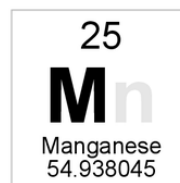
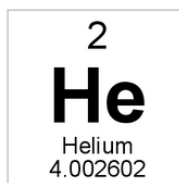
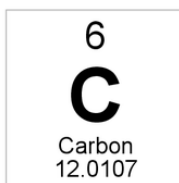
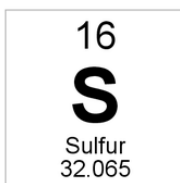
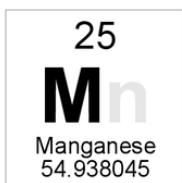


Organic Chemistry HL

IB CHEMISTRY HL



Understandings:

Nucleophilic Substitution Reactions:

- S_N1 represents a nucleophilic unimolecular substitution reaction and S_N2 represents a nucleophilic bimolecular substitution reaction. S_N1 involves a carbocation intermediate. S_N2 involves a concerted reaction with a transition state.
- For tertiary halogenoalkanes the predominant mechanism is S_N1 and for primary halogenoalkanes it is S_N2 . Both mechanisms occur for secondary halogenoalkanes.
- The rate determining step (slow step) in an S_N1 reaction depends only on the concentration of the halogenoalkane, $\text{rate} = k[\text{halogenoalkane}]$.
- For S_N2 , $\text{rate} = k[\text{halogenoalkane}][\text{nucleophile}]$.
- S_N2 is stereospecific with an inversion of configuration at the carbon.
- S_N2 reactions are best conducted using aprotic, polar solvents and S_N1 reactions are best conducted using protic, polar solvents.

Electrophilic Addition Reactions:

- An electrophile is an electron-deficient species that can accept electron pairs from a nucleophile. Electrophiles are Lewis acids.
- Markovnikov's rule can be applied to predict the major product in electrophilic addition reactions of unsymmetrical alkenes with hydrogen halides and interhalogens. The formation of the major product can be explained in terms of the relative stability of possible carbocations in the reaction mechanism.

Electrophilic Substitution Reactions:

- Benzene is the simplest aromatic hydrocarbon compound (or arene) and has a delocalized structure of π bonds around its ring. Each carbon to carbon bond has a bond order of 1.5. Benzene is susceptible to attack by electrophiles.

Reduction Reactions:

- Carboxylic acids can be reduced to primary alcohols (via the aldehyde). Ketones can be reduced to secondary alcohols. Typical reducing agents are lithium aluminium hydride (used to reduce carboxylic acids) and sodium borohydride.

Applications and skills:

Nucleophilic Substitution Reactions:

- Explanation of why hydroxide is a better nucleophile than water.
- Deduction of the mechanism of the nucleophilic substitution reactions of halogenoalkanes with aqueous sodium hydroxide in terms of S_N1 and S_N2 mechanisms.
- Explanation of how the rate depends on the identity of the halogen (ie the leaving group), whether the halogenoalkane is primary, secondary or tertiary and the choice of solvent.
- Outline of the difference between protic and aprotic solvents.

Electrophilic Addition Reactions:

- Deduction of the mechanism of the electrophilic addition reactions of alkenes with halogens/interhalogens and hydrogen halides

Electrophilic Substitution Reactions:

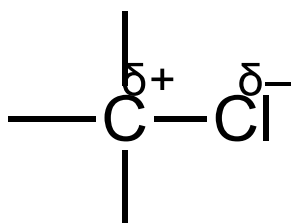
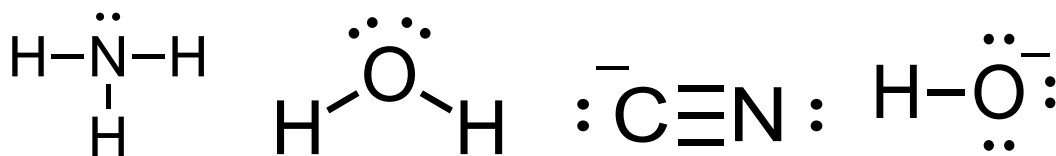
- Deduction of the mechanism of the nitration (electrophilic substitution) reaction of benzene (using a mixture of concentrated nitric acid and sulfuric acid).

Reduction Reactions:

- Writing reduction reactions of carbonyl containing compounds: aldehydes and ketones to primary and secondary alcohols and carboxylic acids to aldehydes, using suitable reducing agents.
- Conversion of nitrobenzene to phenylamine via a two-stage reaction.

Nucleophilic substitution reactions

- S_N stands for substitution nucleophilic reaction (the replacement of one atom by another atom or group).
- Nucleophiles are electron rich species that contain a lone pair of electrons that it donates to an electron deficient carbon.
- Examples of common nucleophiles are shown below.



The halogen is more electronegative than the carbon atom forming a polar bond.

The halogen has a partial negative charge and the carbon has a partial positive charge (electron deficient).

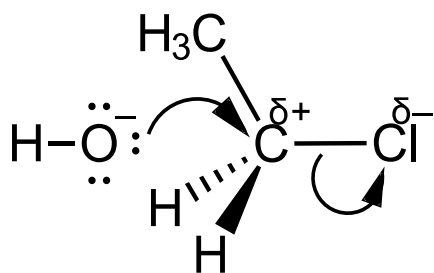
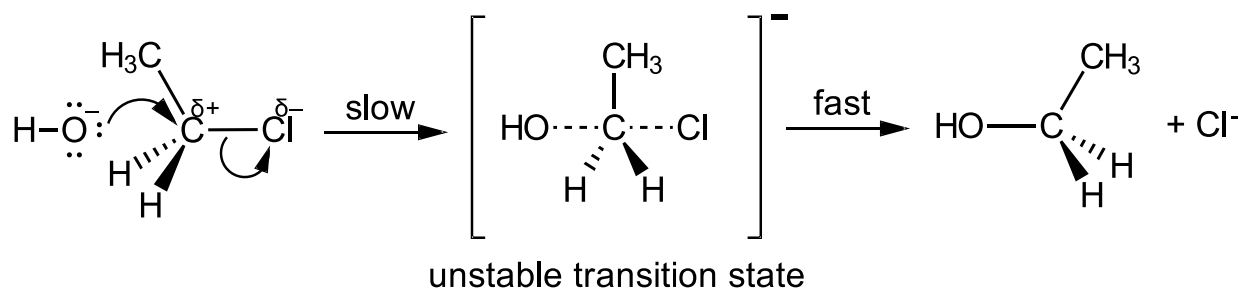
Water vs the hydroxide ion

- OH^- is a better nucleophile than H_2O because it has a negative charge whilst the water molecule only has a dipole.
- Therefore, OH^- is more strongly attracted to a region of positive charge and is a better nucleophile than water.

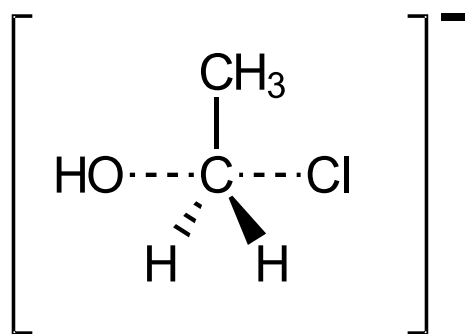


S_N2 - nucleophilic bimolecular substitution reaction

- Primary halogenoalkanes undergo S_N2 reactions.
- It is a one-step reaction that involves the formation of an unstable transition state.

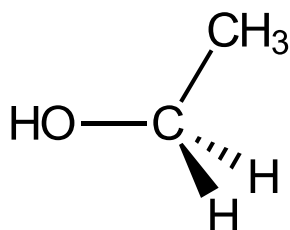


The nucleophile (OH⁻) attacks on the opposite side of the leaving group (Cl⁻) via a backside attack.



