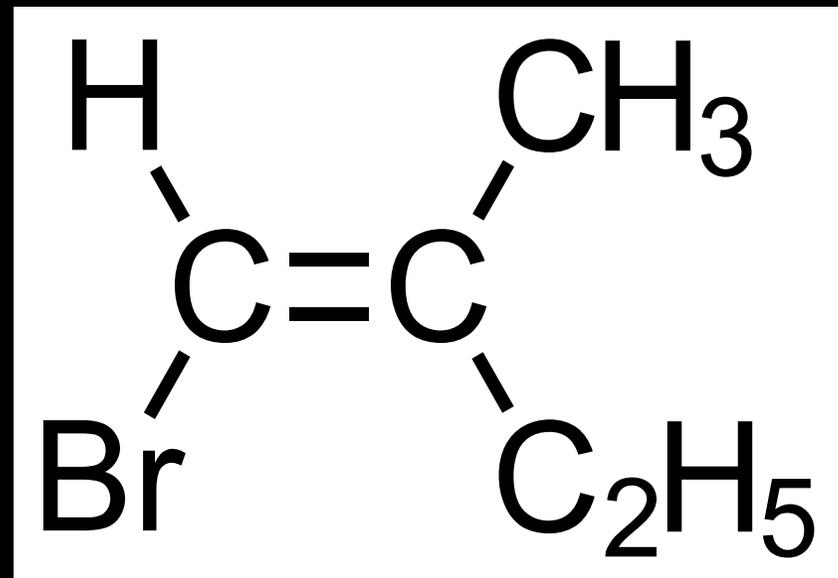
***E/Z* isomerism**

E/Z isomerism

E/Z notation is used when there are up to four different substituents bonded to the two carbon atoms of the C=C bond.



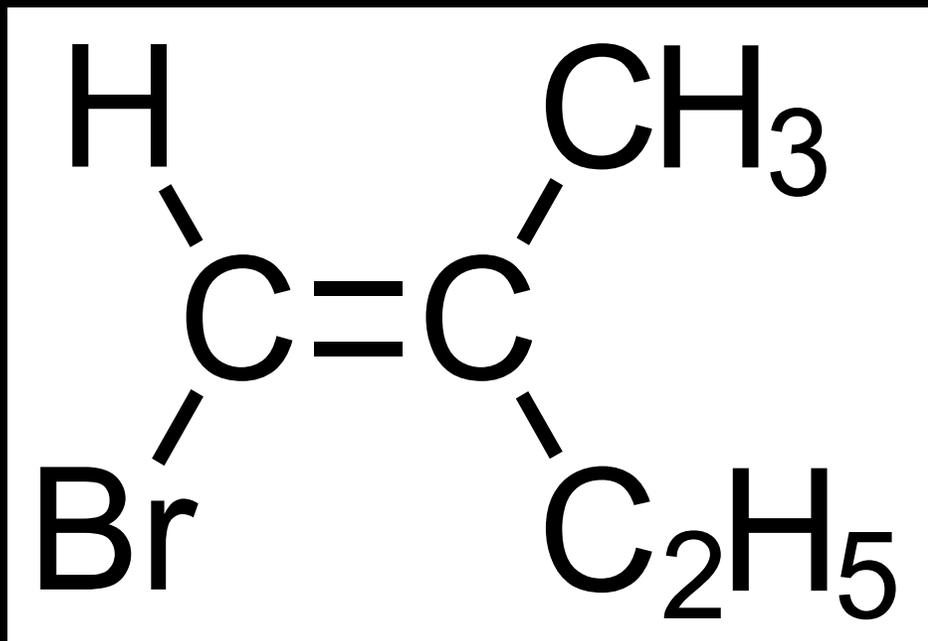
cis-but-2-ene



E/Z isomerism

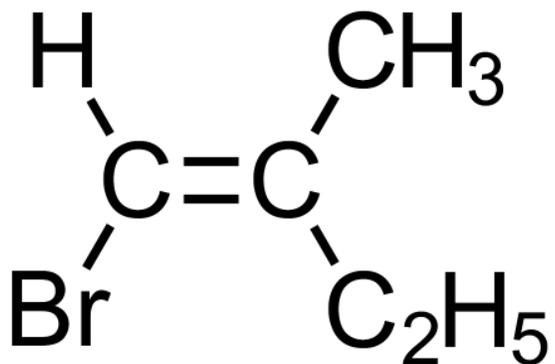
E/Z isomerism is based on the Cahn-Ingold-Prelog (CIP) rules of priority which assign priority to each atom or group of atoms around the C=C bond.

H Z = 1
Br Z = 35

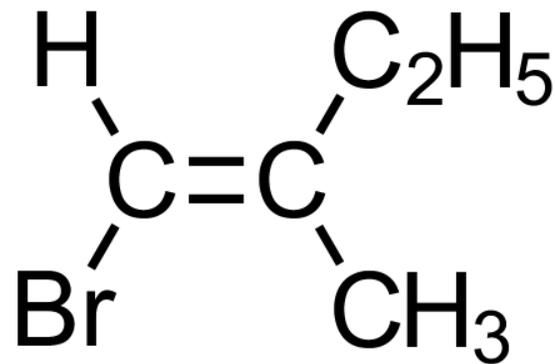


C-H Z = 1
C-C Z = 6

E/Z isomerism



[Z]-1-bromo-2-methylbut-1-ene

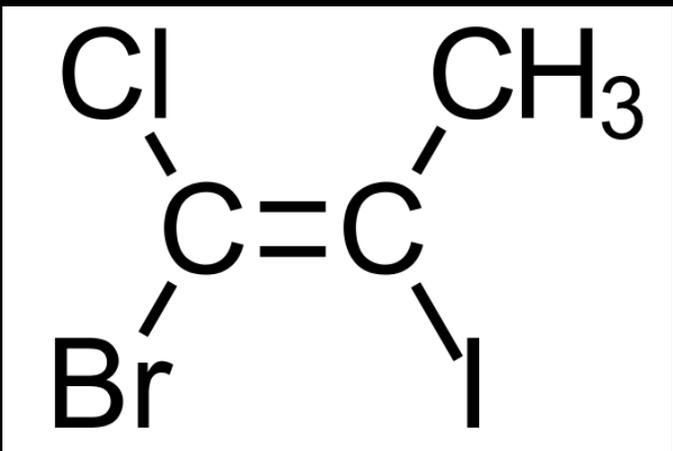


[E]-1-bromo-2-methylbut-1-ene

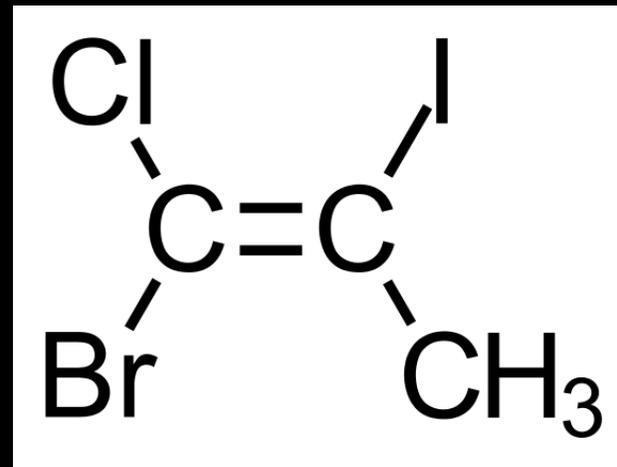
If the highest priority groups are on the same side of the C=C, it is the *Z* isomer.

If the highest priority groups are on opposite sides of the C=C, it is the *E* isomer.

