

Kirkcaldy High School



Chemistry

Advanced Higher

Unit 3 - Organic Chemistry and

Instrumental Analysis

NOTES

Course Overview

Contents

The Advanced Higher Chemistry Course is split into four units. *Italic* shows the contents of this notes booklet.

Unit 1 - Inorganic Chemistry

- (a) Electromagnetic radiation and atomic spectra
- (b) Atomic orbitals, electronic configurations and the periodic table
- (c) Transition Metals

Unit 2 - Physical Chemistry

- (a) Chemical Equilibrium
- (b) Reaction Feasibility
- (c) Kinetics

Unit 3 - Organic Chemistry and Chemical Analysis

- (a) *Molecular Orbitals* *page 3*
- (b) *Synthesis* *page 11*
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- (d) *Experimental Determination of structure* *page 62*
- (e) *Pharmaceutical Chemistry* *page 77*

Unit 4 - Researching Chemistry

- (a) Weighing by difference and gravimetric analysis
- (b) Preparing a standard
- (c) Using a reference or control or blank determination
- (d) Carrying out a complexometric titration
- (e) Carrying out a back titration
- (f) Using a colorimeter or visible spectrophotometer and carrying out dilution to prepare a calibration graph
- (g) Distilling
- (h) Refluxing
- (i) Using vacuum filtration methods
- (j) Recrystallising
- (k) Determining % yield experimentally
- (l) Using thin-layer chromatography
- (m) Using melting point apparatus and mixed melting point determination
- (n) Using a separating funnel and solvent extraction
- (o) Carrying out stoichiometric calculations
- (p) Volumetric Analysis
- (q) Scientific Precision and Uncertainties

Assessment

- There is a **final exam** for Advanced Higher Chemistry. It lasts for 3 h and contains 110 marks scaled to a total of 120. There are.
 - 25 marks of multiple-choice questions
 - 85 marks of written answer questions
- There is a **Project** to write for Advanced Higher Chemistry.
 - The Assignment is **externally marked** by an SQA marker (NOT your teacher)
 - The Assignment contains **25 marks**, but these are scaled to 40 marks such that the assignment is worth one quarter of the total marks.
 - You have unlimited **time to research** and gather data for your Assignment.
 - It must contain data and analysis from experiments you have carried out.

(a) Molecular Orbitals

Combining Atomic Orbitals

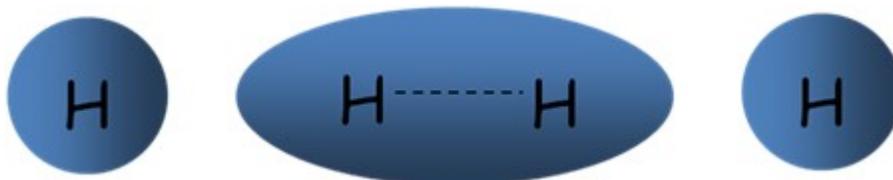
Orbitals can be used to explain the bonding between atoms. Atomic orbitals are the volume of space that the electrons of an atom are likely to be found in.



1s atomic orbitals of hydrogen

When atoms approach each other their separate sets of atomic orbitals merge to form a single set.

The overlap of the 2 atomic orbitals creates molecular orbitals which can be called Bonding Molecular Orbitals.



In the above example, the overlap of two 1s atomic orbitals of hydrogen result in the bonding molecular orbital being formed.

The attraction of positive nuclei to negative electrons occupying bonding molecular orbitals is the basis of bonding between atoms.

Each bonding molecular orbital can accommodate a maximum of 2 electrons - Similarities with the idea of covalent bonding depending on the sharing of a pair of electrons.

Hybridisation

Hybridisation is the process of mixing atomic orbitals within an atom to generate a set of new atomic orbitals called hybrid orbitals.

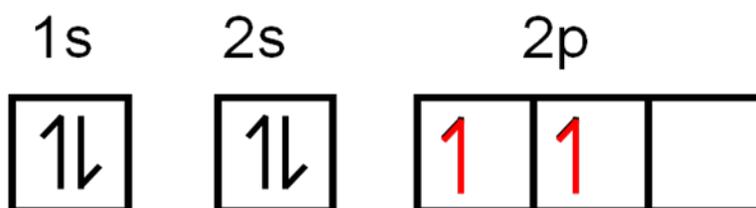
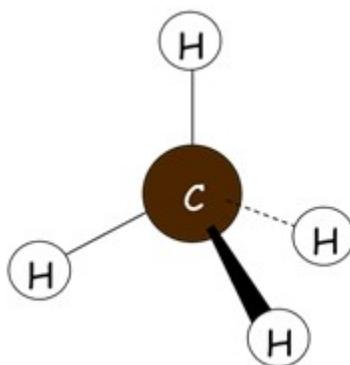
Hybridisation and the basis of covalent bonding can be explained by the concept of hydrocarbons.

Hydrocarbons

Hydrocarbons are compounds composed solely of hydrogen and carbon. We have previously met the familiar homologous series of alkanes, alkenes, cycloalkanes and alkynes.

Alkanes are saturated hydrocarbons which fit the general formula C_nH_{-2n+2} . This means that every carbon atom in an alkane molecule will have 4 single covalent bonds and as we have previously studied have the famous tetrahedral shape.

However, looking at the electron arrangement of a carbon atom in its ground state we see it only has 2 half filled orbitals.

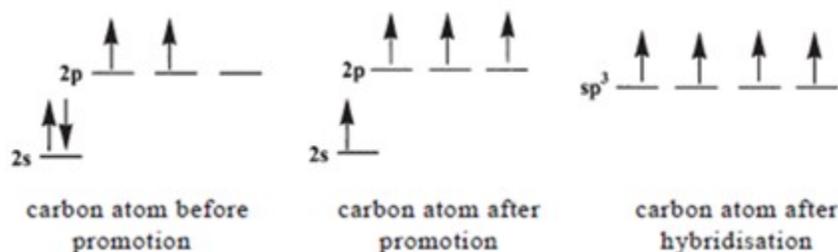


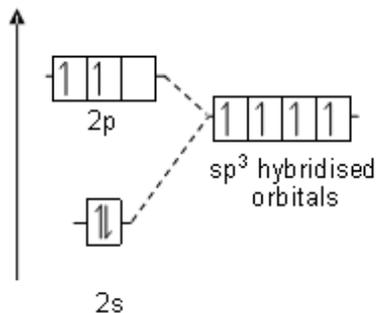
The 2 electrons in the 2p orbitals will individually occupy 2 out of the 3 p orbitals according to **hunds rule**. Therefore if there are only 2 unpaired electrons we would suspect that a carbon atom would create only 2 covalent bonds, clearly this is not the case.

The concept of hybrid orbitals can be used to explain this. These hybrid orbitals are produced from mixing together atomic orbitals in order to produce a new set of orbitals.

In each carbon atom in methane and in other alkanes, the 2s orbital and all three 2p orbitals mix to create four equivalent hybrid orbitals.

The 2s and 2p sublevels are close in energy. One of the 2s electrons has to be promoted to the third 2p orbital. This results in a carbon atom containing four singly occupied orbitals, which can be mixed to produce four hybrid orbitals of equal energy.





The hybrid orbitals found in the carbon atoms of alkane molecules are formed from **one s** orbital and **three p** orbitals. These are known as sp^3 orbitals.

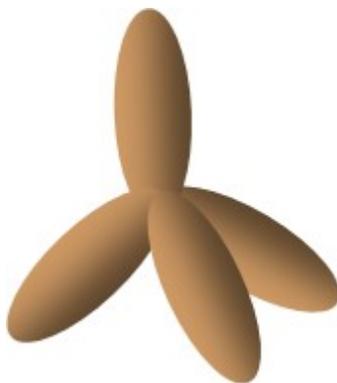


An sp^3 orbital

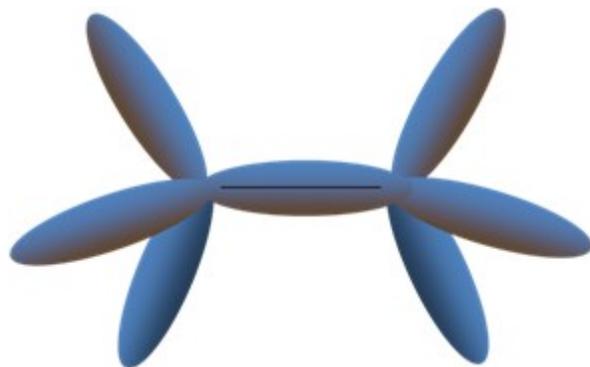
The sp^3 orbitals formed are all half-filled, with the electron far more likely to be found in the larger lobe. When drawn, the smaller lobe is often omitted.

Since electrons repel each other, the four sp^3 hybridised orbitals surrounding a central carbon atom result in a familiar tetrahedral shape, with a maximum possible angle between each orbital of 109.5° .

In methane, all four hybrid orbitals are used to form σ bonds between the central carbon atom and hydrogen atoms. Carbon-to-carbon single bonds in alkanes result from overlapping sp^3 orbitals forming σ bonds.



Sigma - σ bonds are covalent bonds formed by end-on overlap of two atomic orbitals and since σ bonds must lie along the line joining both atoms, there will be free rotation around these orbitals.



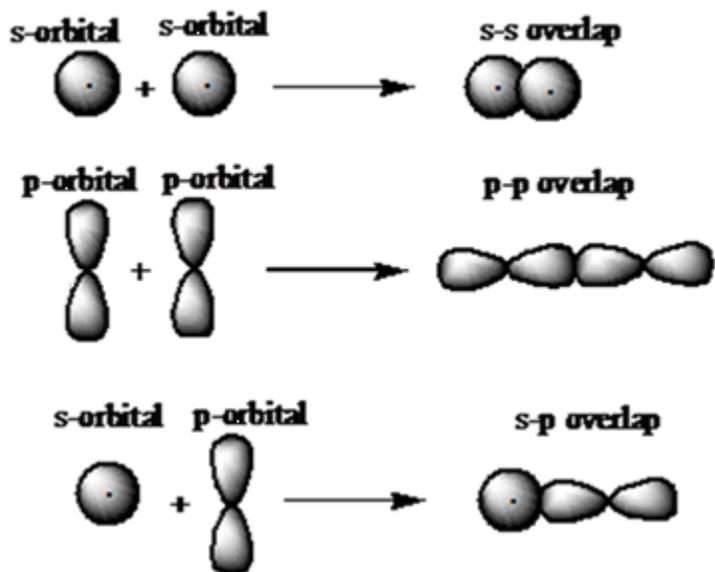
Sigma Bond



Remember that a covalent bond is formed when 2 half filled atomic orbitals come together and overlap. If they overlap along the axis of the bond (“end on”), a covalent bond known as a sigma bond is created.