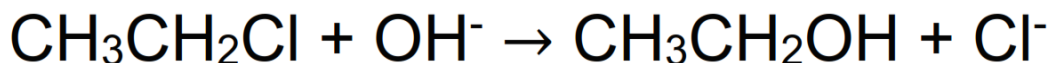
An unstable transition state is formed in which the carbon is weakly bonded to the halogen and the nucleophile.

unstable transition state



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

- Overall equation is shown below:



- The reaction conditions for $\text{S}_{\text{N}}1$ and $\text{S}_{\text{N}}2$ reactions are warm with aqueous NaOH.

Reaction kinetics

- The $\text{S}_{\text{N}}2$ reaction is bimolecular; the rate determining step (slow step) depends on both the concentration of the halogenoalkane and the nucleophile.

$$\text{rate} = k [\text{halogenoalkane}] [\text{nucleophile}]$$

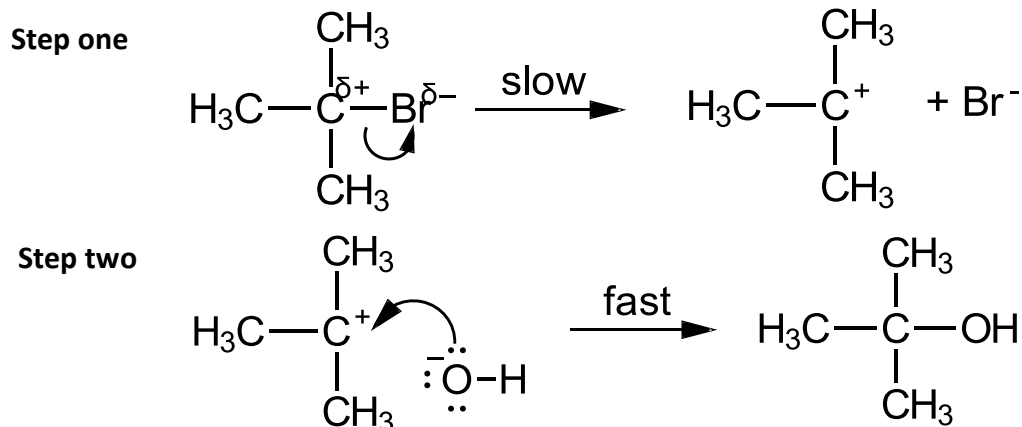
$$\text{rate} = k [\text{CH}_3\text{CH}_2\text{Cl}] [\text{OH}^-]$$

Type of solvent

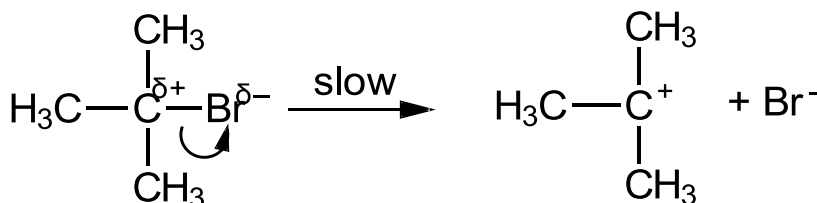
- The $\text{S}_{\text{N}}2$ mechanism is favoured by polar aprotic solvents.
- This is because the polar protic solvents decrease nucleophilic reactivity due to hydrogen bonding. $\text{S}_{\text{N}}2$ reactions are favoured by **polar aprotic** solvents. The nucleophile is not solvated, leaving it 'free' therefore maintaining its effectiveness as a nucleophile.
- Aprotic solvents are not able to form hydrogen bonds as they lack O-H or N-H bonds.
- Suitable solvents include propanone $(\text{CH}_3)_2\text{CO}$ and ethanenitrile (CH_3CN) .

S_N1 - nucleophilic unimolecular substitution reaction.

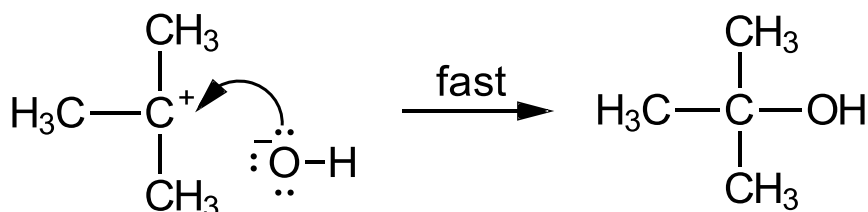
- Tertiary halogenoalkanes undergo S_N1 reactions.
- It is a two-step reaction that involves the formation of a carbocation intermediate.



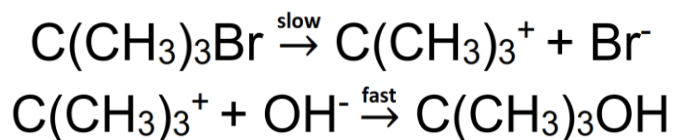
- The presence of the 3 alkyl groups around the carbon – halogen bond make it difficult for an incoming group to attack this carbon (steric hindrance).



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



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



Reaction kinetics

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

$$\text{rate} = k [\text{halogenoalkane}]$$

$$\text{rate} = k [\text{C}(\text{CH}_3)_3\text{Br}]$$

Type of solvent

- The $\text{S}_{\text{N}}1$ mechanism is favoured by polar, protic solvents.
- Protic solvents are able to form hydrogen bonds as they have O-H or N-H bonds.
- Polar protic solvents favour $\text{S}_{\text{N}}1$ reactions as the carbocation intermediate is solvated by ion-dipole interactions by the polar solvent.
- Suitable solvents include water, alcohols and carboxylic acids.

Rates of reaction of nucleophilic substitution reactions

The effect of the leaving group (halogen)

- 1) The polarity of the carbon-halogen bond** – the electronegativity of the halogens decreases as you go down the group, therefore the polarity of the C-X also decreases. This means that the carbon becomes less electron deficient and therefore less vulnerable to attack from a nucleophile.
 - 2) The strength of the carbon – halogen bond** – the C-X bond strength decreases as you go down the group. As the substitution reaction involves breaking this bond, iodoalkane is the most reactive and the fluoroalkane is the least reactive.
- The strength of the carbon-halogen bond dominates the outcome, so the relative rate of reaction is iodoalkane > bromoalkane > chloroalkane > fluoroalkane

The class of halogenoalkane

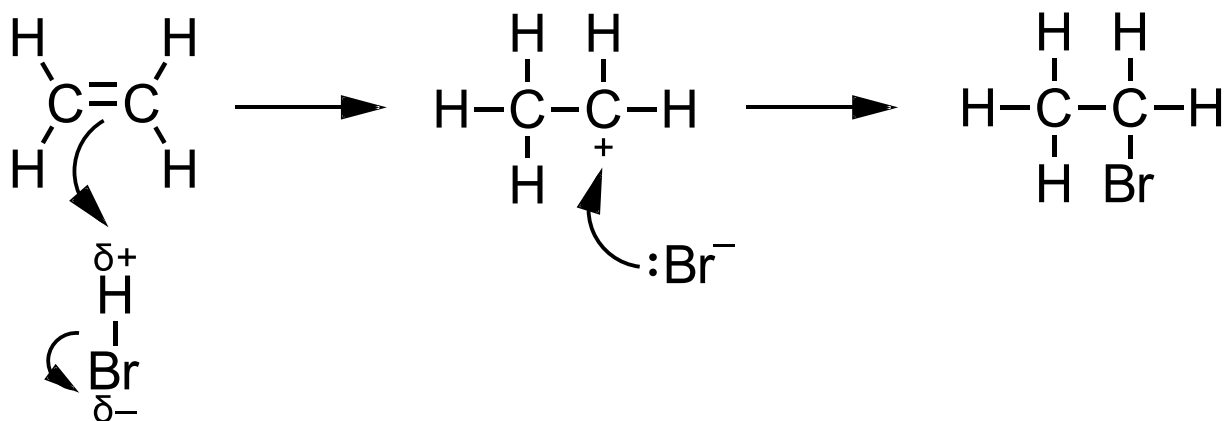
- The $\text{S}_{\text{N}}1$ mechanism, characteristic of tertiary halogenoalkanes is faster than the $\text{S}_{\text{N}}2$ mechanism, characteristic of primary halogenoalkanes.