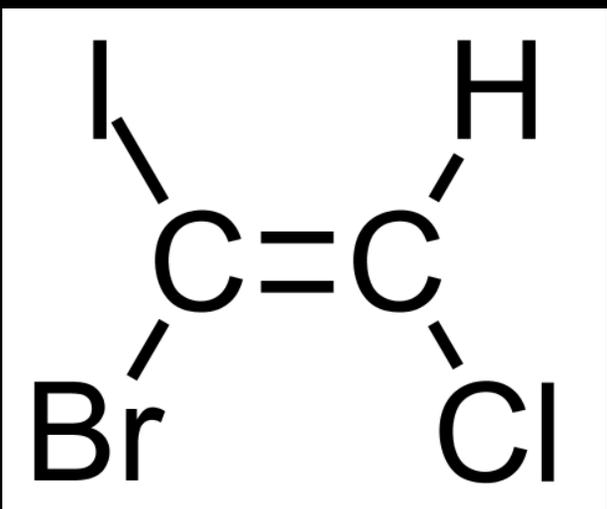
E/Z isomerism



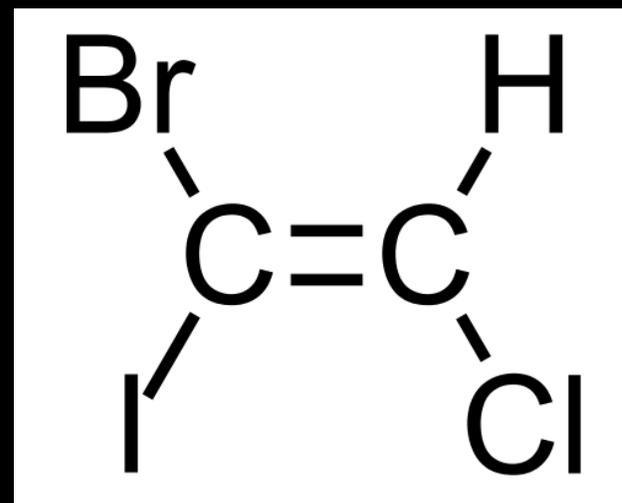
(Z)-1-bromo-1-chloro-2-iodo-1-propene



(E)-1-bromo-1-chloro-2-iodo-1-propene



(E)-1-bromo-2-chloro-1-iodoethene



(Z)-1-bromo-2-chloro-1-iodoethene

E/Z isomerism

How to determine if the isomer is *E* or *Z*:

1. Assign priority to the atoms or groups of atoms on each carbon atom of the C=C double bond



2. If the highest priority groups are on the same side of the C=C bond, it is the *Z* isomer (together).
3. If the highest priority groups are on opposite sides of the C=C bond, it is the *E* isomer (opposite).

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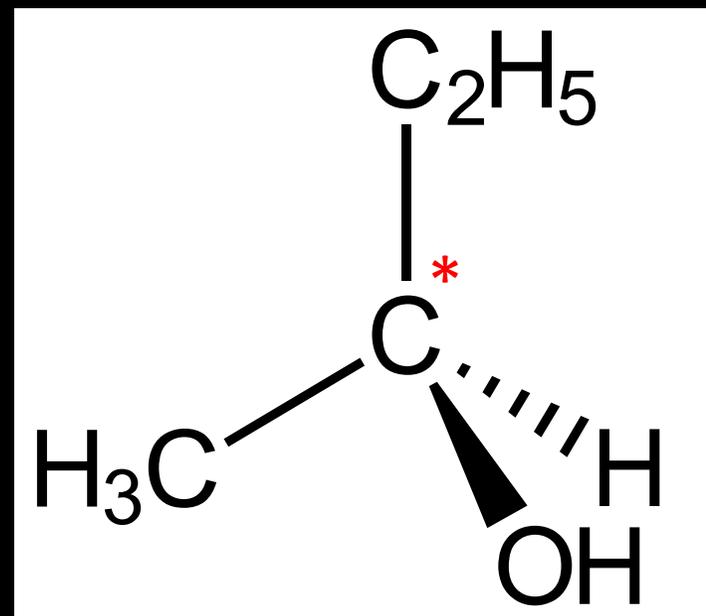
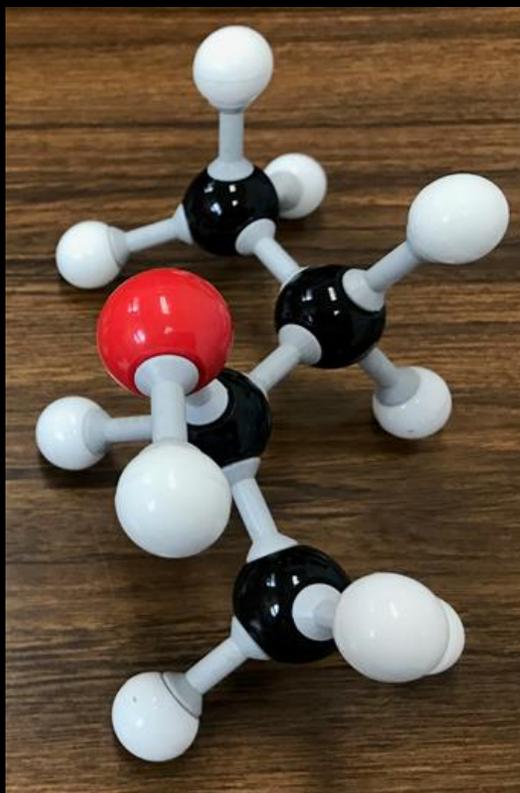
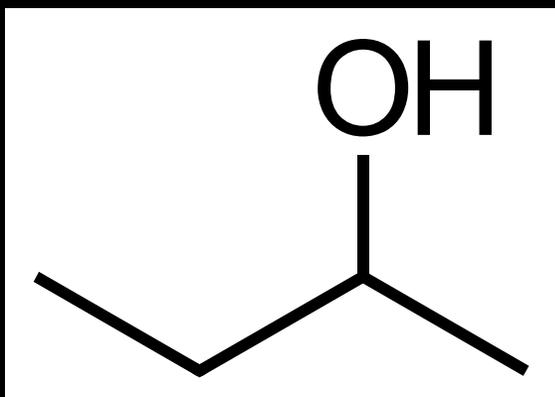
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Optical isomerism

Optical isomerism

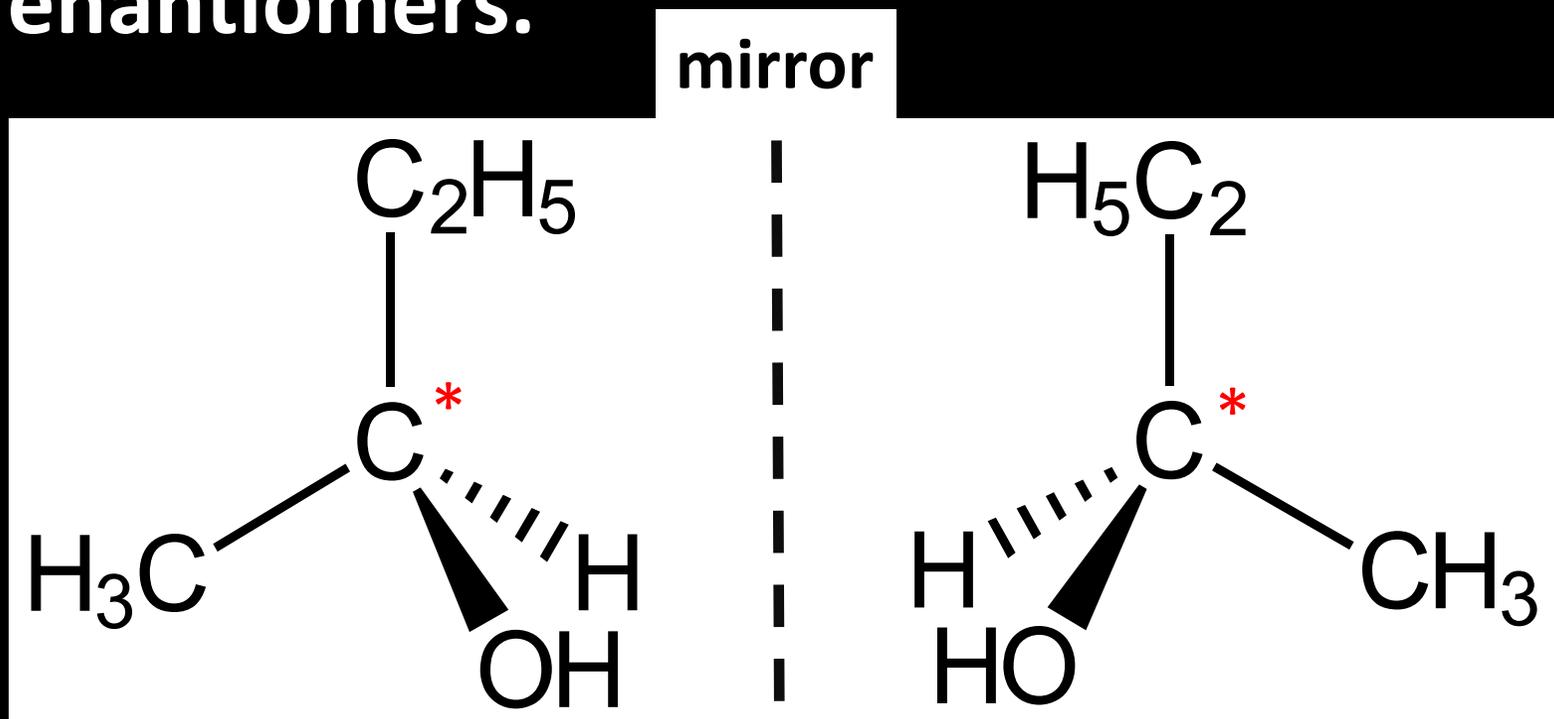
Optical isomerism is shown by chiral molecules that have a carbon atom bonded to four different atoms or groups (chiral center or asymmetric carbon).