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Sigma bond formation

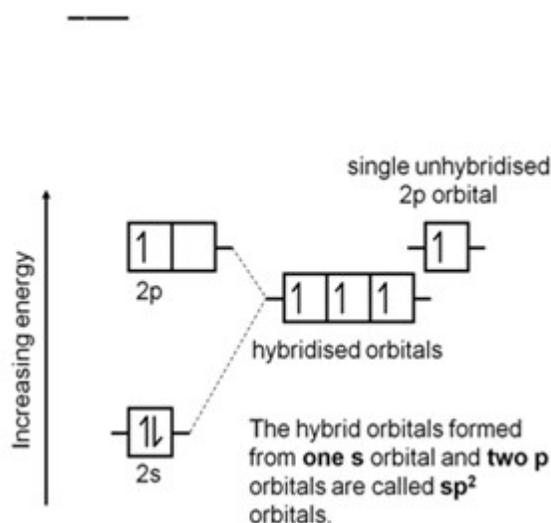


Pi-bonds arise where atoms form multiple bonds. If the two atomic orbitals are perpendicular to the bond and overlap laterally (“side on”) a pi π is formed.

pi bond formation

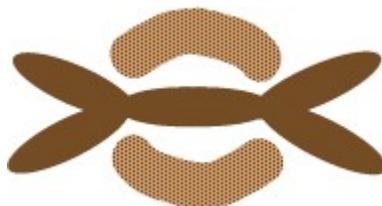


In alkenes the bonding observed is also due to hybridisation. As with alkanes, an electron from the 2s shell is promoted to the empty 2p orbital. This results in the formation of three hybrid orbitals, with one remaining un-hybridised 2p orbital.



The hybrid orbitals formed in alkenes from **one s** orbital and **two p** orbitals are called sp² orbitals. The three sp² orbitals repel each other, resulting in a bond angle of 120° between them, they adopt this trigonal planar structure to try minimise the repulsion.

Each carbon atom uses its three sp² hybrid orbitals to form sigma bonds with two hydrogen atoms and with the other carbon atom. The un-hybridised 2p orbitals left on the carbon atoms overlap side-on to form a pi bond.



The un-hybridised p orbitals are perpendicular to the plane of the molecule. The p orbitals of the carbon atoms are parallel and close enough to overlap sideways. This sideways overlap between the 2p orbitals produces a new molecular orbital between the two carbon atoms. This new orbital is called a pi (π) orbital or more commonly a π bond.

The Bonding Continuum

The shape of the molecular orbital formed from overlapping atomic orbitals will govern the type of intermolecular bonding that is observed.

Non-polar covalent bonds or pure covalent bonds are formed between two atoms of the same element, or two atoms with a very low difference in electronegativities. The molecular orbital formed from overlapping atomic orbitals is symmetrical around a mid-point where the bonding electrons are most likely to be found.



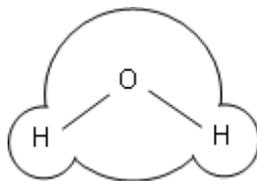
Symmetrical σ bonding orbitals of non-polar covalent bonds.

As shown above, in hydrogen and fluorine molecules, or any non-polar covalent bond, the σ bonding orbital is symmetrical.

This is not always the case. When there is a large difference between the electronegativities of the two elements involved in the bond, the bonding molecular orbital will be asymmetrical.

Water molecules contain highly electronegative oxygen atoms. Because oxygen has a greater attraction for the bonding electrons than hydrogen, the molecular orbital formed will be asymmetrical. The diagram shows that because the bonds in water molecules are polar, bonding electrons are more likely to be found around the δ^- oxygen atom.

When ionic bonds form, there is extreme asymmetry and the bonding molecular orbital is almost entirely around one atom.



Molecular Structure and Skeletal Formula

By now you should be familiar with

Molecular formula is the actual number of atoms of each element in a molecule

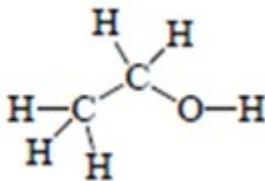
e.g. C_2H_6O for ethanol

Empirical Formula is the simplest whole number ratio of atoms of each element in a molecule

e.g. CH_2 for ethene (from molecular formula $C_2H_4/2$)

Structural Formula shows the relative positioning of atoms and the bonds between them

e.g. for ethanol



In addition you should become familiar with :

Skeletal formula shows just the carbon skeleton and functional groups e.g for ethanol



Skeletal formula show how carbon - carbon bonds and functional groups only. Neither the carbon atoms or any hydrogen atoms attached to the carbon atoms, are shown.

There is a carbon atom at the end of a line and the presence of other carbon atoms are implied by a kink in the back bone.

Alkane e.g. hexane



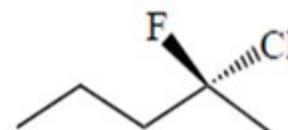
Alkene e.g. hex-3-ene



Alcohol e.g. ethanol



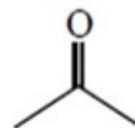
Halogenoalkane e.g. 2-chloro-2-fluoropentane



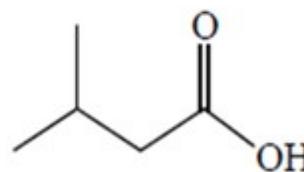
Aldehyde e.g. butanal



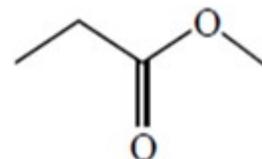
Ketone e.g. propanone



Carboxylic acid e.g. 3-methylbutanoic acid



Ester e.g. methyl propanoate



(b) Synthesis

(i) Overview of Synthesis

Organic synthesis is used to create molecules by design. Synthesis in chemistry allows professionals to produce molecules that are needed as drugs or materials. We can also improve the efficiency of established chemicals by testing a redesigning.

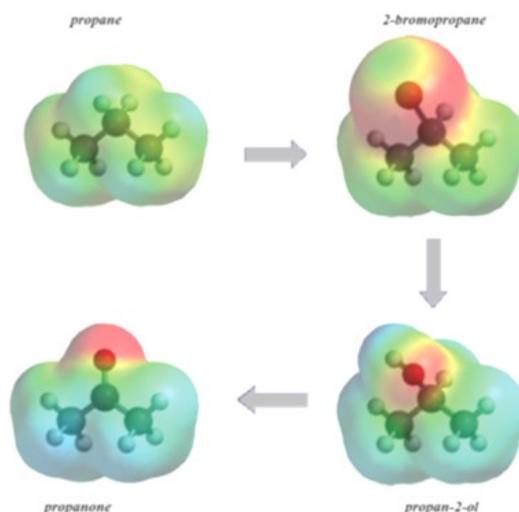
In order to propose a synthesis you must be familiar with named reactions taught in the higher course.

- What they begin with (reactants)
- What they lead to (products)
- How they are accomplished (reagent, mechanisms etc)
- What the limitations are (e.g. Conditions, multiple products, isomeric products, solvents etc)

A synthesis combines a series of proposed steps to go from a defined set of reactants to a specified product. You are expected to devise synthetic routes with up to 3 steps from a given reactant to a final product. Throughout the unit you will encounter and be expected to identify a variety of different types of reactions, some of which will be new to you. These will include :

Addition	Condensation	Hydrolysis	Oxidation
Reduction	Substitution	Elimination	Acid/Base

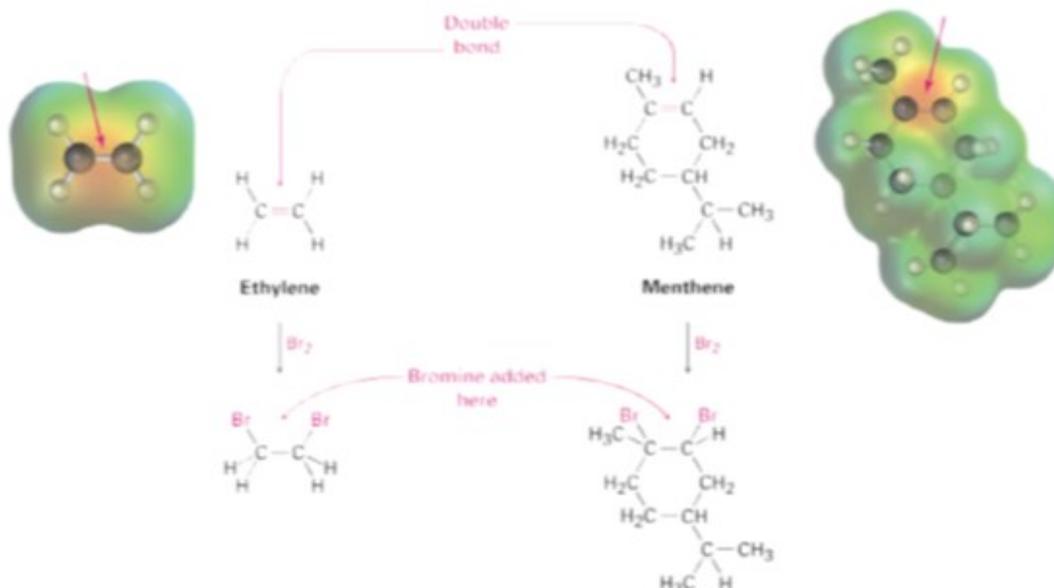
Reaction mechanisms of more complex substances can be clearly outlined and understood using the simple idea of functional groups and intermolecular bonding studied in the higher course.



Functional groups and simple chemical reactions learnt in higher chemistry in the context of simple families can be applied to more complex molecules.

e.g. Breaking a double bond.

Some of the main functional groups studied in chemistry are shown in the table below.