tertiary > secondary > primary

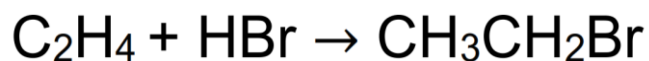
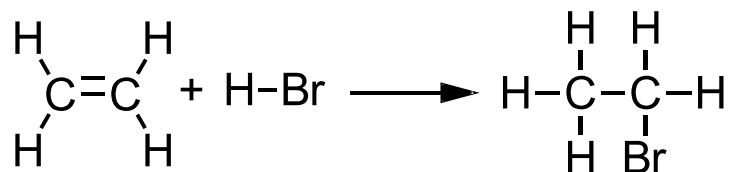
Electrophilic addition reactions

- 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).

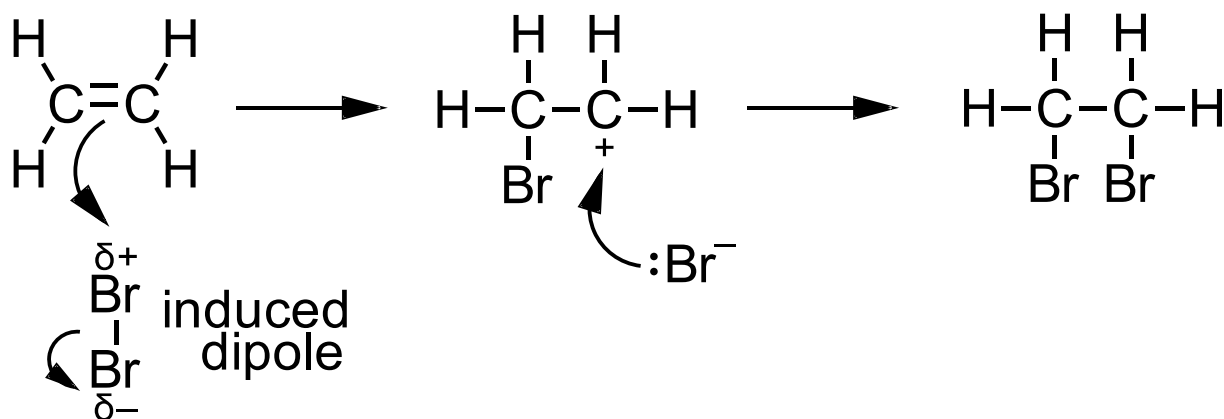
Reaction with HBr



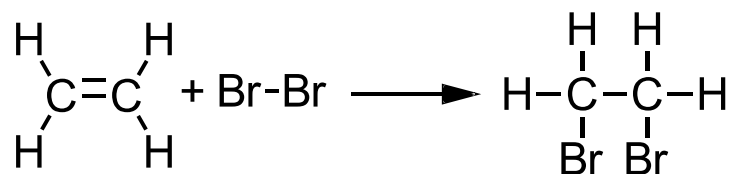
- H-Br is a polar molecule; the hydrogen atom is attracted to the $\text{C}=\text{C}$ double bond.
- The H-Br bond breaks heterolytically forming a bromide ion.
- At the same time, the H atom bonds to one of the C atoms forming a carbocation.
- The carbocation then combines with the Br^- ion forming bromoethane.



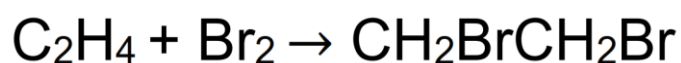
Reaction with Br₂



- 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.

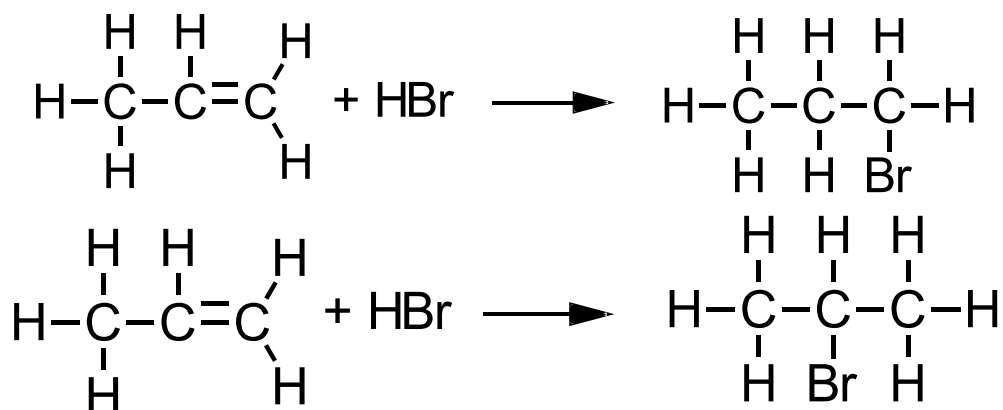


Overall equation:

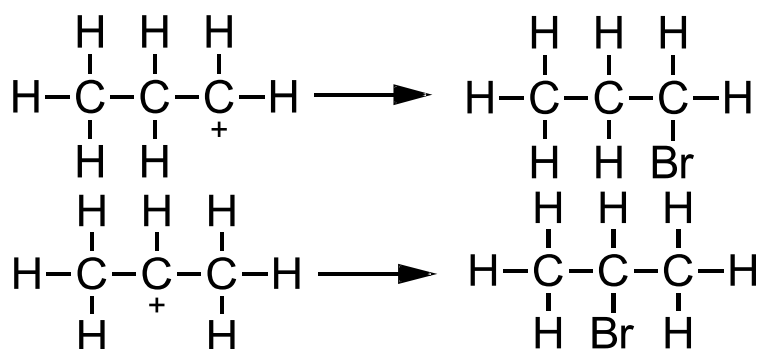


Markovnikov's rule

- When propene (an unsymmetrical alkene) reacts with hydrogen bromide, there are two possible products.



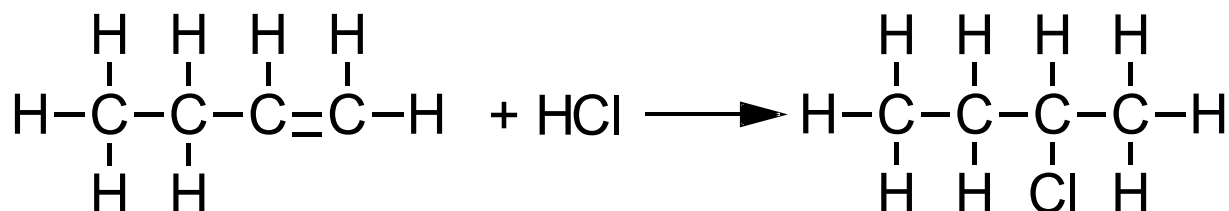
- The product formed depends on the stability of the carbocation



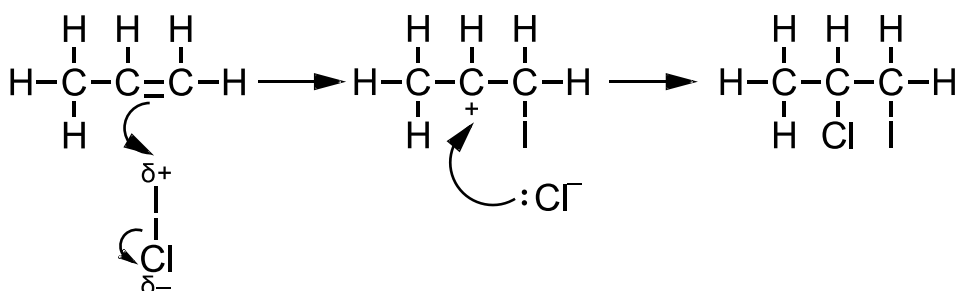
The primary carbocation is less stable than the secondary carbocation.