butan-2-ol



Optical isomerism

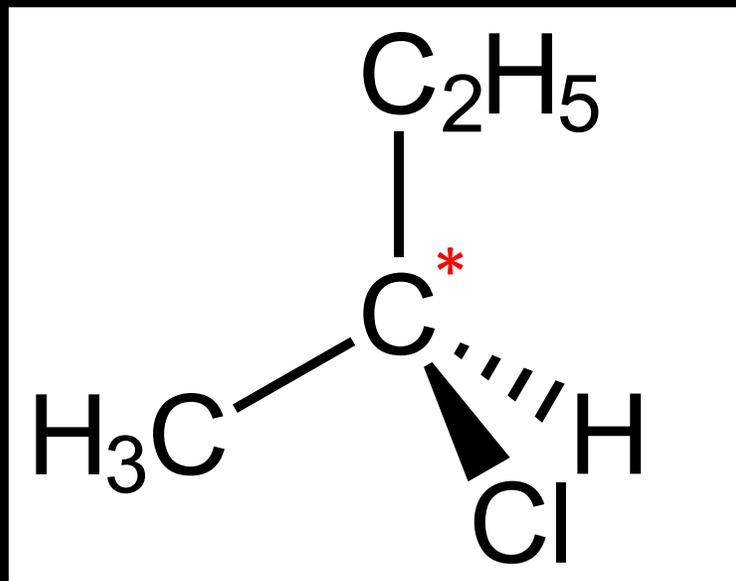
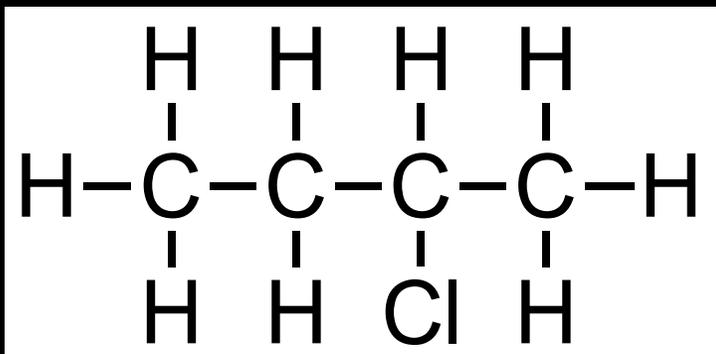
The four groups can be arranged in two three-dimensional configurations which are mirror images of each other. The two mirror images are non-superimposable and are known as enantiomers.



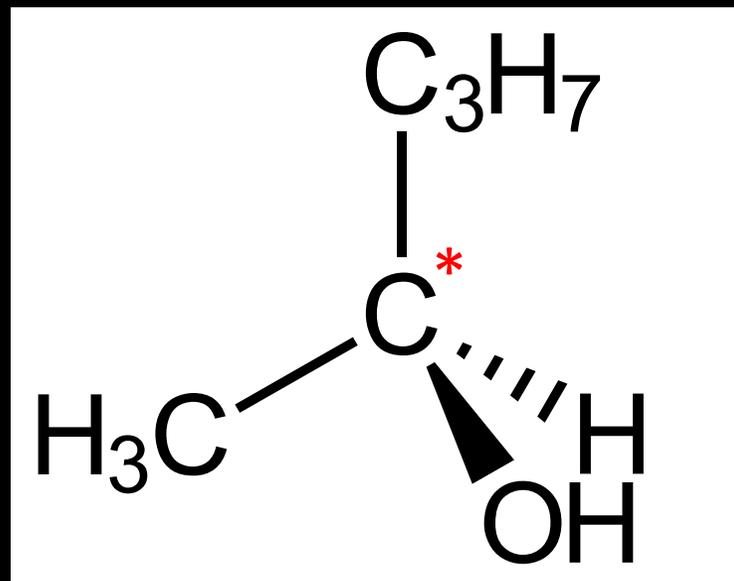
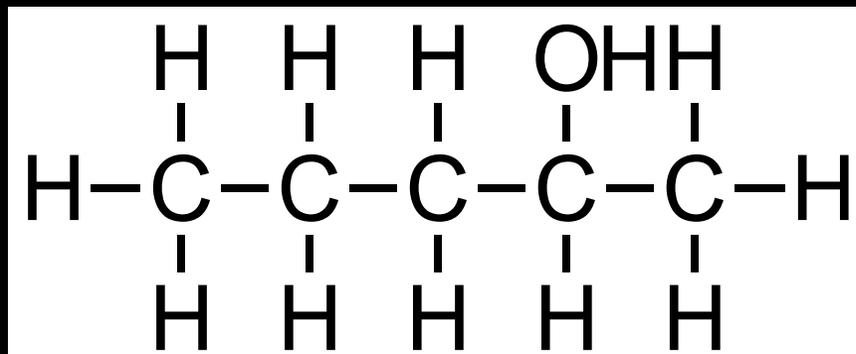
butan-2-ol

Optical isomerism

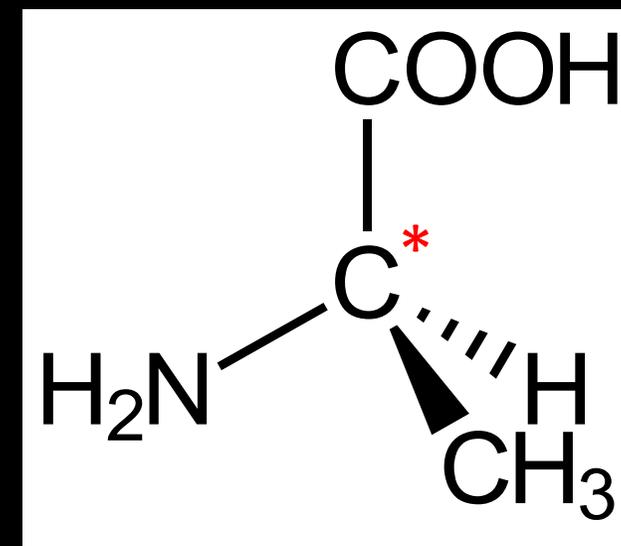
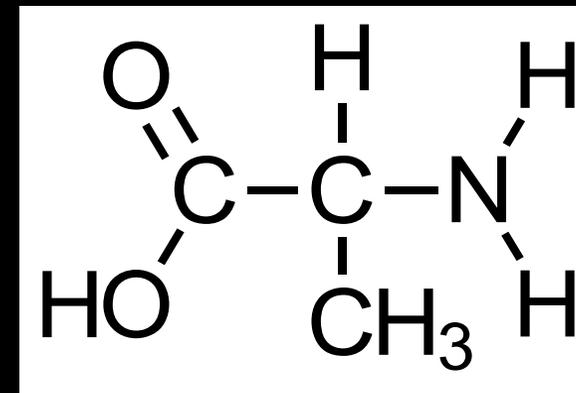
2-chlorobutane