Compound type	Functional group structure	Compound type	Functional group structure
Alcohol	$\begin{array}{c} \delta^+ \\ \\ -C-\overset{\delta^-}{O}H \\ \end{array}$	Carbonyl	$\begin{array}{c} \delta^+ \\ \\ -C=\overset{\delta^-}{O} \\ \end{array}$
Alkene	$\begin{array}{c} \diagup \quad \diagdown \\ C=C \\ \diagdown \quad \diagup \end{array}$ Symmetrical, nonpolar	Carboxylic acid	$\begin{array}{c} \delta^+ \\ \\ -C=\overset{\delta^-}{O} \\ \\ \overset{\delta^-}{O}H \end{array}$
Alkyl halide	$\begin{array}{c} \delta^+ \\ \\ -C-\overset{\delta^-}{X} \\ \end{array}$	Carboxylic acid chloride	$\begin{array}{c} \delta^+ \\ \\ -C=\overset{\delta^-}{O} \\ \\ \overset{\delta^-}{Cl} \end{array}$
Amine	$\begin{array}{c} \delta^+ \\ \\ -C-\overset{\delta^-}{N}H_2 \\ \end{array}$	Aldehyde	$\begin{array}{c} \delta^+ \\ \\ -C=\overset{\delta^-}{O} \\ \\ H \end{array}$
Ether	$\begin{array}{c} \delta^+ \quad \delta^- \quad \delta^+ \\ \quad \quad \\ -C-\overset{\delta^-}{O}-C- \\ \quad \quad \end{array}$		

By thinking about the bonding and structure of molecules we can also work out how they will perform in a chemical reaction.

Intermolecular attractions such as hydrogen bonding and London dispersion forces are all dependant on the polarity of the molecule.

Non-polar molecules such as butane—an alkane- rely on London dispersion forces.

Propanal—an aldehyde and acetone which is a ketone will contain polar attractions between the molecules.

This is generally down to the presence of the highly electronegative oxygen atom

Propanol which is an alcohol and thus contains the OH group will also display hydrogen bonding.

Thinking back to the higher course each of the intermolecular attractions will give rise to differences in both the physical and chemical properties of a molecule.



Butane, bp 0°C



Propanal, bp 50°C



Acetone, bp 56°C



Propanol, bp 97°C

Boiling Points—most organic molecules contain mainly hydrogen and carbon. As the hydrocarbon chain increases in these molecules the strength of London dispersion forces also increases giving rise to a higher boiling point.

As a result, more energy is require to move the molecules further apart. Branched chain molecules have fewer attractions and are overall more compact therefore they do tend to have lower boiling points than the equivalent chain only molecules.

Molecules which display a degree of polarity will have higher boiling points again reflecting the extra energy needed to overcome the stronger attractions between their molecules.

Polarity is clearly a very important factor when assessing the properties of a molecule and how it will undergo specific reaction.

Bond Fission

When considering reactions of organic molecules polarity of the carbon bonds may influence the way they react.

A single covalent bond can be broken in the following ways.



Homolytic fission is shown above.

This method of bond breaking produce **free radicals**.

Free radicals are a very reactive species which contain unpaired electrons.

Homolytic fission is when each atom keeps the electrons it was contributing to the covalent bond..



The R and Z each share one electron to form the covalent bond.

The dots beside the symbol tell us a free radical has been formed

Homolytic fission normally occurs when non polar bonds are broken.



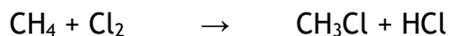
Above is an example of heterolytic fission.

This is when one of the atoms take both the electrons being shared in the covalent bond. This type of fission takes place when a polar bond is broken.

Remember a polar bond is when the carbon atom in this case is bonded to a highly electronegative atom.

Alkanes

The alkanes are a family of hydrocarbons which are not very reactive at all. This is largely due to the non polar nature of their bonds. The alkanes do however react with halogens in the presence of sunlight or UV exposure.



The above reaction is an example of homolytic fission. We can therefore assume free radicals will be created and by looking at three steps to the reaction we can deduce the reaction mechanism.

Chlorination of methane is an example of a **chain reaction**.

A chain reaction can be broken down into 3 different steps

- Initiation
- Propagation
- Termination

Initiation



The initiation step used to break the non polar bond between the Cl atoms involves UV light.

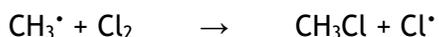
Propagation

Each chlorine radical produced in the initiation step goes on to attack the methane molecule.



The chlorine radical removes a hydrogen from the methane molecule forming hydrogen chloride and a methyl radical.

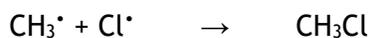
The methyl radical produced can then go on to attack a chlorine molecule to form chloromethane and another chlorine radical.



In each of the propagation steps one radical enters and another radical is produced. These steps “propagate” or sustain the reaction.

Termination

As the number of radicals build up from both initiation and propagation steps collisions between these super reactive unstable atoms occur and so form stable molecules.



Termination steps are reactions in which the free radicals are used up and so the overall reaction is brought to an end.

The three steps which make up a chain reaction in which a halogenoalkane is formed is also known as a **substitution reaction**.

A substitution reaction is the reaction in which an atom or group of atoms in a molecule is replaced by another atom or group of atoms.

The initiation step in the reaction between methane and chlorine is slow and is used to determine the rate of the reaction. Similar reactions occur with other halogen molecules but this is an unsatisfactory method of creating halogenoalkanes as a mixture of products are formed.

Alkenes

Alkenes are another subset of hydrocarbons which contains at least one carbon to carbon double bond. Remember alkenes different hybridisation occurs.

sp^2 Hybridisation

3 new atomic orbitals are formed using the 2s and two of the 2p orbitals, leaving the 3rd p orbital unhybridised.

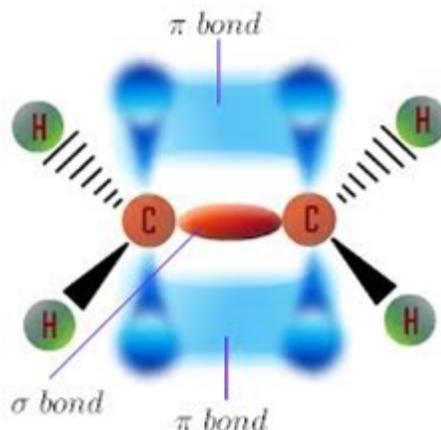
sp^2

1 s orbital 2 p orbitals

Sp^2 hybrid orbitals form sigma bonds. (like the alkanes). The remaining p orbitals on each carbon merge together above and below the plane of the sigma bond.

A pi bond is formed from the sideways overlap of the 2 parallel atomic orbitals.

A double bond which is contained in the alkane homologous series is therefore made up of one sigma bond and one pi bond.



The extra attractions of the pi bonds pull the carbon atoms closer together making the double bond length shorter than a single bond. The pi bond of the C=C is weaker than the sigma bond and so it is this that allows the alkenes to react easily. The pi bond is the bond which is broken during a normal addition reaction.

Synthesis of Alkenes

Alkenes are produced by elimination reactions.

An elimination reaction occurs when a single reactant breaks up to form two products.

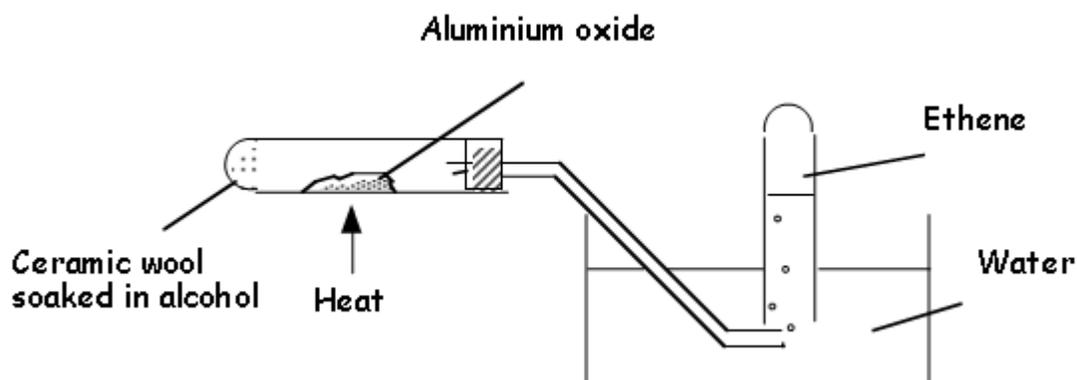
- One product is a small molecule such as water
- The other product will contain multiple bonds.

Alkenes can be prepared by

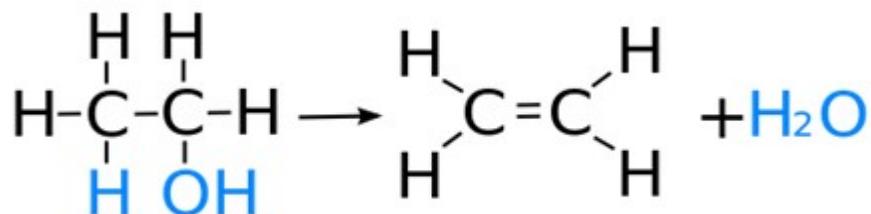
- Dehydration of alcohols
- Base induced elimination of hydrogen halides from monohalogenoalkanes

In the lab dehydration of alkanes can be brought about by passing alcohol vapour over a heated aluminium oxide catalyst or reacting the alcohol with a strong acid such as sulphuric or phosphoric.

The reaction taking place could be



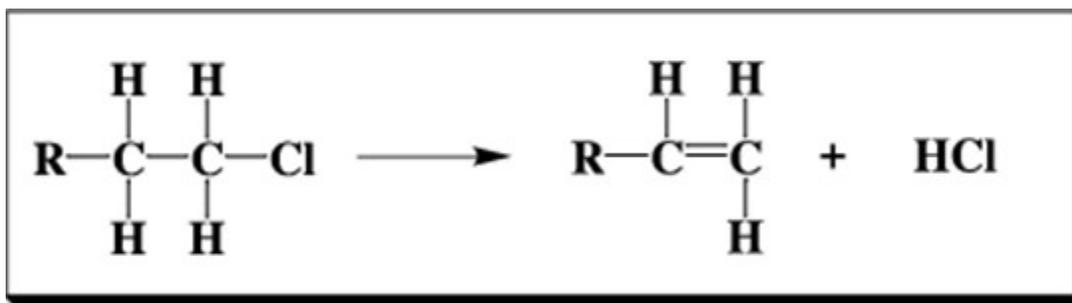
During this dehydration the OH group is removed along with a hydrogen atom on an adjacent carbon.