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

- The major product will be 2-bromopropane because of the stability of the secondary carbocation (due to the positive inductive effect).
- When an unsymmetrical alkene reacts with a hydrogen halide, the hydrogen adds to the carbon that is already bonded to the greatest number of hydrogens.

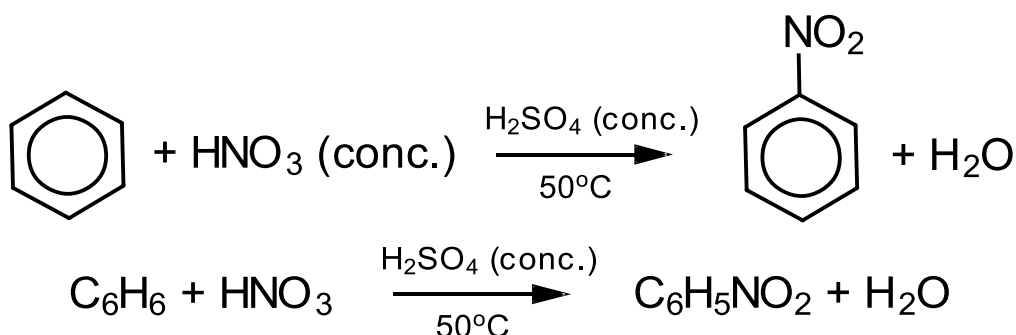


- When an unsymmetrical alkene reacts with an interhalogen (I-Cl), the electrophilic portion of the molecule bonds to the carbon that is bonded to the greatest number of hydrogens (mechanism shown below).

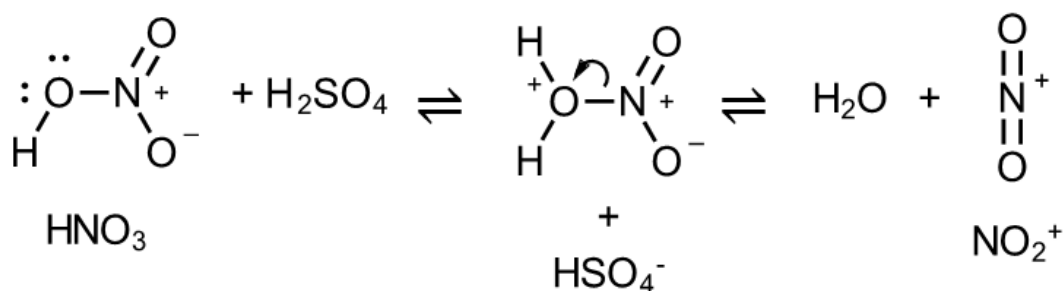


Nitration of benzene (electrophilic substitution reaction)

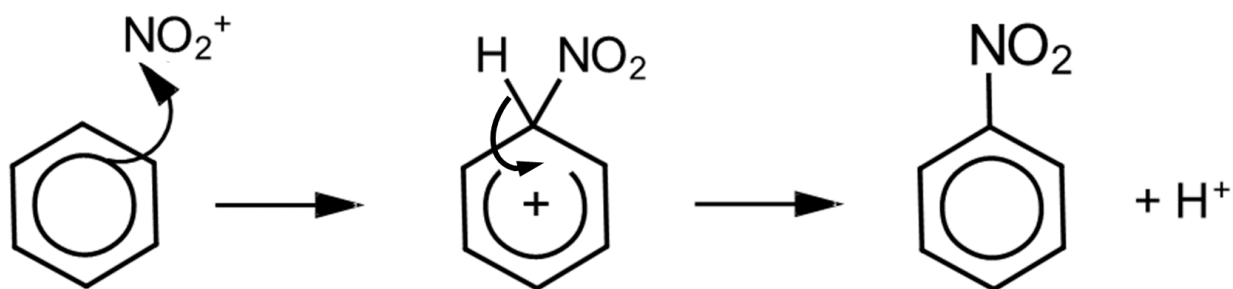
- Benzene reacts with a mixture of concentrated nitric acid (HNO_3) and concentrated sulfuric acid (H_2SO_4) to form nitrobenzene ($\text{C}_6\text{H}_5\text{NO}_2$) and water.



- The concentrated H_2SO_4 acts as a catalyst.
- The mixture of concentrated nitric acid and concentrated sulfuric acid is known as a nitrating mixture.
- The sulfuric acid protonates the nitric acid, which then loses a molecule of water to form the nitronium ion (NO_2^+).

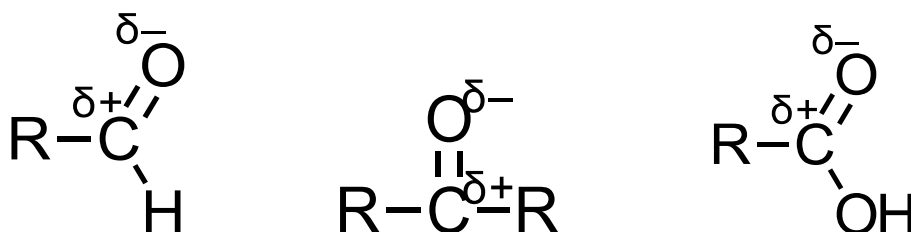


Reaction mechanism



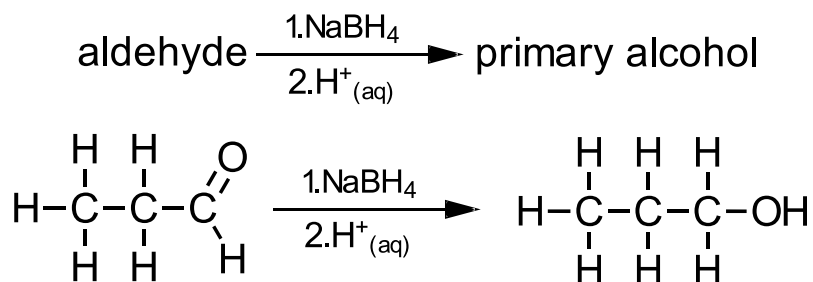
- NO_2^+ is a strong electrophile and is attracted to the delocalized π electron cloud in benzene. It then reacts with the π electrons to form a carbocation intermediate.
- The loss of a hydrogen ion (proton) leads to the reformation of the arene ring in the nitrobenzene. The hydrogen ion released reacts with the HSO_4^- to reform the sulfuric acid catalyst.