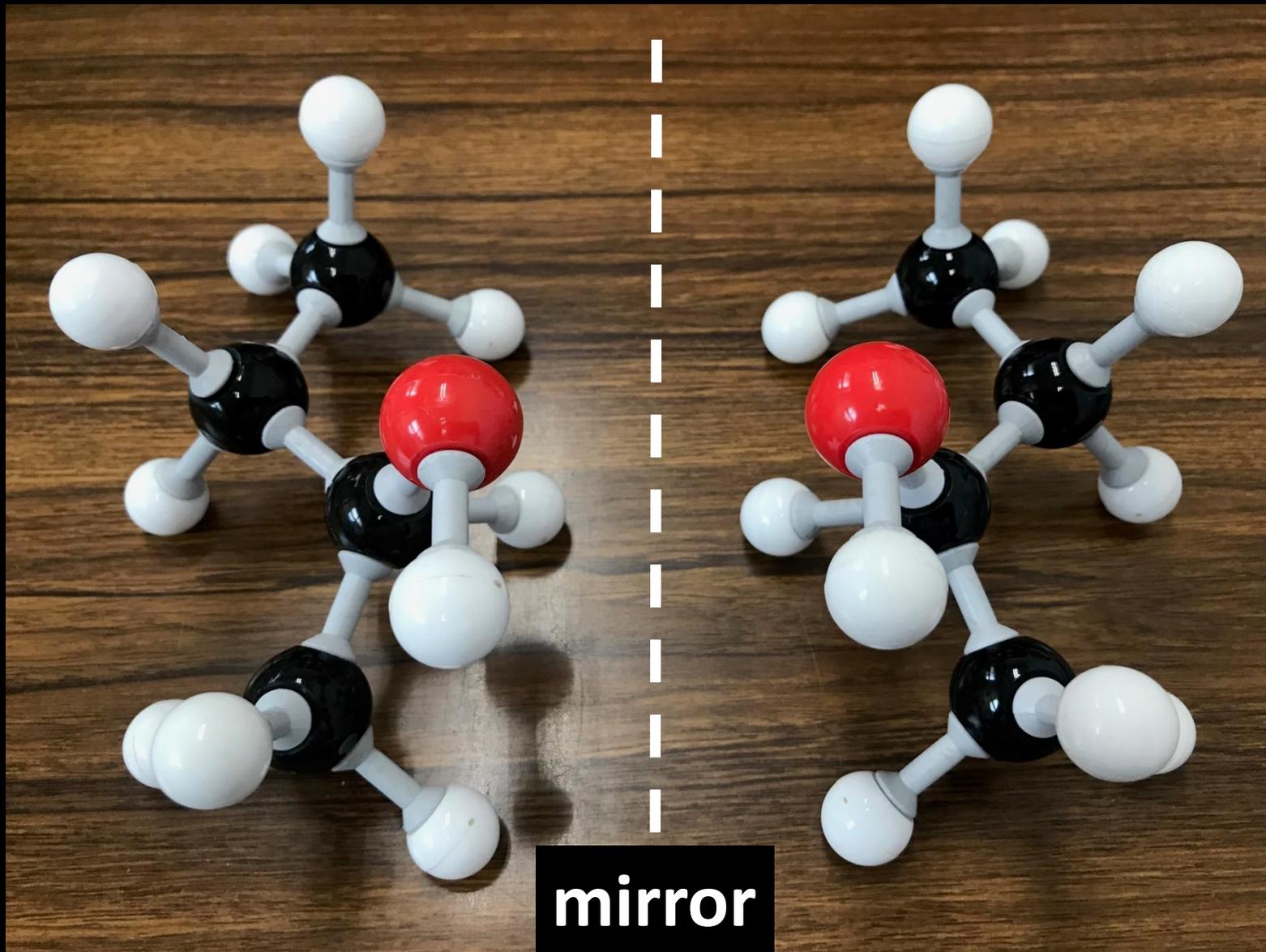
Pentan-2-ol



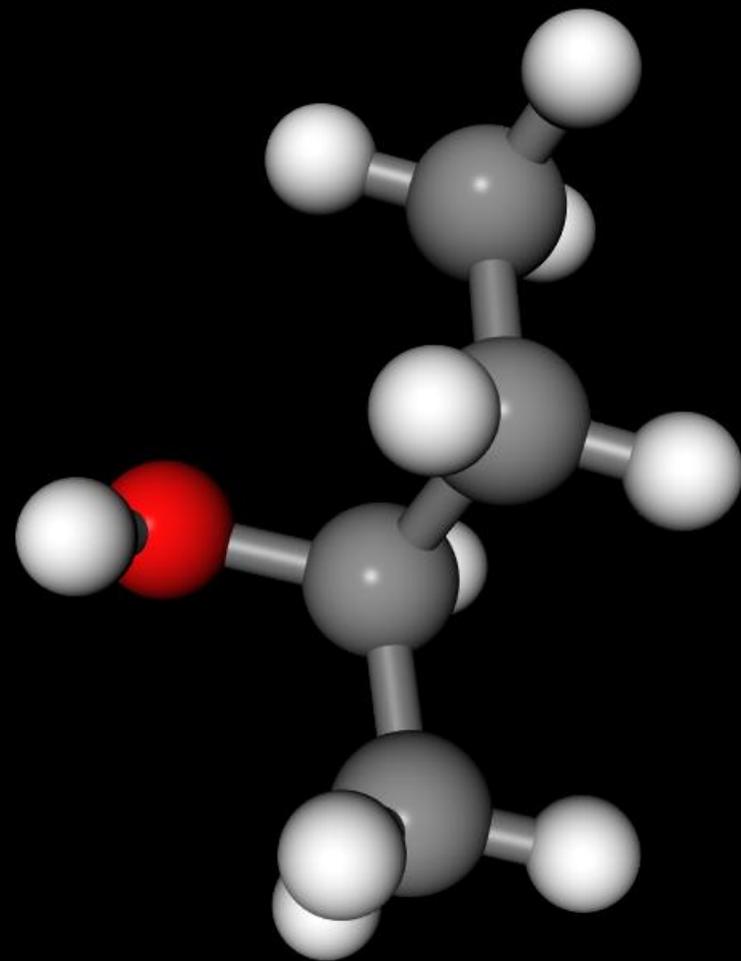
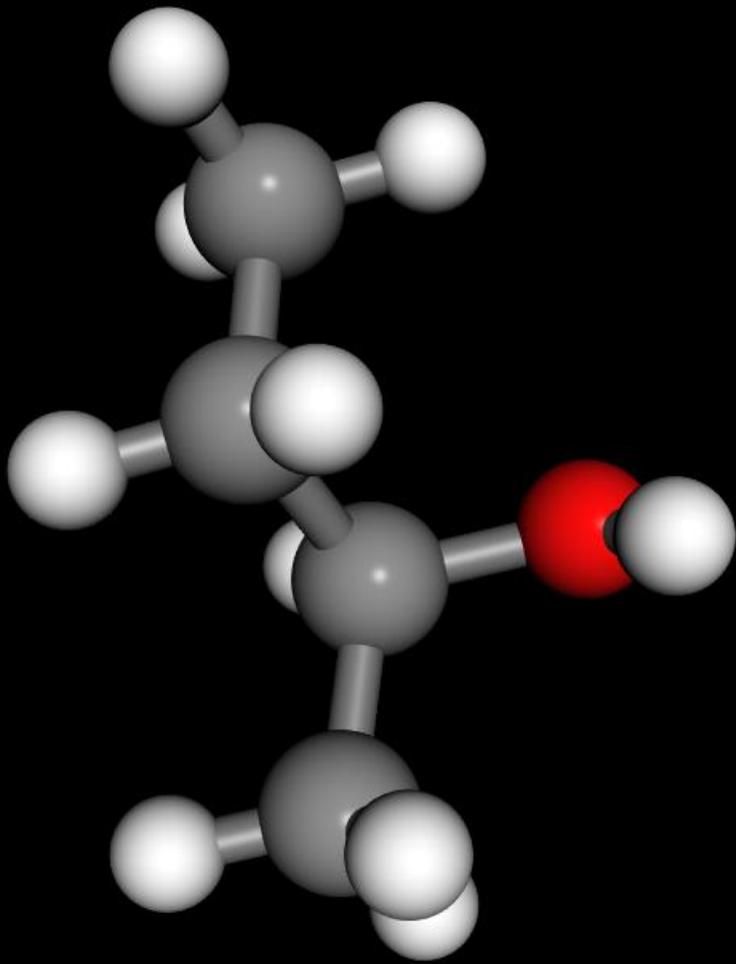
Alanine