When using the strong acid method for the elimination reaction, phosphoric acid is preferred. This is due to the extra side reactions that occur when Sulphuric acid is instead used.

Base induced elimination of hydrogen halides to form monohalogenoalkanes is another example of an elimination reaction used to prepare alkenes.

The mechanism involves heating the monohalogenoalkane with ethanolic potassium or sodium hydroxide. Ethanolic potassium hydroxide is just a solution of potassium hydroxide in ethanol.



The reaction can be called a base induced elimination since it is the presence of the base which actually drives the reaction.

If there are more than three carbon atoms in the reactant which is undergoing elimination—alkenes may be formed.

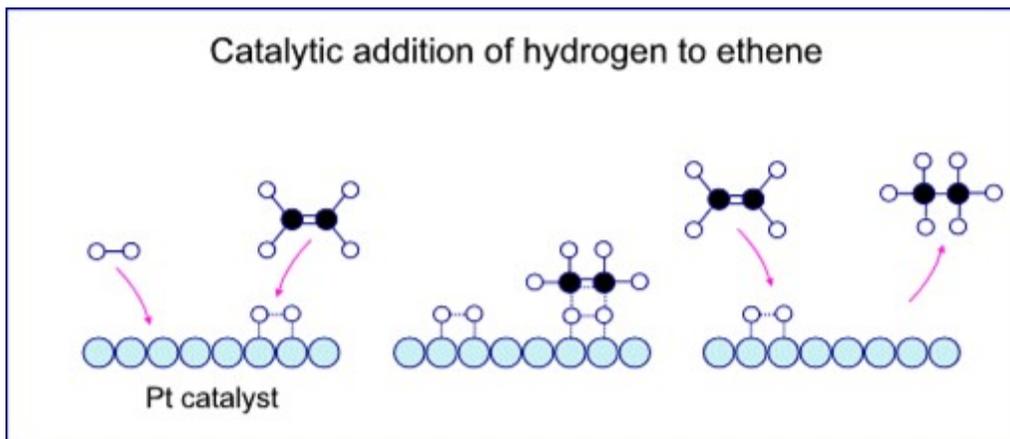
For example heating 2-bromobutane with ethanolic potassium hydroxide produces but-1-ene and but-2-ene.

Reactions of Alkenes

Alkenes may also undergo various addition reactions. They can react with hydrogen to form alkanes, halogens to form dihaloalkanes, hydrogen halides to form Monohalogenoalkanes and water to form alcohols.

Catalytic addition of hydrogen

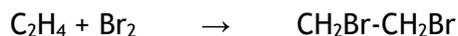
The addition of hydrogen is also known as hydrogenation and is catalysed by nickel or platinum.



The addition of hydrogen to ethene allows for the breaking of the C=C producing an alkane.

Addition of halogens to form dihaloalkanes

The addition of a halogen to an alkene can also be known as halogenations. This test can also be used to detect unsaturation in a molecule.



Because alkenes contain a C=C they can behave as nucleophiles.

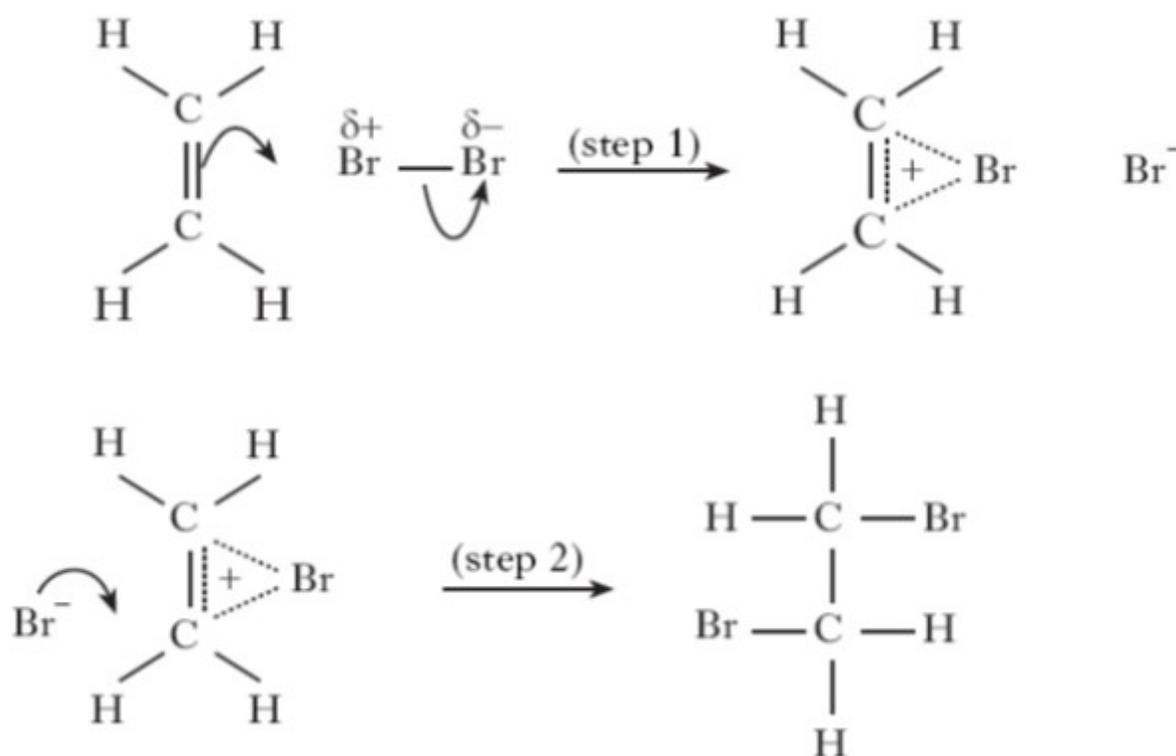
Nucleophiles— nucleophiles are nucleus loving particles. These are attracted to positively charged species and so are generally negatively charged,

e.g. nucleophiles can be

- Negative ions such as OH⁻ CN⁻
- Molecules with lone pairs
- Negatively charged polar atoms.

Reaction Mechanisms

The following reaction mechanism details the addition of a halogen to an alkene.

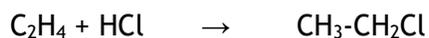


Note: The curly arrow is used to represent the movement of electrons

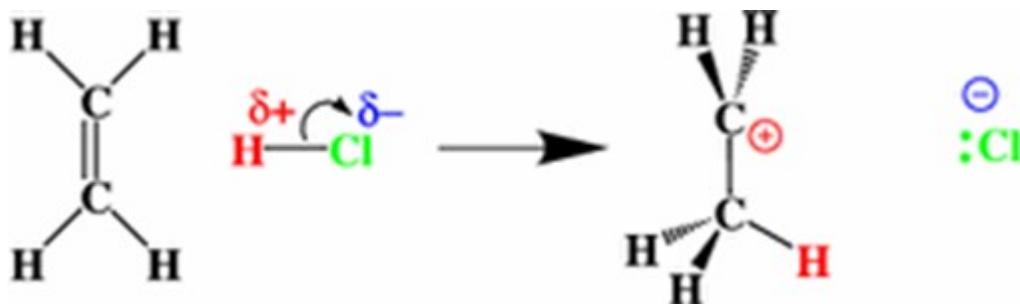
Step1: a positive **BROMONIUM** ion is formed between the alkene and the positive bromine atom (The bromonium ion is described as a **cyclic ion intermediate**.)

Step 2: The second stage of the reaction is a rapid, **NUCLEOPHILIC** attack by the bromide ion. Remember the bromide ion will act as nucleophile as it has a negative charge and therefore will be attracted to the positive charge (carbocation) in the molecule.

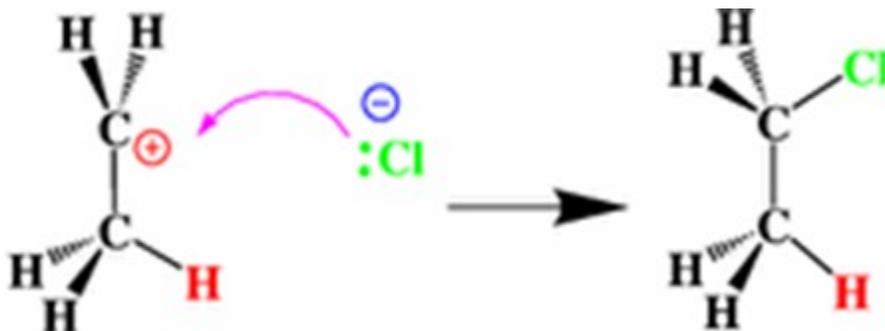
Addition of hydrogen halides to produce monohalalkanes.



Step 1: Electrophilic attack forming CARBOCATION (a carbon carrying a positive charge)



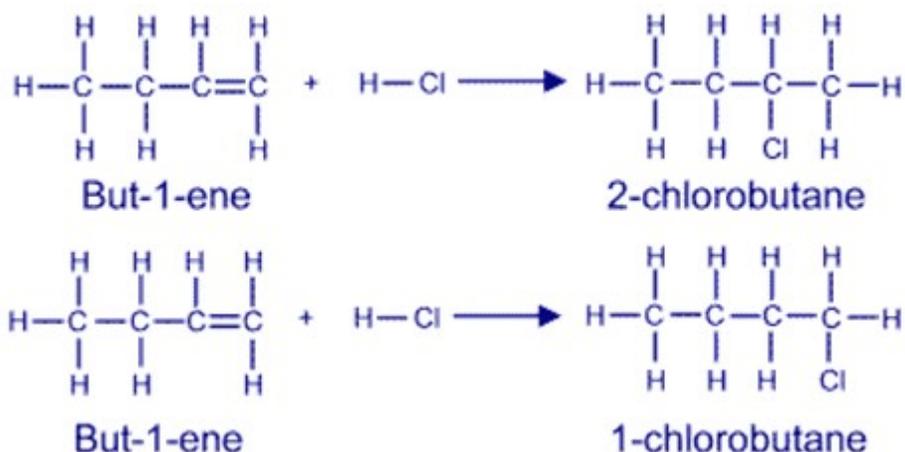
Step 2: Nucleophilic attack



As the bond forms between the H atom and the C atom, the H-Cl bond breaks **heterolytically** (**Heterolytic Fission**: both of the shared electrons go to only **one** of the two atoms producing **ions**)
Addition of hydrogen halides to asymmetrical alkanes like propane can result in the formation of 2 possible products.