Reduction of carbonyl compounds

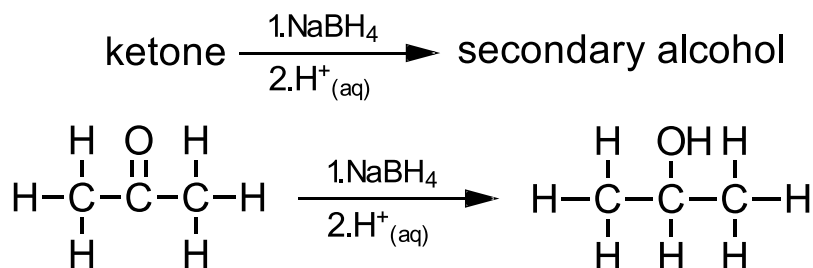


- The carbon to oxygen bond is a polar bond because of the difference in electronegativity between carbon and oxygen.
- Primary and secondary alcohols can be oxidized to aldehydes, ketones or carboxylic acids depending on the conditions.
- These oxidation reactions can be reversed by using a suitable 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.

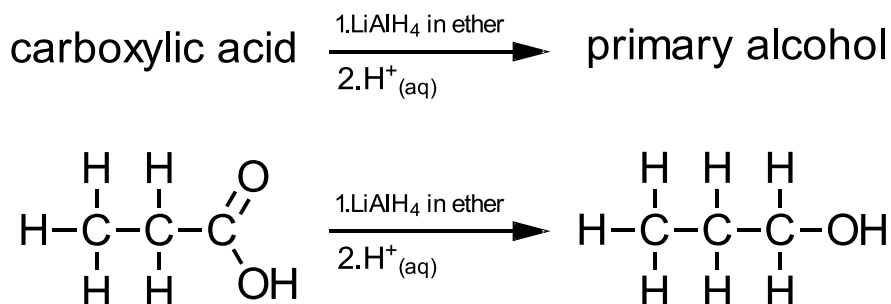
Reduction of aldehyde to primary alcohol



Reduction of ketone to secondary alcohol



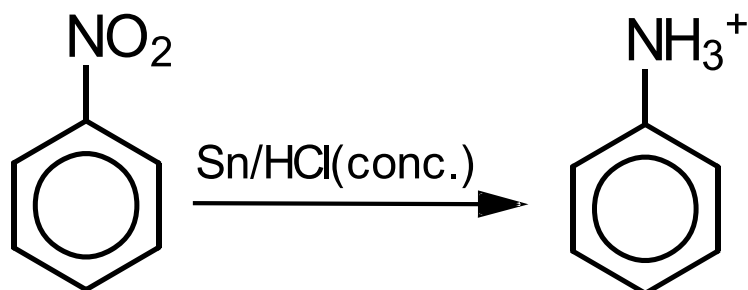
Reduction of carboxylic acid to primary alcohol



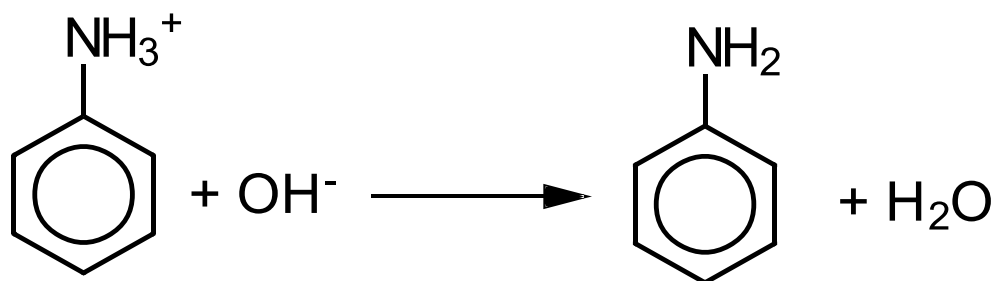
- Conditions: heat with LiAlH_4 in dry ether, then acidify (NaBH_4 is not a strong enough reducing agent to reduce carboxylic acids).

Reduction of nitrobenzene

- Nitrobenzene ($\text{C}_6\text{H}_5\text{NO}_2$) can be reduced to phenylamine ($\text{C}_6\text{H}_5\text{NH}_2$) in a two-stage reaction.
- Stage 1 – $\text{C}_6\text{H}_5\text{NO}_2$ is reacted with Sn and concentrated HCl (heat under reflux in a boiling water bath).
- The product is the phenylammonium ion ($\text{C}_6\text{H}_5\text{NH}_3^+$)



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



20.2 Synthetic routes

Understandings:

- The synthesis of an organic compound stems from a readily available starting material via a series of discrete steps. Functional group interconversions are the basis of such synthetic routes.
- Retro-synthesis of organic compounds.

Applications and skills:

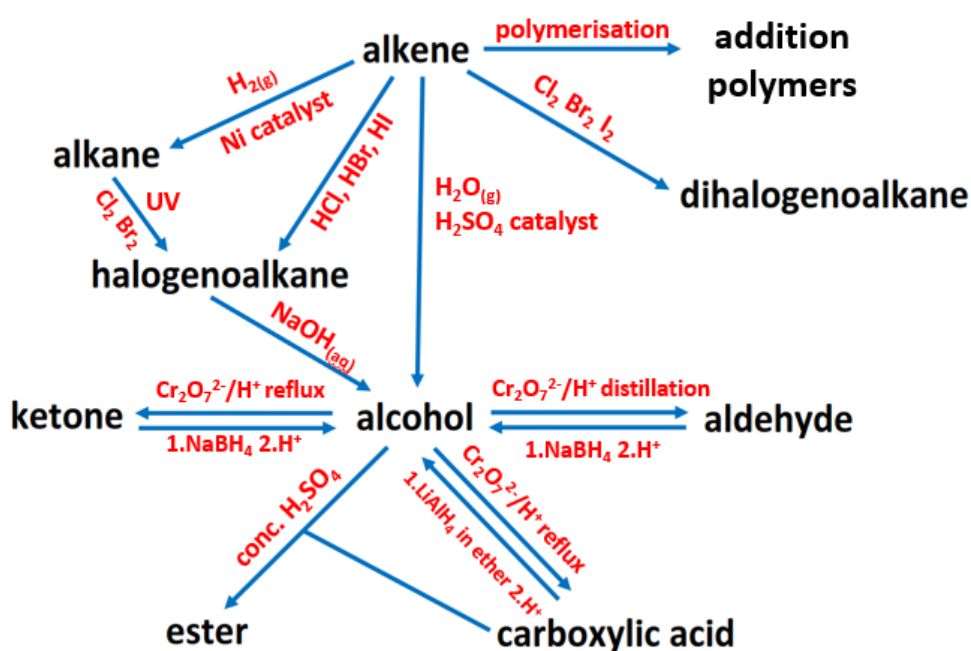
- Deduction of multi-step synthetic routes given starting reagents and the product(s).

Guidance:

- Conversions with more than four stages will not be assessed in synthetic routes.
- Reaction types can cover any of the reactions covered in topic 10 and sub-topic 20.1.

Synthetic routes

- Below is a summary of all the synthetic routes in SL and HL (excluding the reactions of benzene).



Exercises

Outline the steps including all the reactants and conditions for the following synthesis:

- The conversion of but-2-ene to butanone.
- The conversion of 2-chloroethane to ethanoic acid.

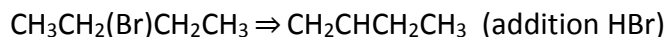
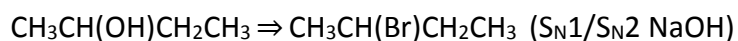
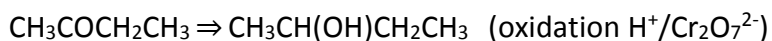
Retrosynthesis

- 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).
- Retro-synthesis involves thinking backwards from relatively complex molecules to simpler ones.