Optical isomerism

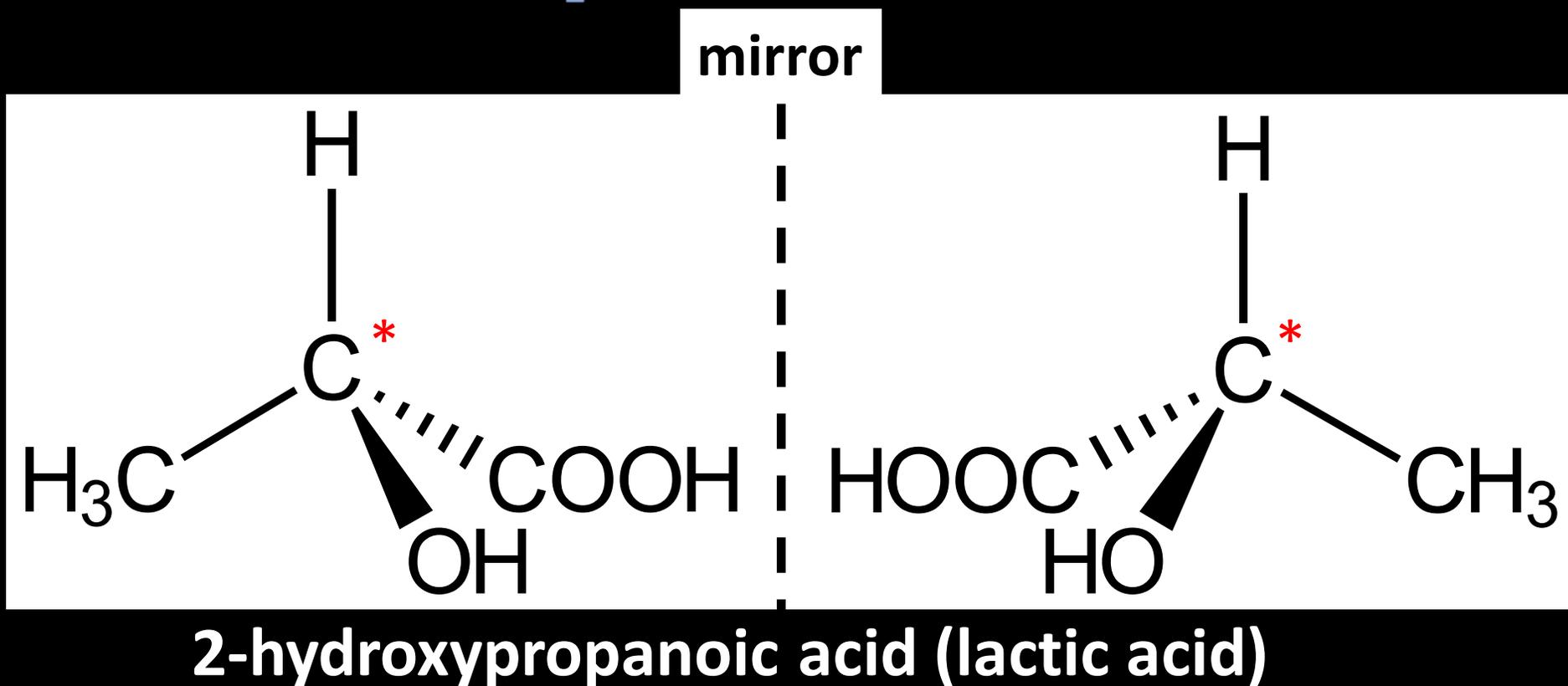


Optical isomerism



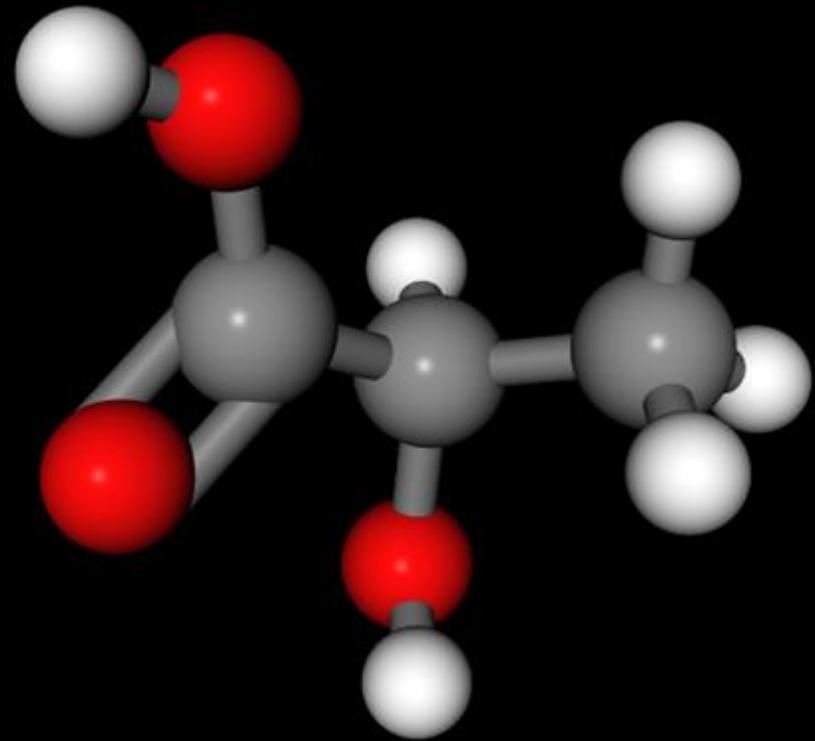
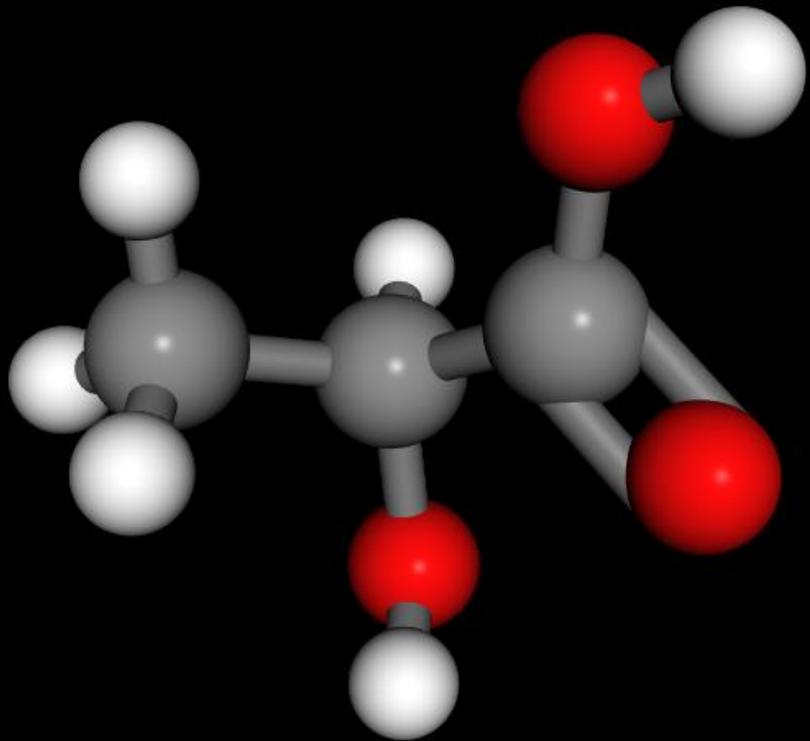
mirror

Optical isomerism



The two optical isomers (enantiomers) are optically active with plane-polarised light.

Optical isomerism



mirror

Optical isomerism

Enantiomers have identical physical properties, such as melting point and boiling point, except that they rotate the plane of plane-polarised light in opposite directions (optically active).

This property is used to distinguish between the two enantiomers of a chiral molecule.

The chemical properties of two enantiomers are also identical, except when they react with other chiral molecules (such as those found in the human body).

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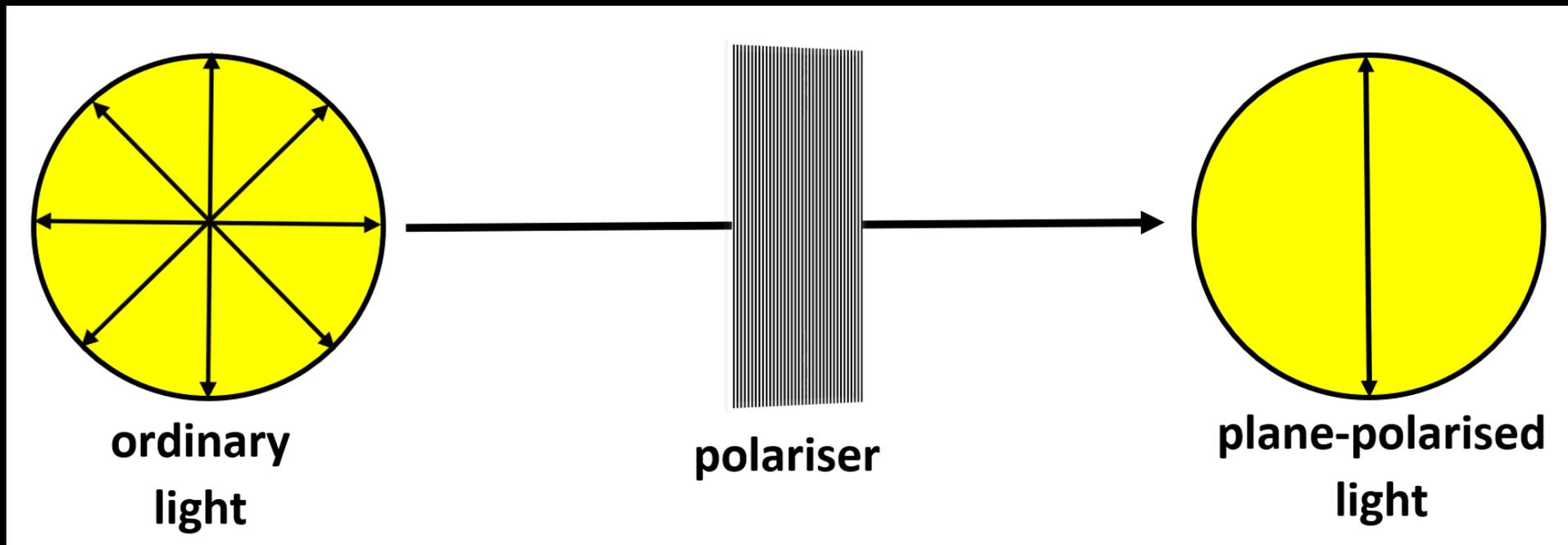
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**How to distinguish
between enantiomers of
a chiral compound**