Markovnikov's Rule

Addition reactions can produce isomers when the alkene is **asymmetric** (the double bond is not symmetrically placed in the molecule). *e.g.*



Markovnikov's Rule can be used to predict the major product of this type of reaction. It states:

“the H atom of H-X adds to the carbon atom which already has more hydrogen atoms”

e.g. In the equation above, the **more likely product** of the addition of H-Cl to but-1-ene will be:

2-chlorobutane

with a smaller quantity of 1-chlorobutane.

2-chlorobutane will be the more likely product as the hydrogen has attached to the carbon atom with the highest number of hydrogen atoms.

Addition of Water(Hydration) forming Alcohols

The addition of water to an alkene is done in the presence of an acid catalyst. Again this process can produce more than one product.

The more likely product of the reaction can be predicted by using Markovnikov's rule.

When water adds across an asymmetrical double bond the major product formed is the molecule in which hydrogen adds to the carbon atom in the double bond with the greater number of hydrogen atoms attached.

The production of an alcohol from an alkene can be a significant step in organic synthesis as it opens up the route to oxygen containing compounds such as aldehydes, ketones, esters and acids.

Note:

the above reaction is **catalysed** with **sulfuric acid**

follows carbocation reaction mechanism

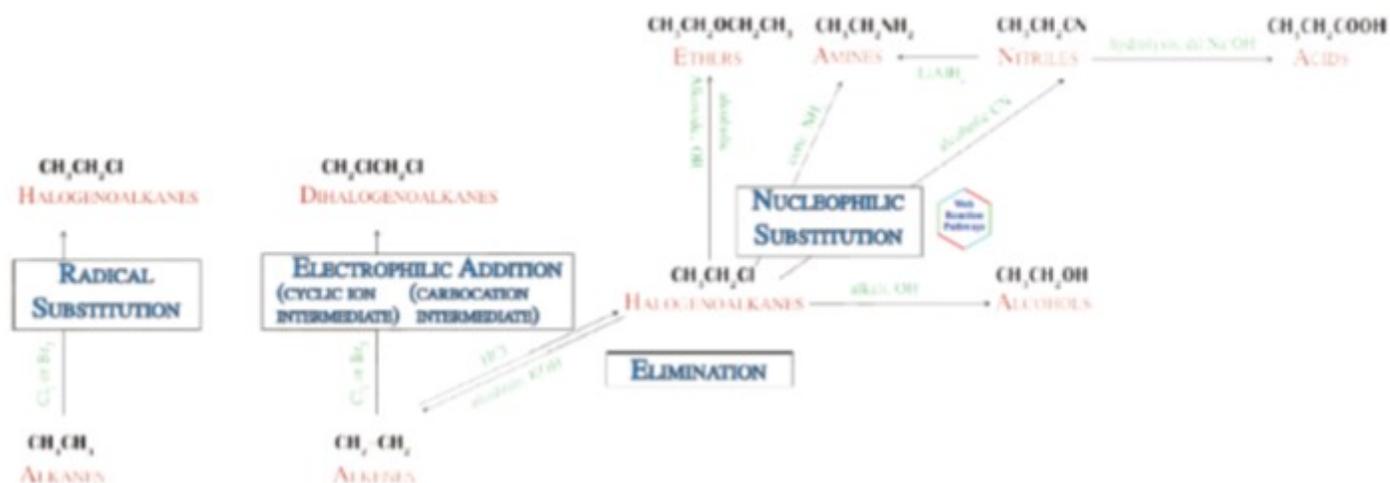
Markovnikov's Rule applies

This reaction is an example of electrophilic addition . electrophiles are molecules or positively charged ions which are capable of accepting a lone pair of electrons.

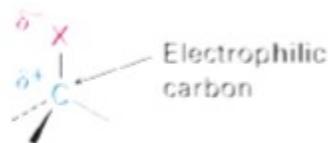
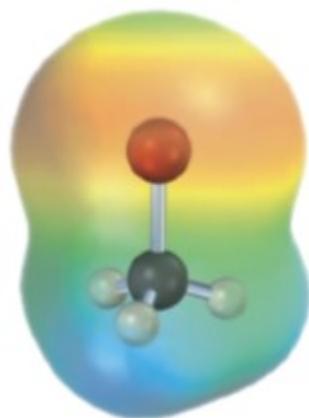
Both hydrohalogenation and hydration are examples of electrophilic addition with a carbocation intermediate.

Halogenoalkanes

Halogenoalkanes or otherwise known as alkyl halides are not particularly important in the higher chemistry course. In advanced higher however the significance of halogenoalkanes cannot be overstressed. They can be a very important part in many synthesis pathways. Organic compounds containing halogen substituent are comparatively rare in the natural world and therefore most of them have to be synthesised in the laboratory.

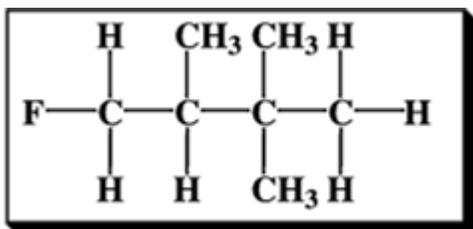


Halogenoalkanes are very important in the modern world and can be used not only in medicine but also in agriculture and the manufacture of plastics. In the advanced higher course we are able to manipulate the products of reactions involving halogenoalkanes. One of the most significant features of a halogenoalkane is the production of a dipole and in particular a positively charged carbon atom. This positively charged carbon will now be vulnerable to attack by a number of different nucleophiles leading to NUCLEOPHILIC SUBSTITUTION.

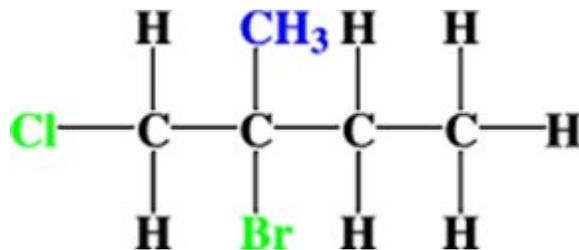


Halogenoalkanes are named according to the IUPAC(International Union of Pure and Applied Chemistry) rules. The presence of halogen substituent is shown by the appropriate prefix:

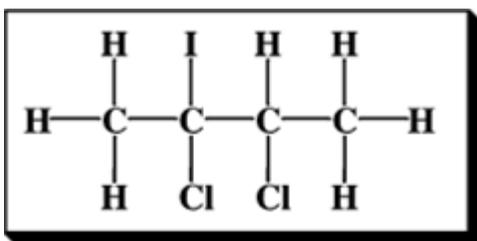
Halogen	prefix
fluorine	fluoro-
chlorine	chloro-
bromine	bromo-
iodine	iodo-



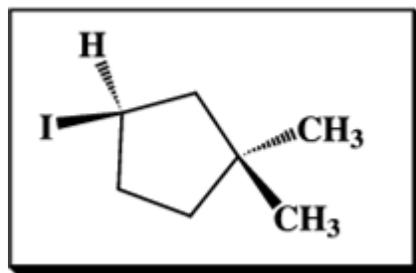
1- fluoro,- 2,3,3 - trimethyl butane



2-bromo-1-chloro-2-methylbutane



2,3-dichloro-2-iodo-butane

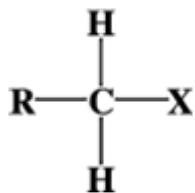


1-iodo-3,3-dimethylcyclopentane

Types of MonoHalogenoalkanes

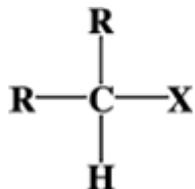
Monohalogenoalkanes can be classified as primary, secondary or tertiary

Primary ; carbon bonded to the halogen group is bonded to **1 other carbon**:



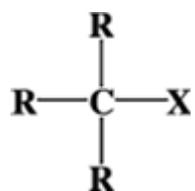
General formula RCH_2X

Secondary ; carbon bonded to the halogen is bonded to **2 other carbons**



General formula $(\text{R})_2\text{CH-X}$

Tertiary ; carbon bonded to the halogen is bonded to **3 other carbons**



General formula $(\text{R})_3\text{C-X}$

In the general formulae shown the “R” groups correspond to to an alkyl group $\text{C}_n\text{H}_{2n+1}$ With the X used to represent the Halogen.

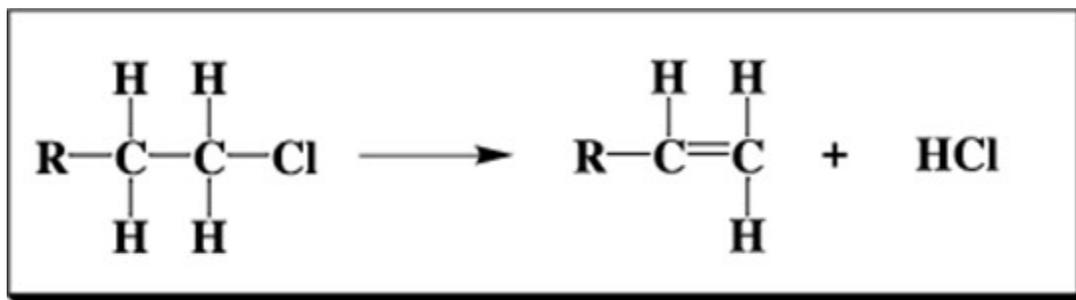
Reactions of Monohalogenoalkanes

Halogenoalkanes undergo **two** main types of reaction:

The easiest of these being

1. ELIMINATION reactions (forming alkenes):

e.g. Reaction with alkali (dissolved in ethanol)



When a monohaloalkane is refluxed with alcoholic potassium hydroxide hydrogen halide is eliminated. This produces the corresponding alkene from the monhaloalkane.