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

Example:

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



Exercises

Outline the steps involved in the retro-synthesis of the following:

1. Propanoic acid from 1-bromopropane.

2. Ethanol from an alkane.

20.3 Stereoisomerism

- Stereoisomers are subdivided into two classes—conformational isomers, which interconvert by rotation about a σ bond and configurational isomers that interconvert only by breaking and reforming a bond.
- Configurational isomers are further subdivided into cis-trans and E/Z isomers and optical isomers.
- Cis-trans isomers can occur in alkenes or cycloalkanes (or heteroanalogues) and differ in the positions of atoms (or groups) relative to a reference plane. According to IUPAC, E/Z isomers refer to alkenes of the form $R_1R_2C=CR_3R_4$ ($R_1 \neq R_2$, $R_3 \neq R_4$) where neither R_1 nor R_2 need be different from R_3 or R_4 .
- A chiral carbon is a carbon joined to four different atoms or groups.
- An optically active compound can rotate the plane of polarized light as it passes through a solution of the compound. Optical isomers are enantiomers. Enantiomers are non-superimposable mirror images of each other. Diastereomers are not mirror images of each other.
- A racemic mixture (or racemate) is a mixture of two enantiomers in equal amounts and is optically inactive.

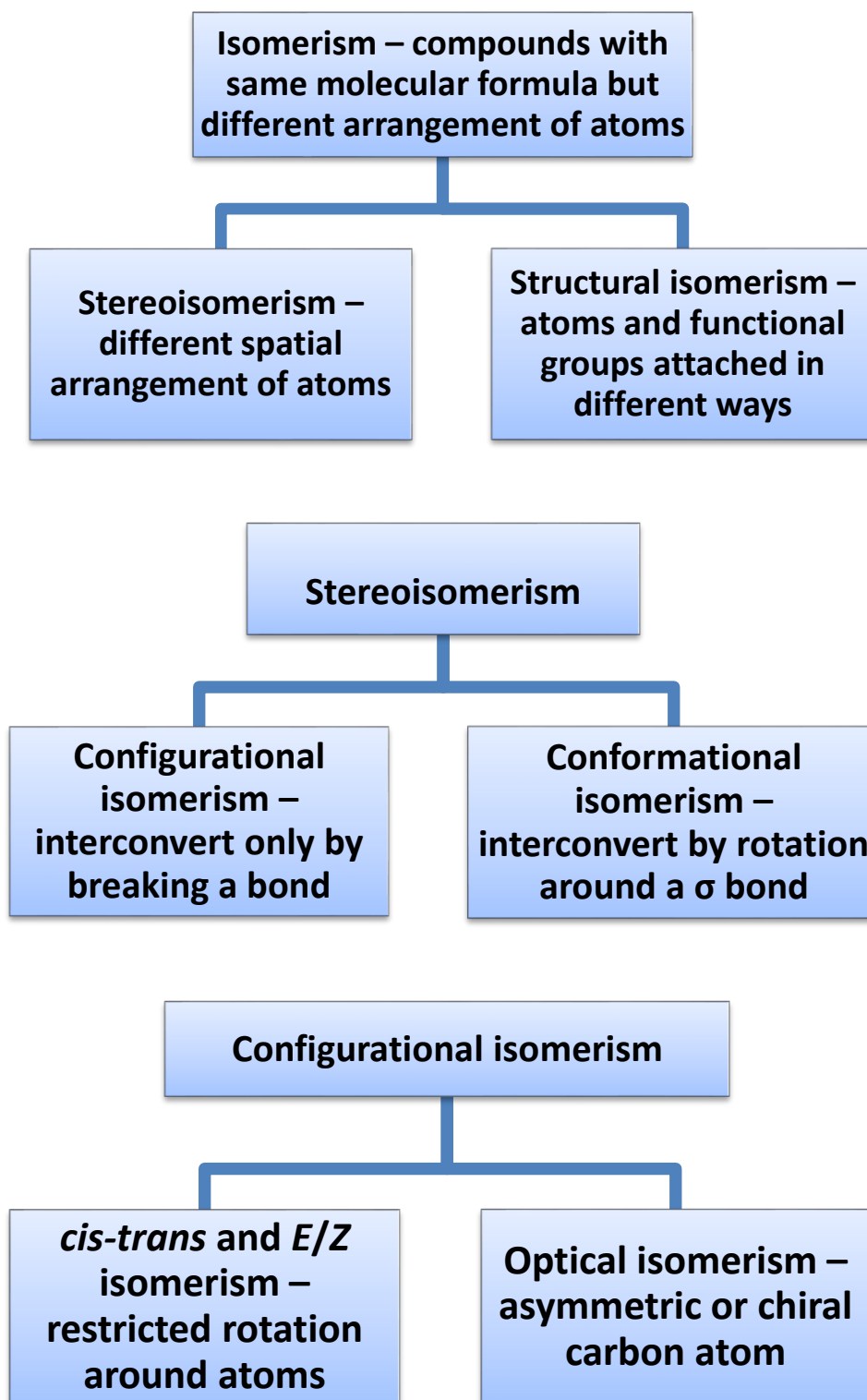
Applications and skills:

- Construction of 3-D models (real or virtual) of a wide range of stereoisomers
- Explanation of stereoisomerism in non-cyclic alkenes and C₃ and C₄ cycloalkanes.
- Comparison between the physical and chemical properties of enantiomers.
- Description and explanation of optical isomers in simple organic molecules.
- Distinction between optical isomers using a polarimeter.

Guidance:

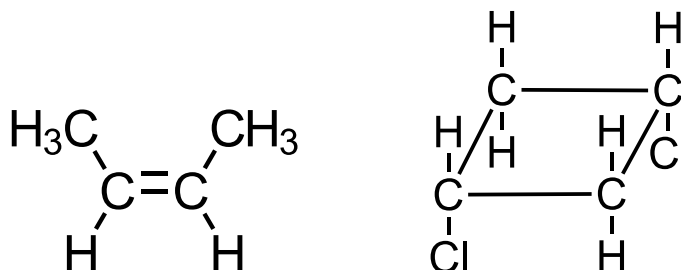
- The term geometric isomers as recommended by IUPAC is now obsolete and cis-trans isomers and E/Z isomers should be encouraged in the teaching programme.
- In the E/Z system, the group of highest Cahn–Ingold–Prelog priority attached to one of the terminal doubly bonded atoms of the alkene (ie R_1 or R_2) is compared with the group of highest precedence attached to the other (ie R_3 or R_4). The stereoisomer is Z if the groups lie on the same side of a reference plane passing through the double bond and perpendicular to the plane containing the bonds linking the groups to the double-bonded atoms; the other stereoisomer is designated as E.
- Wedge-dash type representations involving tapered bonds should be used for representations of optical isomers.

Types of isomerism



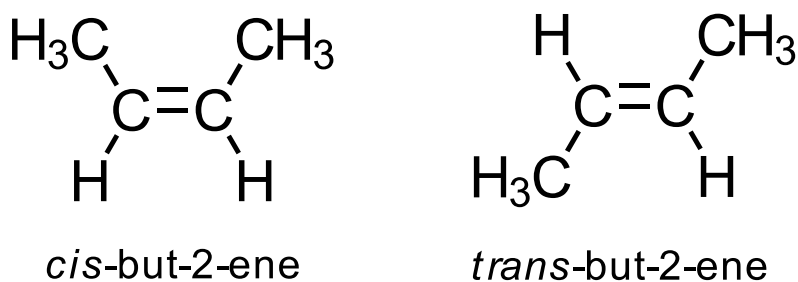
***cis-trans* isomerism**

- cis-trans* isomerism occurs where there is restricted rotation around a bond either because of a double bond or as a result of the ring structure in a cyclic molecule.