Optical isomerism

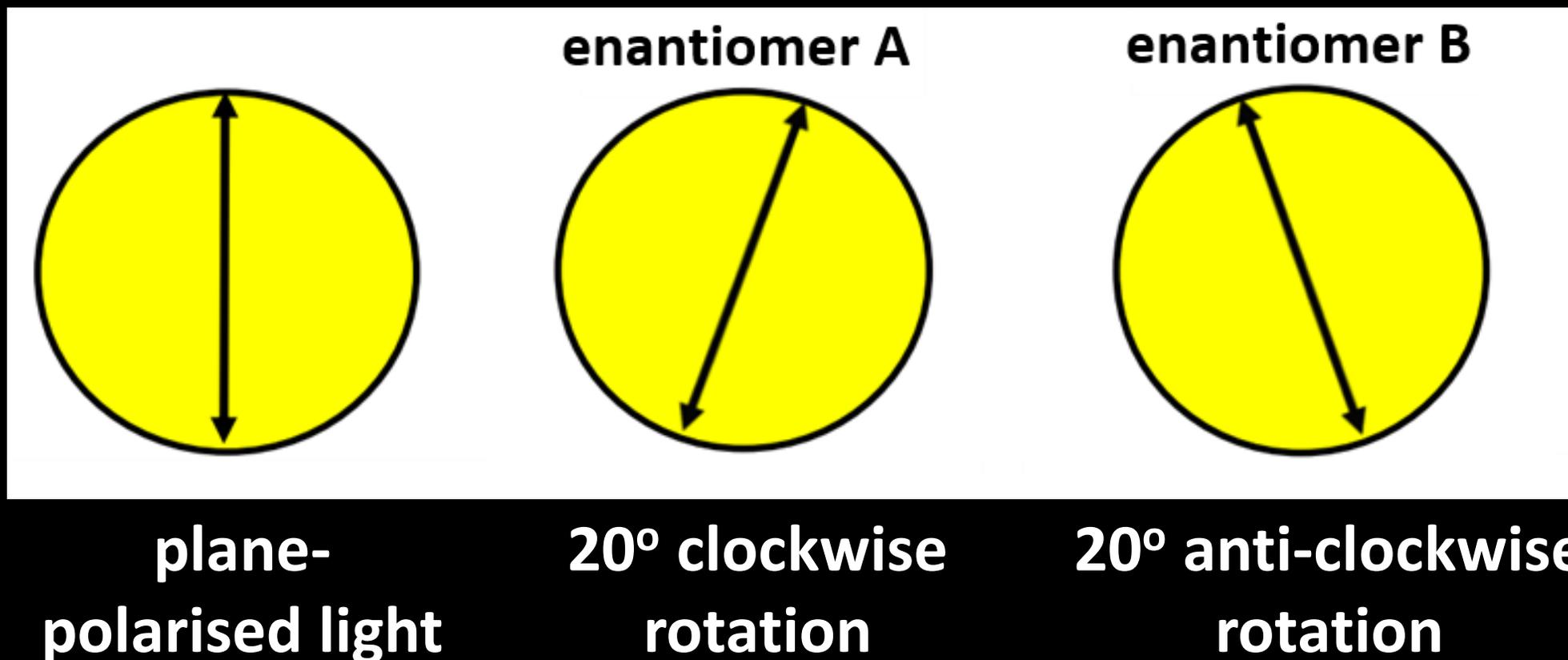
Ordinary light consists of waves that vibrate in all planes perpendicular to its direction of travel.

Plane-polarised light consists of waves vibrating in one plane only.

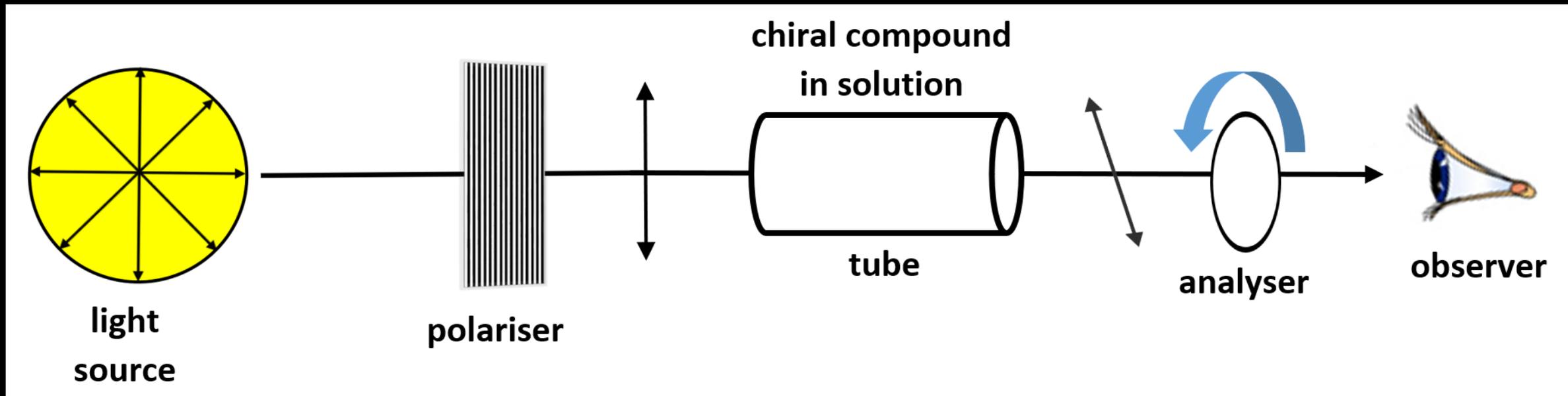


Optical isomerism

The two enantiomers of a chiral compound rotate the plane of plane-polarised light by the same angle but in opposite directions.



Optical isomerism



Plane-polarised light is passed through a tube containing a solution of the enantiomer.

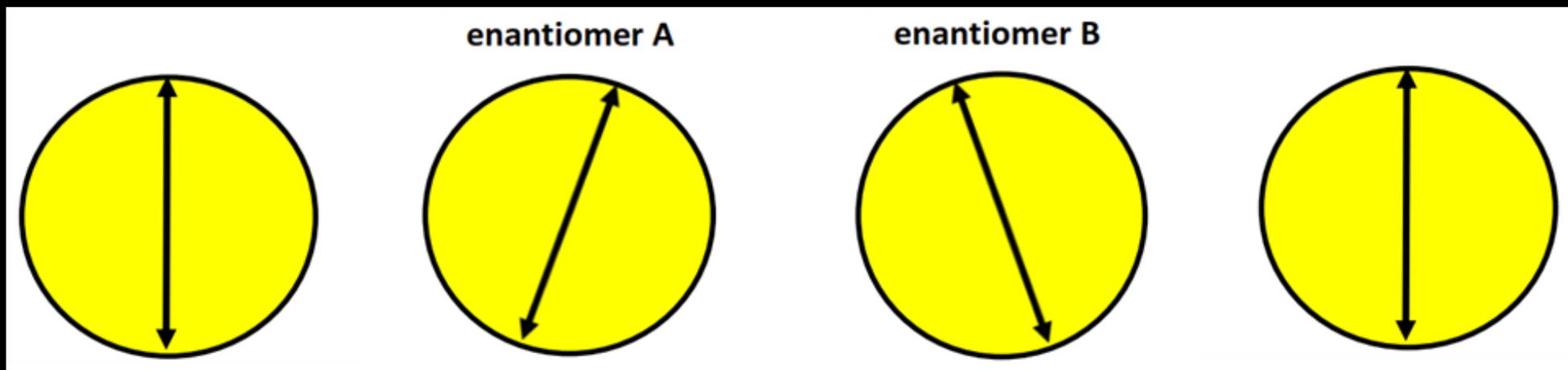
The plane of the plane-polarised light is rotated which then passes through the analyser.

The analyser is rotated until the light passes through and the angle and direction of rotation can be measured.

Optical isomerism

A solution containing equal amounts of both enantiomers is known as a racemic mixture (racemate).

If both enantiomers are present in equal amounts, the two rotations cancel out and the mixture is said to be optically inactive.



plane-
polarised light

20° clockwise
rotation

20° anti-clockwise
rotation

no overall
rotation

Optical isomerism

When chiral compounds are made in the laboratory, they often occur as a 50/50 mixture of the two enantiomers, which is optically inactive (no effect on plane-polarised light).