Substitution reactions involving monohaloalkanes

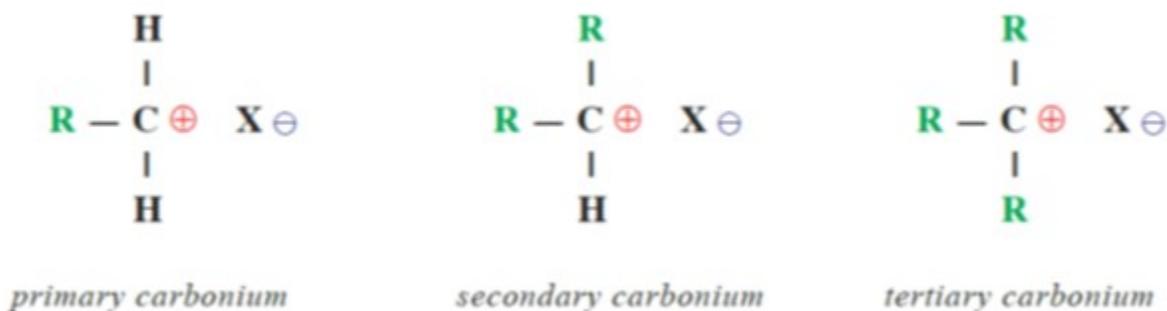
The most common reaction monohaloalkanes will undergo is known as a substitution reaction. In this particular substitution the monohaloalkane will undergo a nucleophilic attack of the carbon atom in the polar carbon-halogen.

The polarity of the carbon-halogen bond will differ causing changes in strength dependent on the electronegativity of halide attached.

Fluorine is the most electronegative of the halogens and therefore when bonded to carbon in the alkyl halide the strength of the bond will be high as well as the polarity.

One mechanism for the production of the carbonium (positive carbon) ion in the alkyl halide is the removal of the halogen as a halide ion.

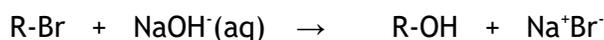
As previously seen and shown through the Markovnikov's rule the inductive effect of the alkyl groups will help stabilize the carbonium ion thus meaning there is a much higher chance of this mechanism taking place in the tertiary haloalkanes than with primary haloalkanes.



where the halogen atom is replaced by a **nucleophile**

e.g.

Reaction with **Aqueous ALKALIS** to form **ALCOHOLS**:



Reaction with **ALKOXIDES** (dissolved in alcohol) to form **ETHERS**:



(Alkoxides have the formula R-O^{\ominus} where R = an alkyl group such as $\text{C}_2\text{H}_5^{\ominus}$.)

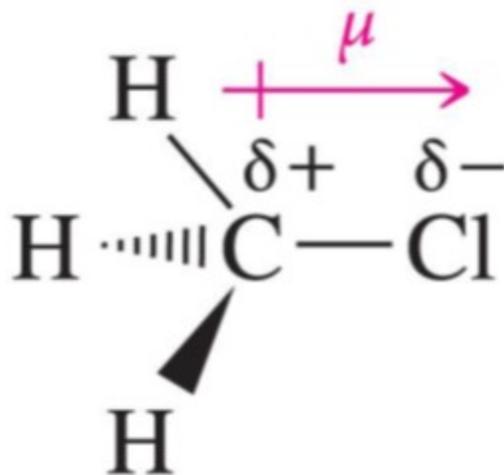
The ethoxide ion has the formula $\text{C}_2\text{H}_5\text{O}^{\ominus}$)

Nucleophilic substitution

Looking again at the polar nature of the carbon-halide bond we can understand why the nucleophilic attack will take place.

The electronegativity of the halogen will induce a slight positive charge on the carbon atom it is attached to

Remember - nucleophiles are substances which seek out a positive charge. Nucleophiles will all possess unpaired electrons (electrons are negatively charged).



There are many products which may be formed when monohaloalkanes undergo nucleophilic substitution reactions with different reactants

- Alkalis to form alcohols
- Alcoholic alkoxides to form ethers
- Ethanolic cyanide to form nitriles. Nitriles can then be hydrolysed to carboxylic acids.

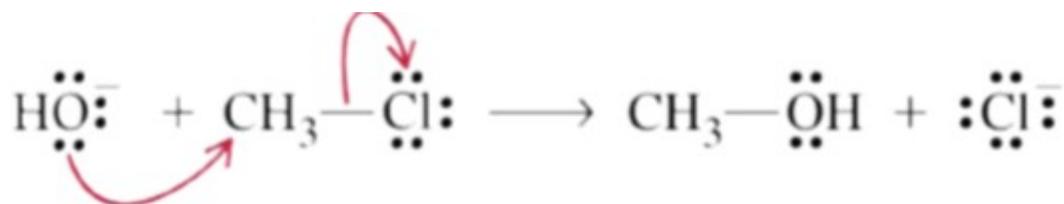
Mechanism Description

The nucleophile which attacks the carbon atom, with the slight positive charge, donates an electron pair and by doing so forms a covalent bond with the carbon atom of the C-X bond. At the same time the halogen is thrown out and replaced by the nucleophile.

Reaction with alkalis to form alcohols

The production of an alcohol during a synthesis reaction is extremely important. This will open up the door to many other reactions and allow us to create an array of organic compounds.

When refluxed with an alkali a monohaloalkane undergoes nucleophilic substitution to form the corresponding alcohol.



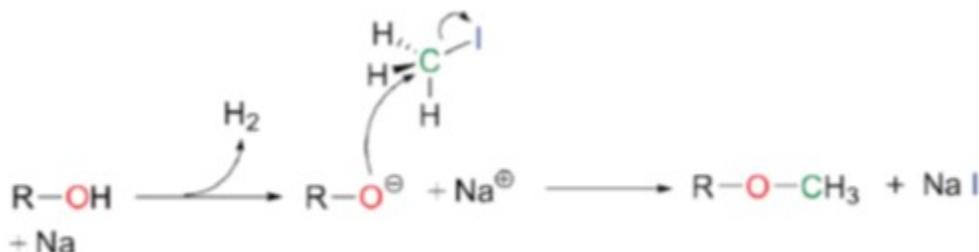
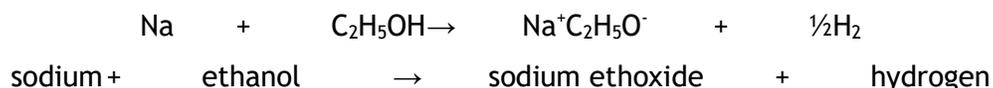
Reaction with alcoholic sodium alkoxides to form ethers.

When sodium is reacted with an alcohol a sodium alkoxide is formed.

The key to the above reaction is the production of what's known as the alkoxide ion



It is this ion which becomes our nucleophile and therefore allows for the nucleophilic substitution.

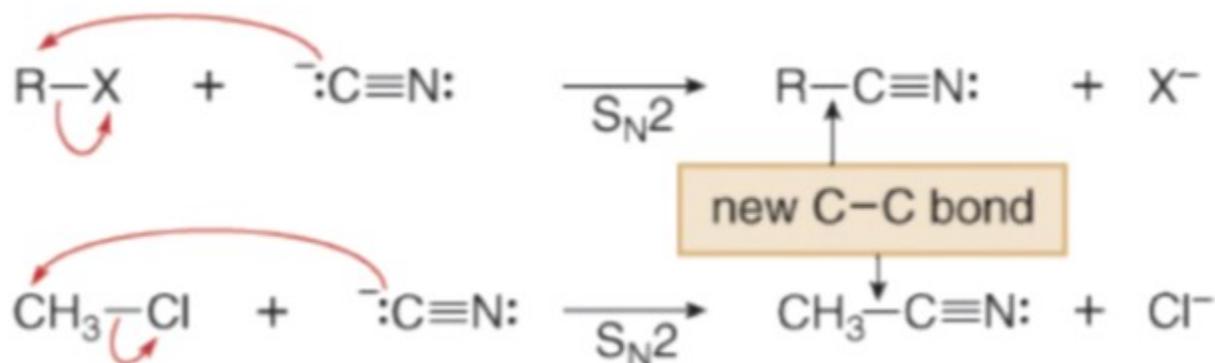


It appears in the above mechanism that there are two different reagents but in reality it is the same reagent and therefore allows production of the ether.

Reaction with sodium cyanide to form nitriles

When a monohaloalkane is reacted with sodium cyanide the production of the nucleophilic substitution reaction is a nitrile.

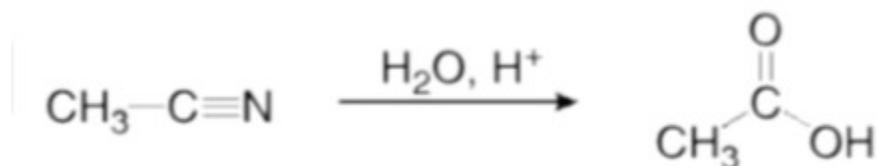
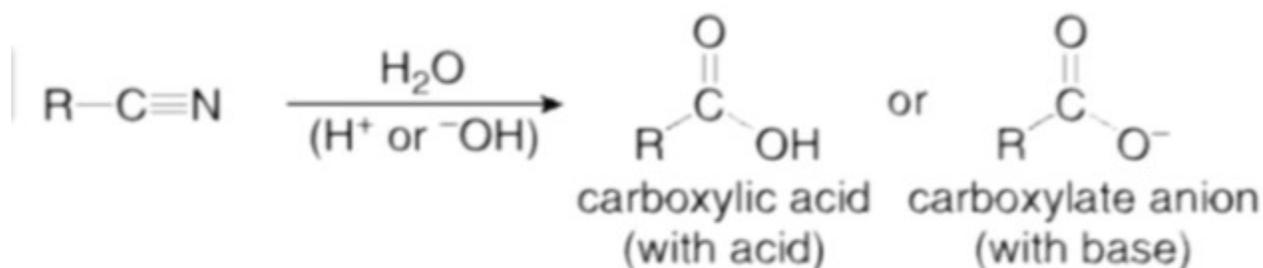
The production of the new C-C bond can be seen as a very important step in organic chemistry as this allows the alkane chain to grow.



After producing the nitrile the next is normally to hydrolyse this new substance with an acid.

Acid hydrolysis of the nitrile will allow for the production of a carboxylic acid.

The methane nitrile above will go on and produce ethanoic acid after the acid hydrolysis step.