Molecules with carbon to carbon double bonds

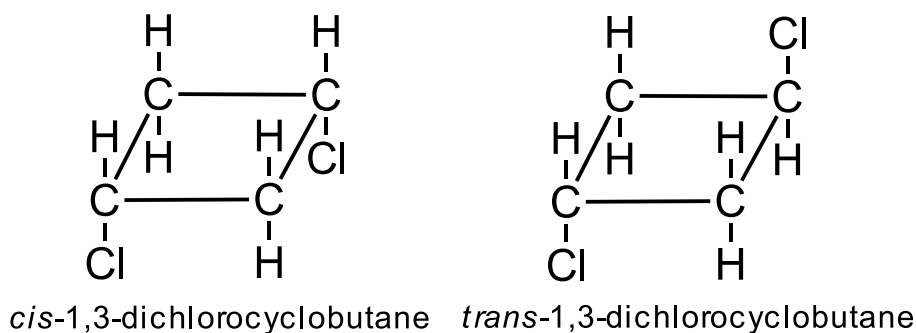
- The π bond in the carbon to carbon double bond restricts rotation, forming two different isomers.



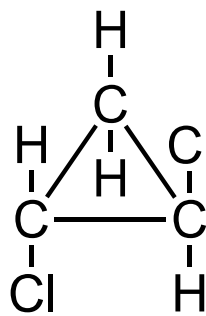
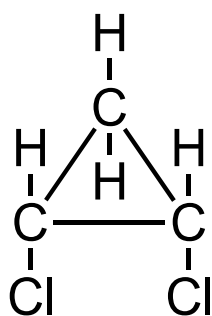
- cis* isomers have the same groups on the same side of the double bond, *trans* isomers have the same groups on opposite sides of the double bond.

Cyclic structures

- Cycloalkanes contain a ring structure that restricts rotation.
- When the molecule contains two or more different groups attached to the ring, two different isomers are formed.



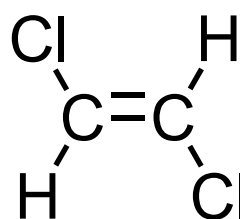
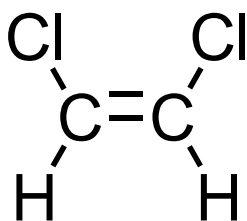
- cis* isomers have the same groups on the same side of the ring, *trans* isomers have the same groups on opposite sides of the ring.



cis-1,2-dichlorocyclopropane trans-1,2-dichlorocyclopropane

Physical properties of cis-trans isomers

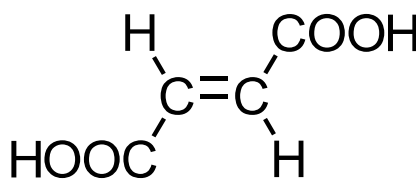
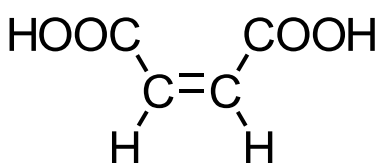
polar molecule
B.P 60 °C
M.P -80 °C



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).

M.P.
139 °C

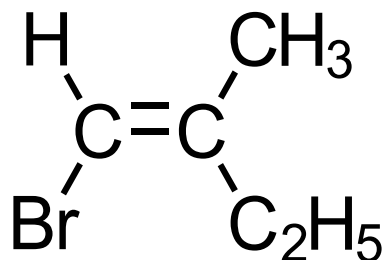


M.P.
287 °C

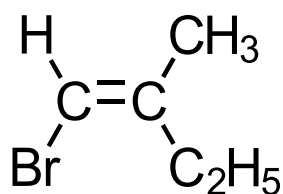
- The cis-isomer forms intramolecular hydrogen bonds (within the molecule).
- The trans-isomer forms intermolecular hydrogen bonds (between molecules).

***E/Z* isomerism**

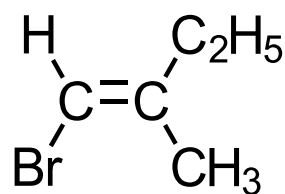
- *E/Z* isomerism is based on the Cahn-Ingold-Prelog (CIP) rules of priority which assign priority to each atom or group of atoms around the double bond.



- The atom (or group of atoms) attached to the carbon atoms of the double bond with the higher atomic number have priority.
- If both of the highest priority groups are on the same side of the double bond, it is the *Z* isomer.
- If the highest priority groups are on opposite sides of the double bond, it is the *E* isomer.



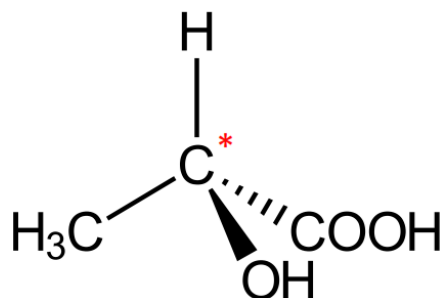
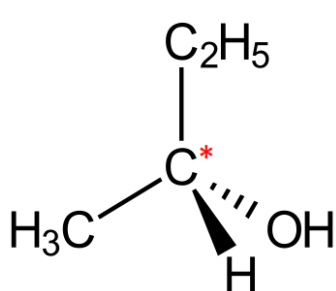
[*Z*]-1-bromo-2-methylbut-1-ene



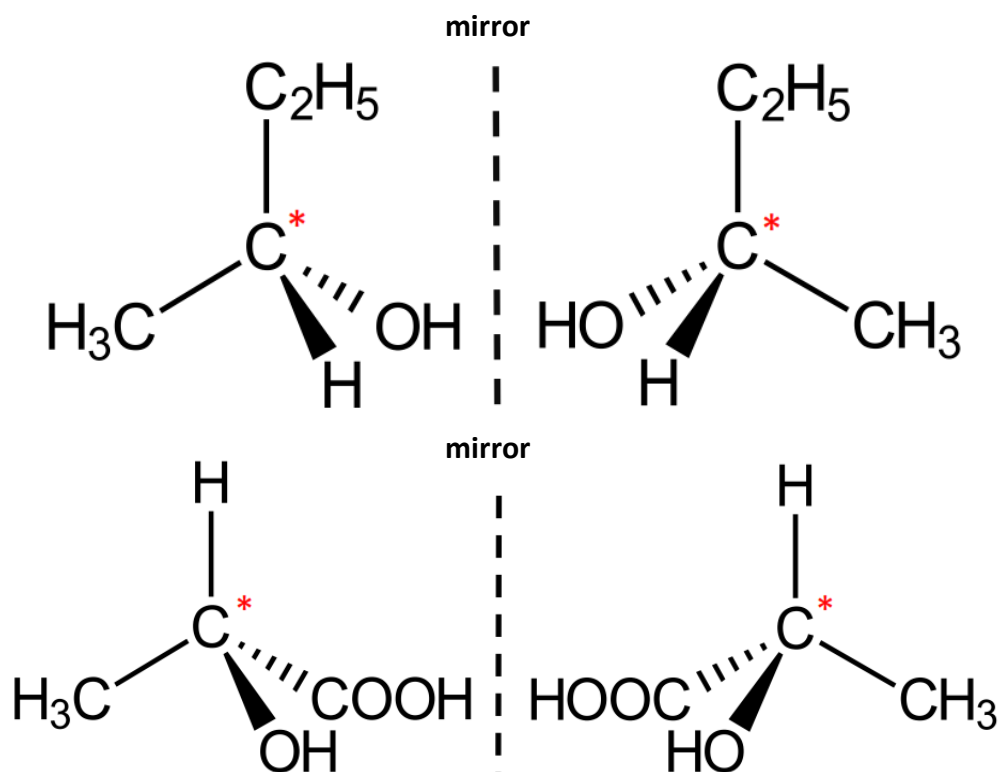
[*E*]-1-bromo-2-methylbut-1-ene

Optical isomerism

- Optical isomerism is shown by compounds that have a chiral or asymmetric carbon within the molecule.
- A chiral carbon is a carbon atom bonded to four different atoms or groups.