Biological processes within cells produce only one form of the enantiomer and are therefore optically active (rotate the plane of plane-polarised light).

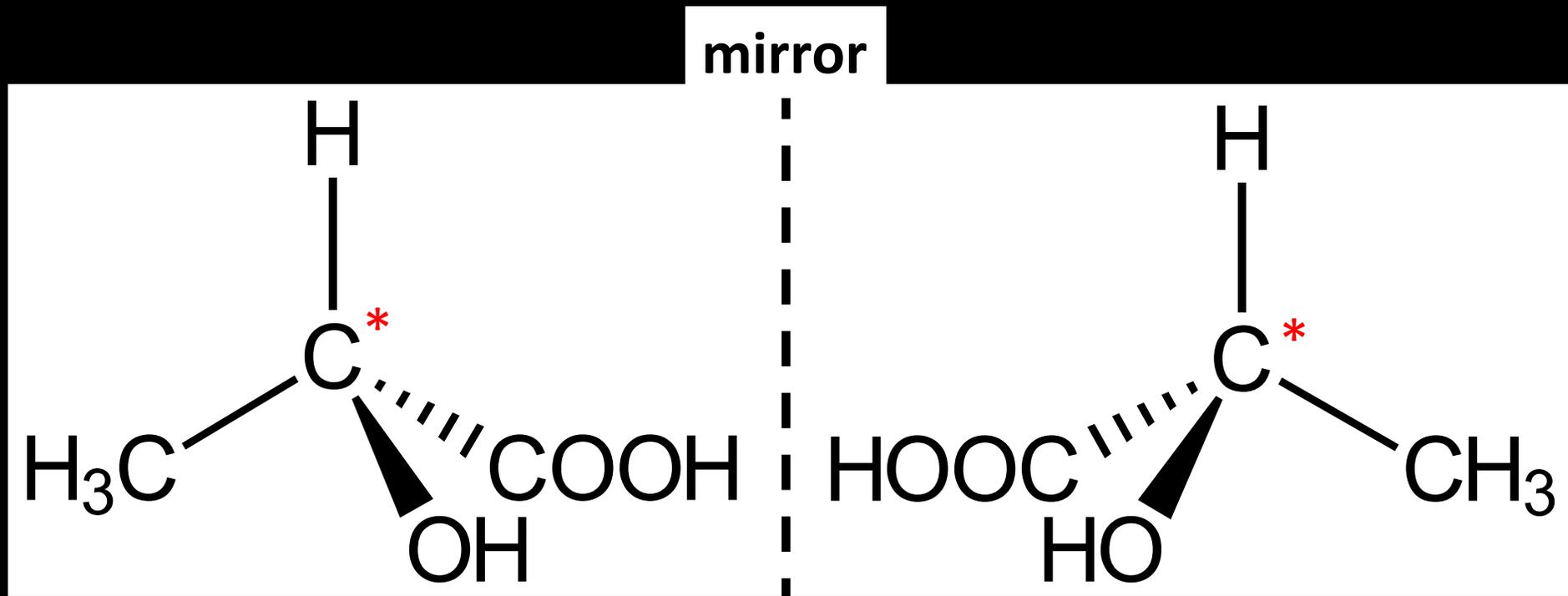
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Diastereomers

Enantiomers

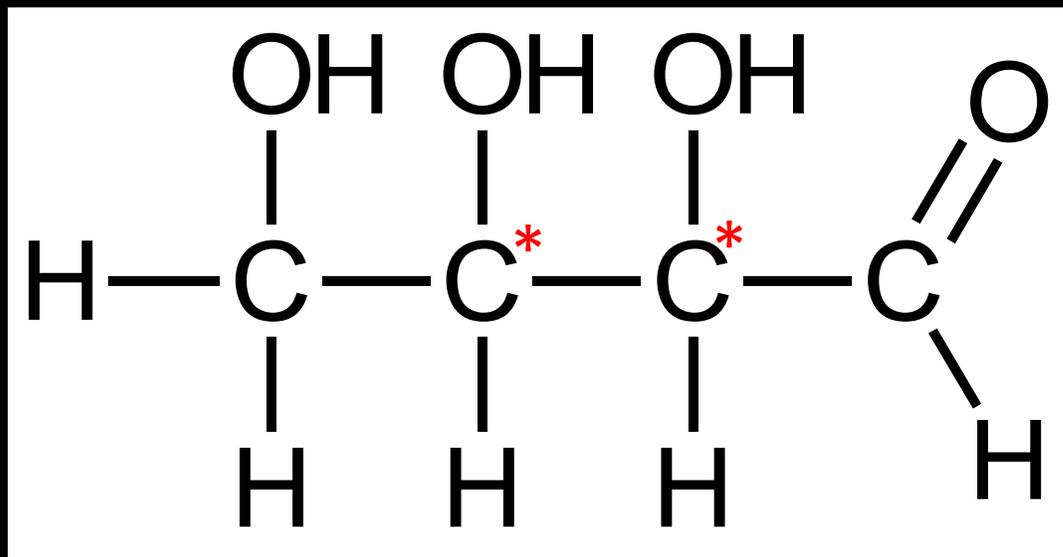
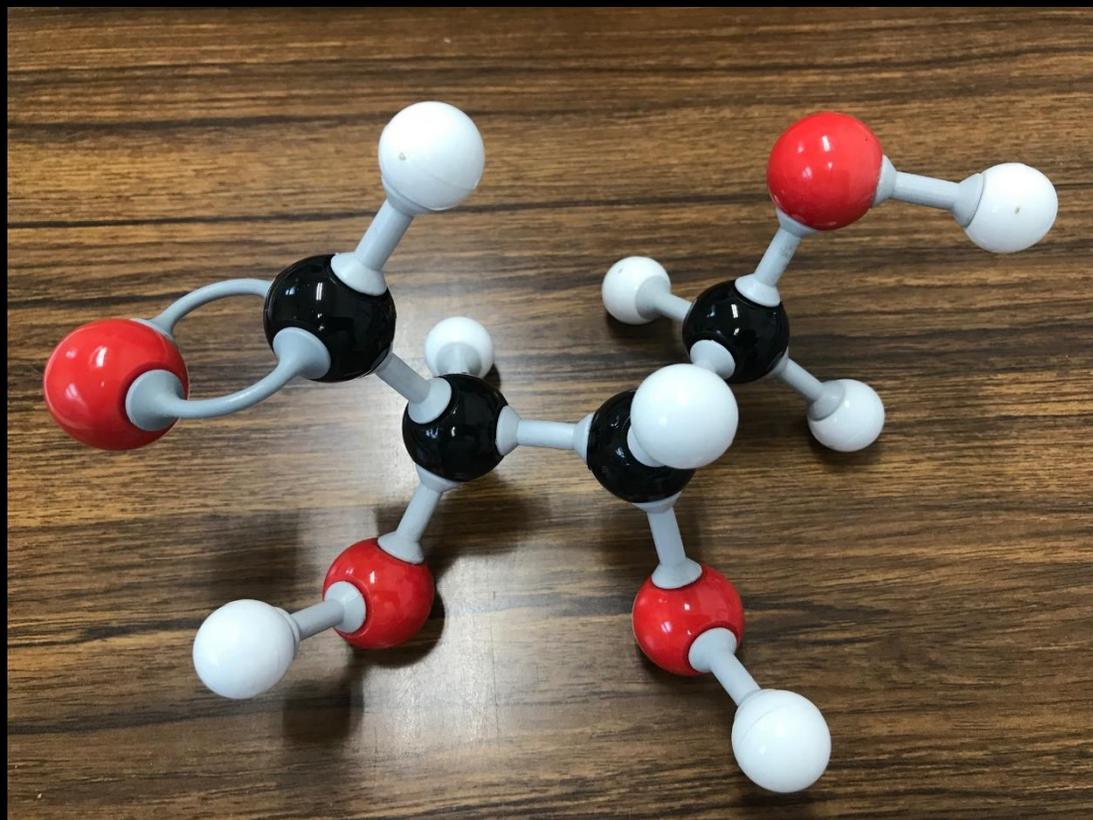
Enantiomers are stereoisomers that are mirror images of one another and are non-superimposable.