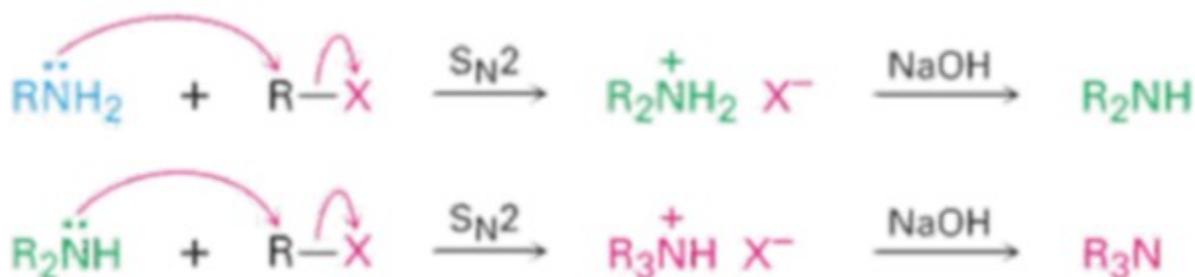
Nucleophilic substitution reaction to form amines

When a monohaloalkane is reacted with ammonia the product of the nucleophilic substitution is an amine.



It is important to be aware that the ammonia can initiate what can be classed as a 2 step reaction mechanism. The ammonia will as shown above produce a primary amine however this amine due to the lone pairs of the nitrogen atom can then go on and act as a nucleophile.

The use of the amine as a nucleophile can therefore produce both secondary and tertiary amines.



Another way in which amines may be produced by the nucleophilic substitution reaction again can be shown by a two step reaction mechanism involving

1. Reaction with sodium cyanide to form a nitrile
2. Reduction of the nitrile to form an amine

Nitriles can be REDUCED to produce AMINES:



Nucleophilic Substitutions

Substitutions may be classified into two categories:

A. First-Order Nucleophilic Substitution 2 step process (S_N1)

- Only 1 molecule involved in the rate determining step
- Transition state is planar trigonal with 3 groups attached to the carbon atom
- Isomeric forms are possible if the alkyl halide is a chiral molecule
- The nucleophile can attach from either side
- Least likely for primary alkyl halide and most likely for tertiary
- Think about inductive effect

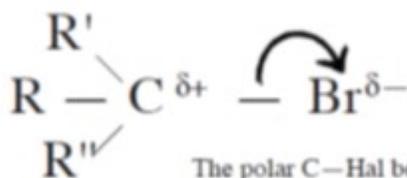
B. Second-Order Nucleophilic Substitution 1 step process (S_N2)

- 2 molecules involved in the rate determining step
- Transition state will be trigonal bipyramidal—5 groups attached to carbon atom
- There will be no isomeric products formed
- Nucleophile will have to attach from opposite side to the departing hydrogen
- S_N1 mechanisms most likely for primary alkyl halide and least likely for tertiary alkyl halide
- Think about steric hindrance



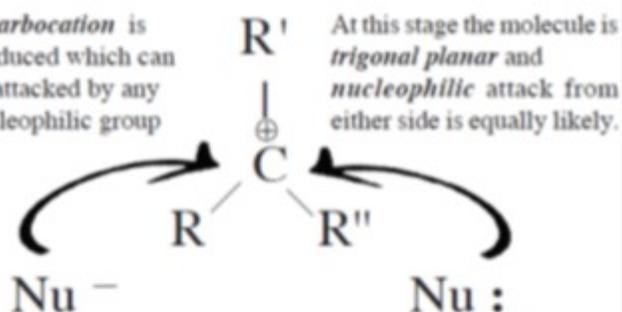
NUCLEOPHILIC SUBSTITUTION

(S_N1)



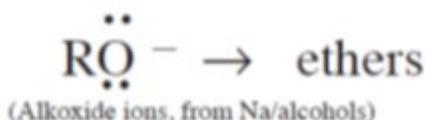
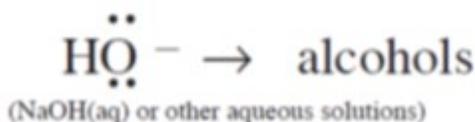
The polar C—Hal bond breaks *heterolytically*.

A *carbocation* is produced which can be attacked by any nucleophilic group



If R, R' and R'' are all different (asymmetric carbon), then a mixture of *optical isomers* will be produced.

Nucleophiles include:



A variety of products can be made by this reaction but overall the reaction can be represented by the equation:



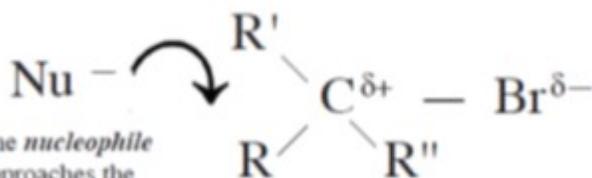
SUBSTITUTION

The first step is the *rate determining step* and, since it only involves one substance, the reaction is *first order*



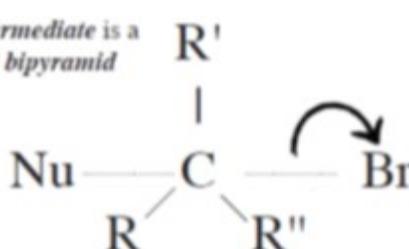
NUCLEOPHILIC SUBSTITUTION

(S_N2)



The *nucleophile* approaches the *electron deficient* carbon

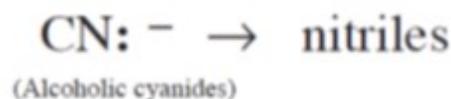
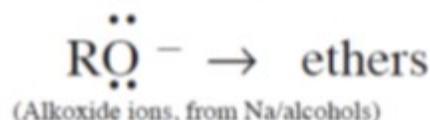
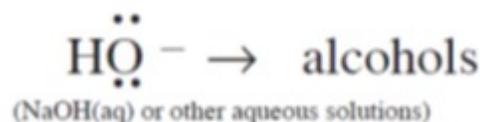
The *intermediate* is a *trigonal bipyramid* shape



As the *nucleophiles'* electron pair moves in, the electrons of the C—Br bond move onto the bromine

Even if R, R' and R'' are all different (asymmetric carbon), only *one possible isomer* can be produced.

Nucleophiles include:



A variety of products can be made by this reaction but overall the reaction can be represented by the equation:



SUBSTITUTION

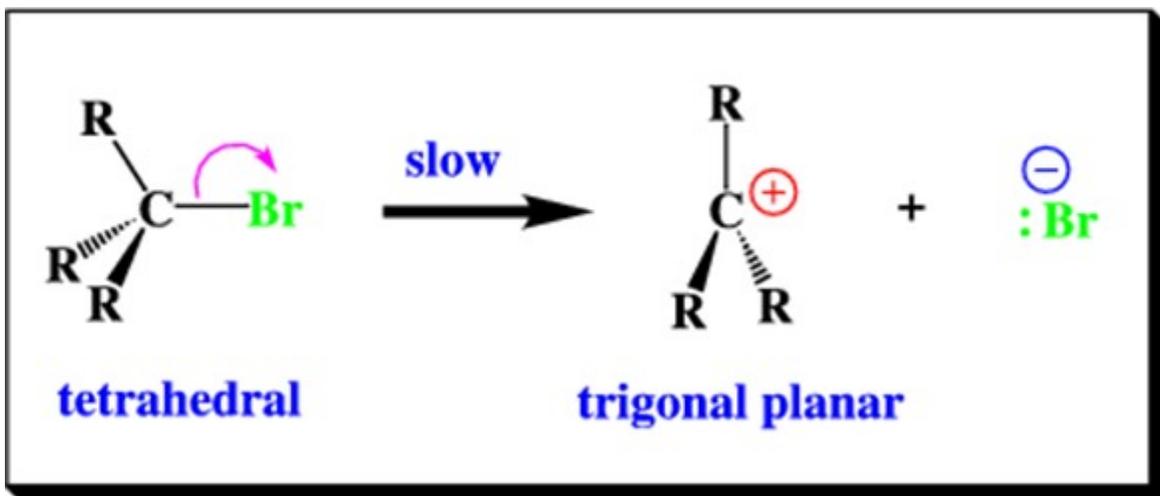
The *rate determining step* involves both chemicals so the reaction is *second order*

First-Order Nucleophilic Substitution (S_N1)

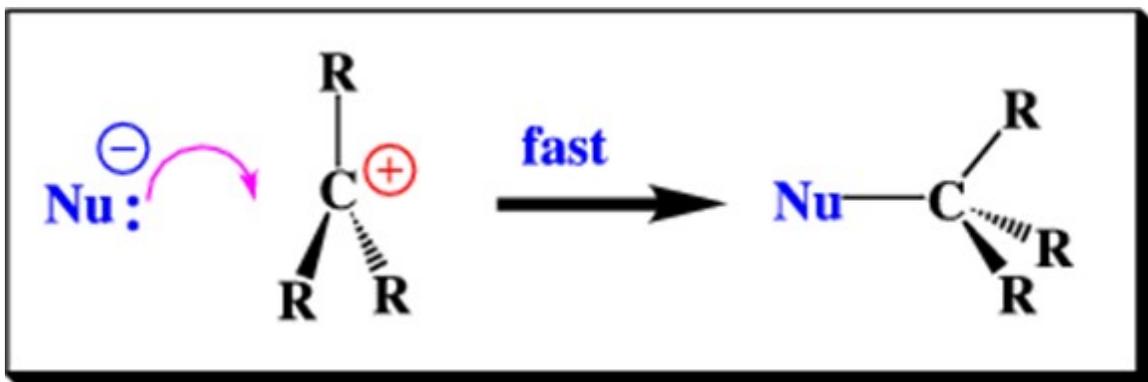
TERTIARY HALOGENOALKANES react in first-order reactions.