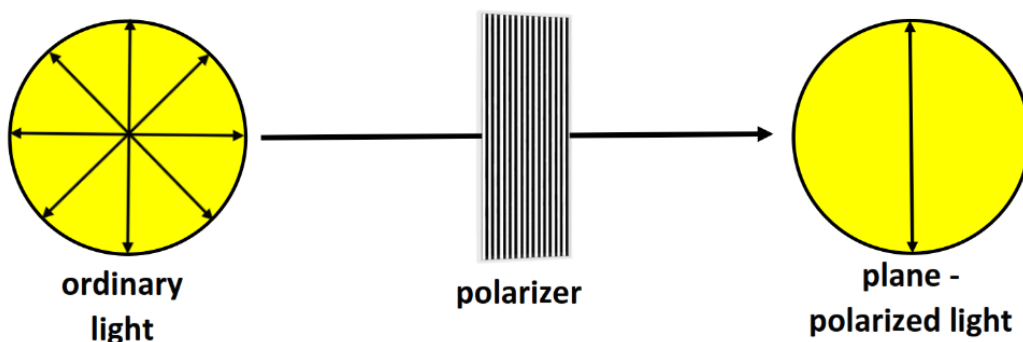
- The four groups can be arranged in two three dimensional configurations which are mirror images of each other.
- The two mirror images are non-superimposable and are known as enantiomers.



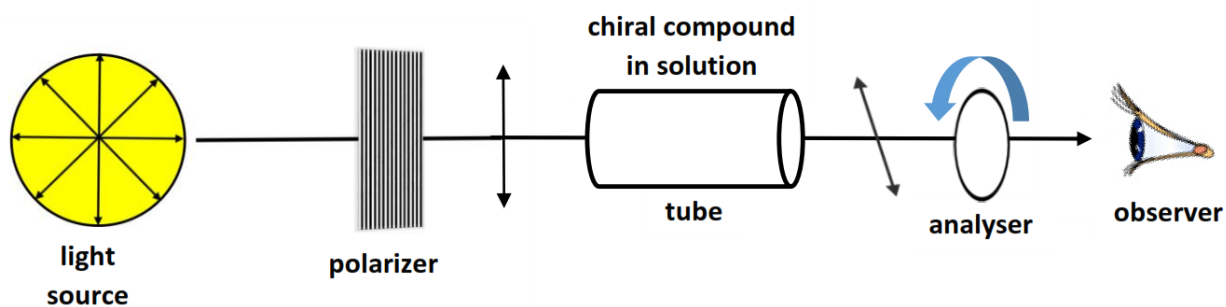
- The two optical isomers (enantiomers) are optically active with plane-polarized light - they rotate the plane of plane-polarized light in opposite directions.

Plane-polarized light

- Ordinary light consists of waves that vibrate in all planes perpendicular to its direction of travel.
- Plane-polarized light consists of waves vibrating in one plane only.

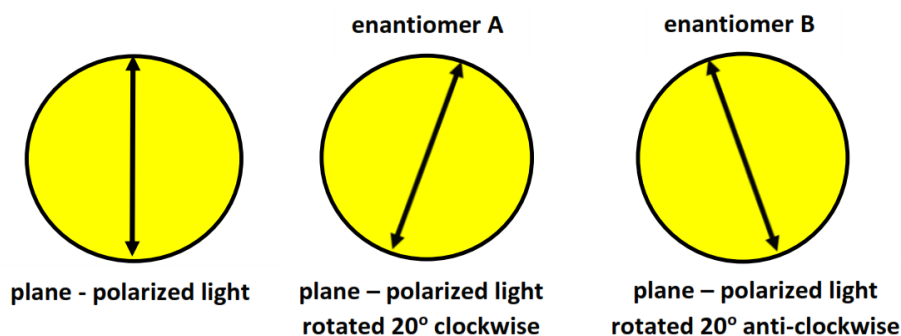


Use of polarimeter



- Plane-polarized light is passed through a tube containing a solution of optical isomers.
- The plane of the plane-polarized light is rotated which then passes through the analyser.
- The analyser is rotated until the light passes through and the extent and direction of rotation can be determined.

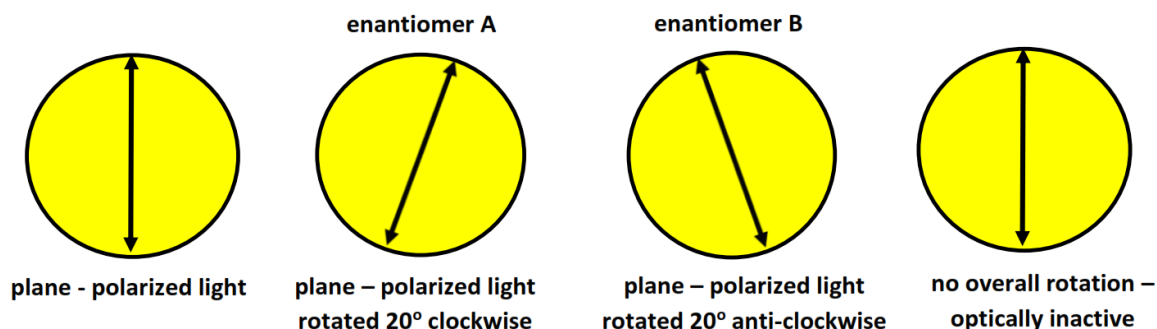
Rotation of plane-polarized light



- The two enantiomers of a chiral compound rotate the plane of plane-polarized light in equal amounts but in opposite directions.

- This property can be used to distinguish between the two enantiomers of a chiral compound.

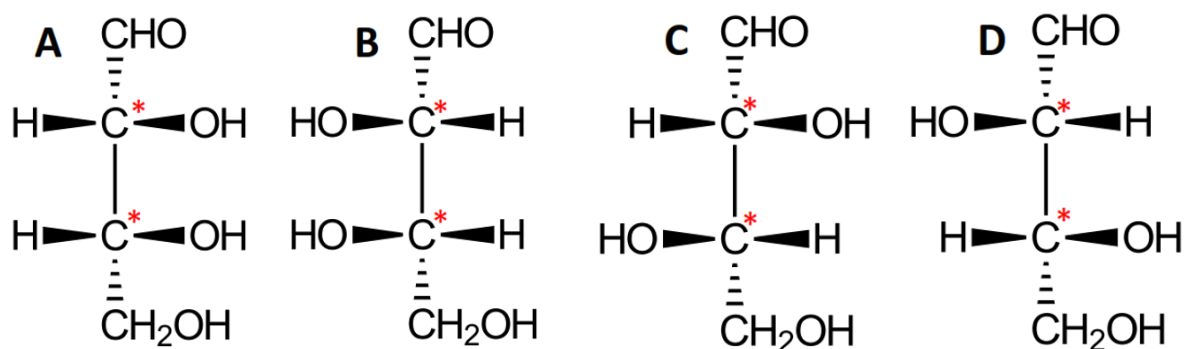
Racemic mixture



- 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 each other out and the mixture is said to be optically inactive.
- When optically active substances 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-polarized light).
- Biological processes within cells produce only one form of the enantiomer and are therefore optically active (rotate the plane of plane-polarized light).

Diastereomers

- Enantiomers have opposite configurations at both chiral centres – they are mirror images of each other.
- Compounds A and B and C and D are enantiomers – mirror images of each other.



- Diastereomers have opposite configurations at only one chiral centre – they are not mirror images of each other.
- Compounds A and B below are enantiomers, but B and D are diastereomers; they have opposite configurations at only one chiral centre.