2-hydroxypropanoic acid (lactic acid)

Diastereomers

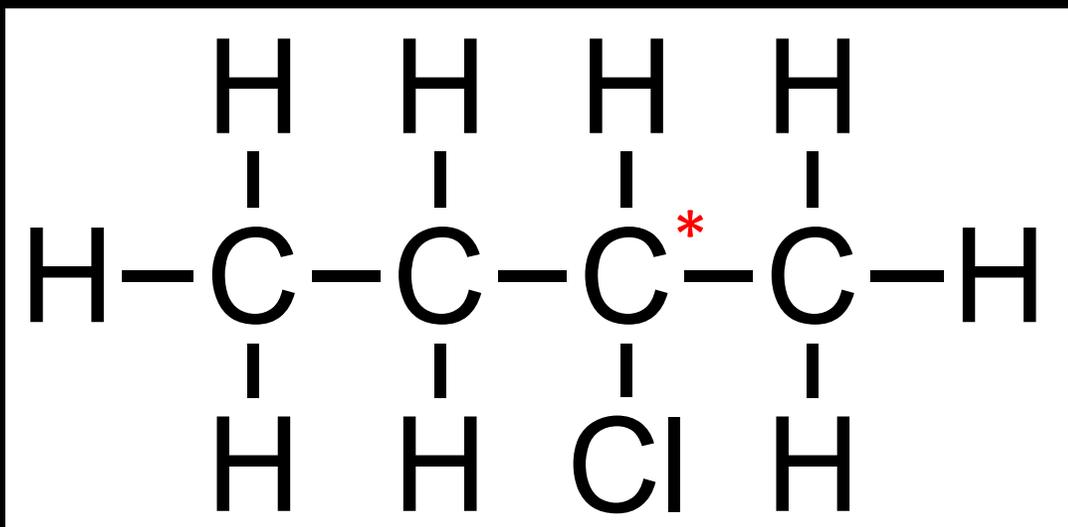
Diastereomers are stereoisomers that are not mirror images of one another and are non-superimposable.



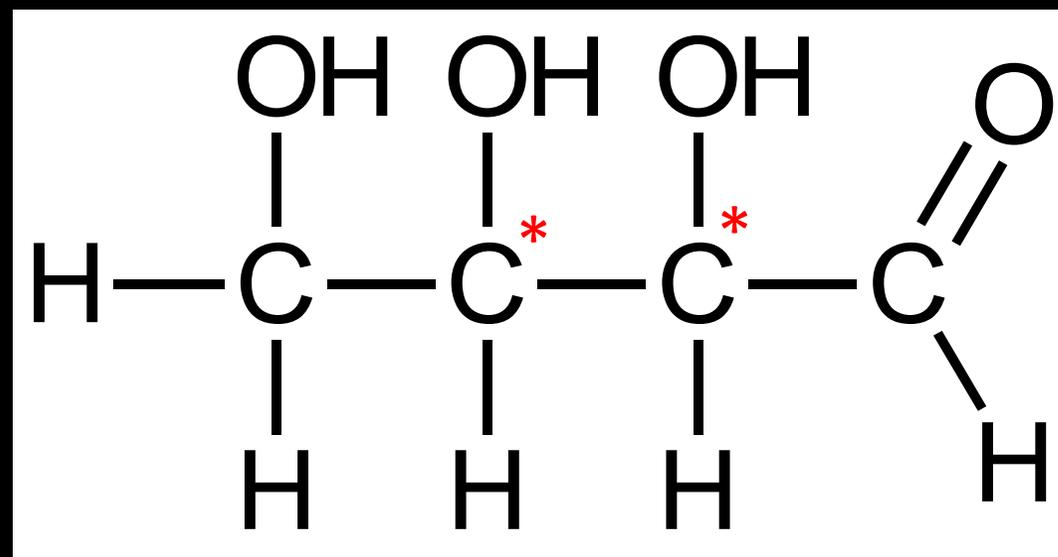
2,3,4-trihydroxybutanal

Diastereomers

The number of possible optical isomers for a chiral molecule is $2n$, where n is the number of chiral centres in the molecule.



2-chlorobutane

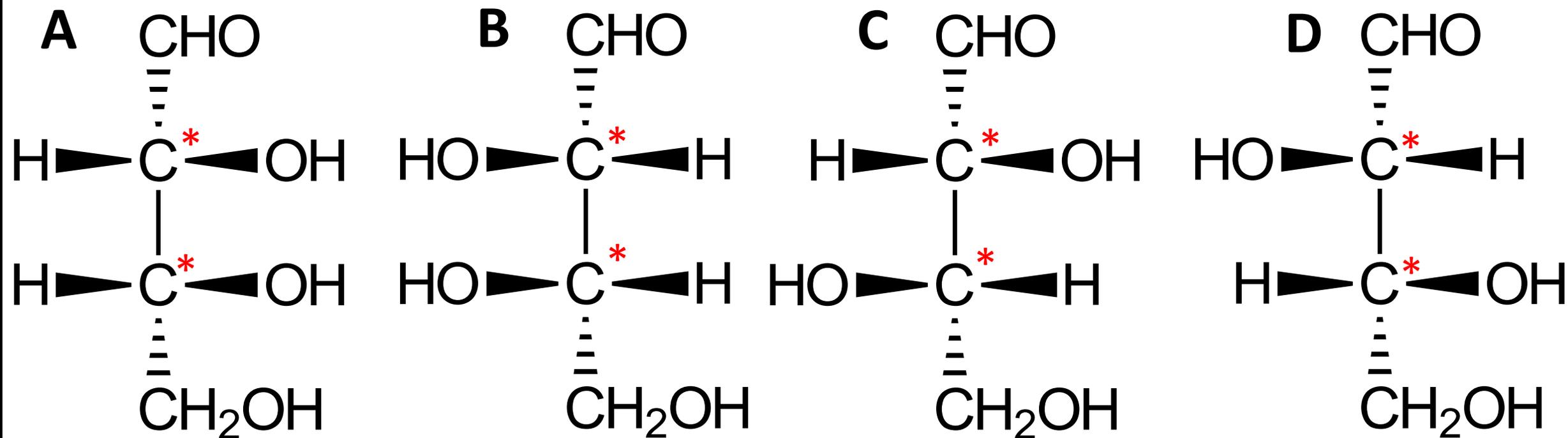


2,3,4-trihydroxybutanal

Diastereomers

A and B are enantiomers

C and D are enantiomers

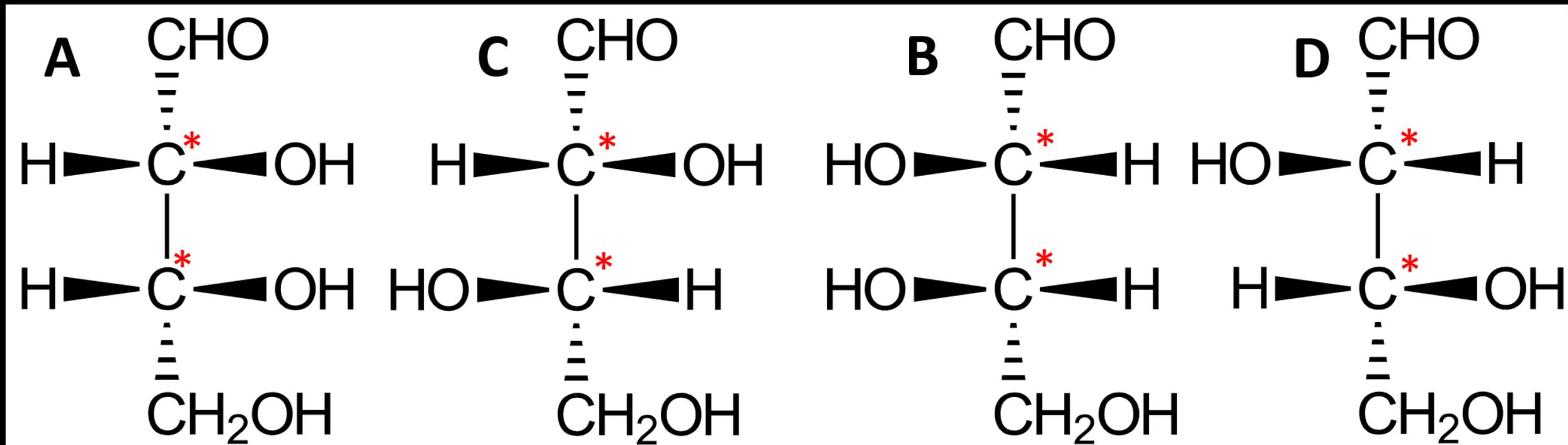


Enantiomers are mirror images and non-superimposable. They have opposite configurations at all chiral centres.

Diastereomers

A and C are diastereomers

B and D are diastereomers



Diastereomers are not mirror images and are non-superimposable. They have opposite configurations at some, but not all of the chiral centres.

Diastereomers

Enantiomers	Diastereomers
Are mirror images and are non-superimposable	Are not mirror images and are non-superimposable
Have one or more chiral centres	Have at least two chiral centres
Have opposite configurations at all chiral centres	Have opposite configurations at some, but not all chiral centres
Have the same physical and chemical properties	Have different physical and chemical properties
Are optically active	Not all diastereomers are optically active