Reaction Mechanism:

Step 1: heterolytic fission of the carbon-halogen bond (RDS)



Step 2: nucleophilic attack

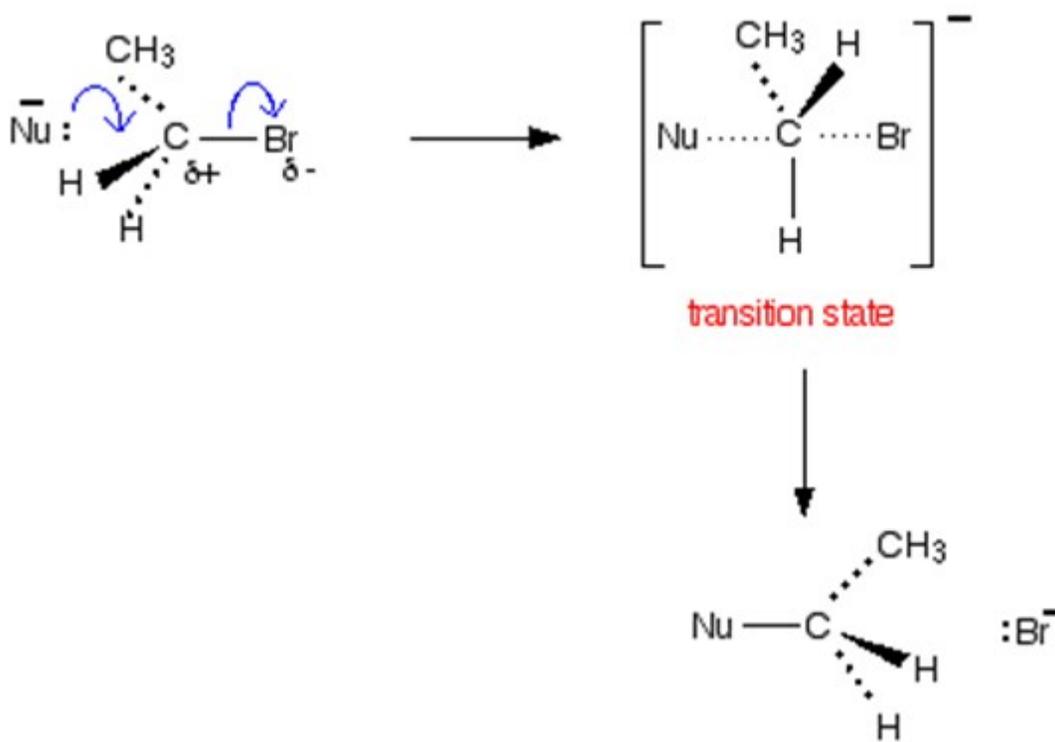


Note: The reaction rate depends solely on the haloalkane concentration. Therefore, FIRST ORDER.

Second-Order Nucleophilic Substitution (S_N2)

PRIMARY AND SECONDARY HALOGENOALKANES react in second-order reactions.

Reaction Mechanism:



A nucleophile attacks the **positively polar carbon atom**. This results in the heterolytic fission of the carbon-halogen bond.

Note: the reaction rate depends on **both** the halogenoalkane and the nucleophiles concentration. Therefore, **SECOND ORDER**.

Note: The above mechanisms must be drawn in 3d

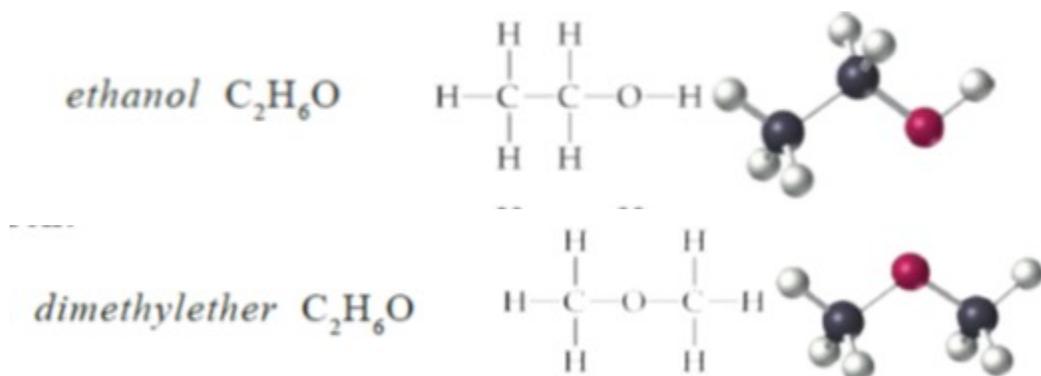
Alcohols

Alcohols are compounds which contain the hydroxyl group (OH) and composed of the elements C, H and O. From Higher chemistry you should be able to

- Name both straight and branched chain alcohols
- Explain the properties of alcohols and how they arise
- Understand the process of oxidation and how aldehydes and ketones can be produced from primary and secondary alcohols.

Properties

Alcohols and ethers are isomeric and you would therefore think there could be problems in distinguishing them. The two families however exhibit very different chemical and physical properties.



Alcohols exhibit hydrogen bonding and so will have very high melting points and boiling points when compared to many other organic compounds of comparable shape and relative formula mass.

Ethers do not hydrogen bond and are only slightly polar therefore are compounds which can be distinguished by their nature of being very volatile, flammable liquids

	Compound	Molar Mass	Boiling Point (°C)	Soluble in Water?
Alkane	$CH_3-CH_2-CH_3$	44	-42	No
Ether	CH_3-O-CH_3	46	-23	Yes
Alcohol	CH_3-CH_2-OH	46	78	Yes

Preparation of Alcohols

Alcohols can be prepared from the following reactions

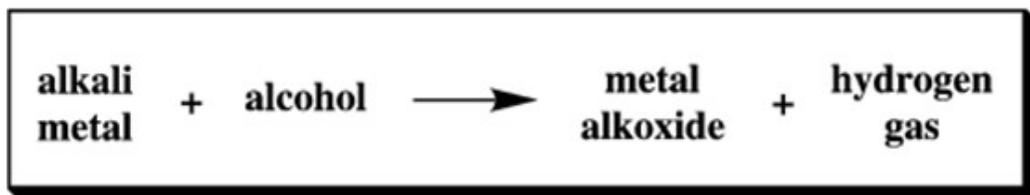
1. Acid catalysed hydration of alkenes (shown in reactions of alkenes page 18)
2. Substitution reactions of alkanes (shown in haloalkanes page 25)

Alcohols have not only played a large part in National Five Chemistry but many reactions of alcohols have previously been shown in Higher Chemistry.

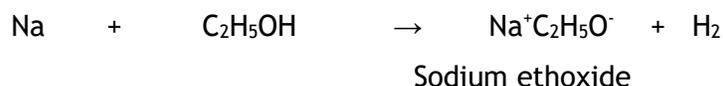
Reactions of alcohols include

- Alcohols being reacted with reactive metals to form alkoxides
- Dehydration of alcohols to form alkenes
- Condensation of an alcohol with carboxylic acid/acid chloride to form ester
- Oxidation reaction of alcohols to form aldehydes/ ketones
- Reduction reaction of aldehyde/ ketone to produce alcohols.

Reaction with reactive metals to produce alkoxides.



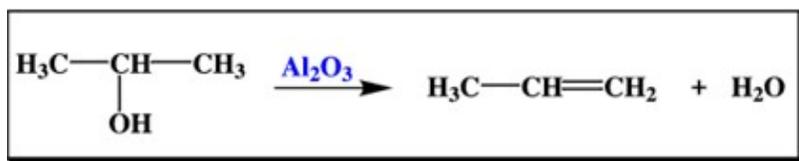
Reactive metals such as sodium and potassium (group 1) can be reacted with alcohols to form alkoxides.



Dehydration of Alcohols to form Alkenes

Dehydration of an alcohol to form an alkene can be brought about by two methods

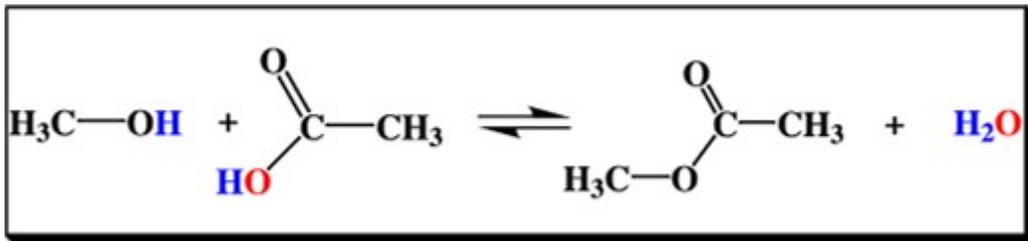
- Alcohol vapour passed over heated aluminium oxide (page 17)
- Alcohol heated with an excess of sulfuric acid.



Ester Formation

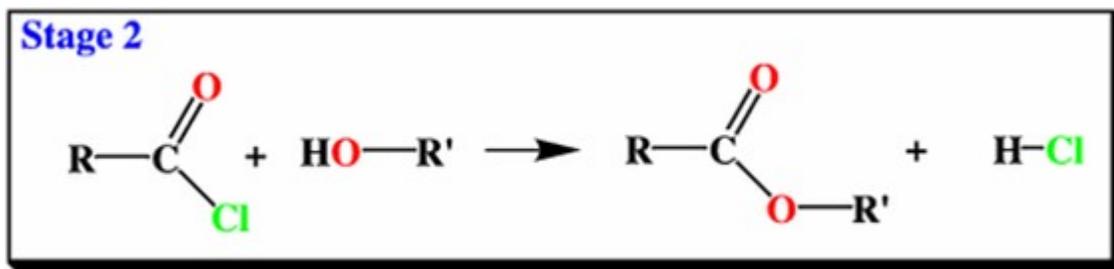
Condensation reactions have previously been covered in your chemistry career in particular thinking about esterification.

Esterification is a great example of a condensation reaction in which an alcohol is reacted with a carboxylic acid also producing 1 mole of water



The above reaction would be carried out under the influence of a concentrated sulfuric acid catalyst.

The general condensation reaction for the production of an ester can however be carried out instead with an acid chloride and an alcohol. This makes the overall esterification process faster and more vigorous.

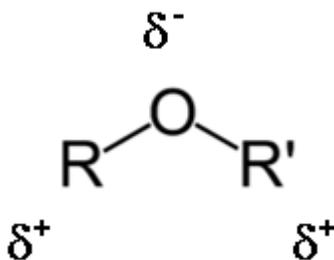


Remember during a condensation reaction a small molecule is lost. This small molecule does not always have to be a water molecule. In the reaction above hydrogen chloride is produced. As the product

Ethers

Alcohols are substances which are isomeric with ethers. Ethers are also organic compounds with the general formula $\text{R}-\text{O}-\text{R}'$ where R and R' are both alkyl groups. Due to their low molecular masses and their lack of hydrogen bonding ethers have low boiling point liquids which are generally insoluble in water.

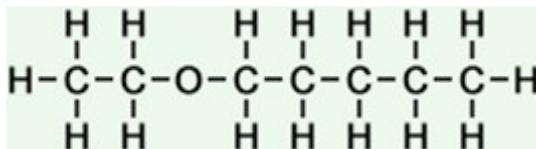
Comparison with alcohols can be made not only with the melting point and boiling point but also with the miscibility in water. Alcohols are soluble with water and the solubility is an increasing factor with the increasing chain length of the alcohol, however ethers are insoluble. The lack of hydrogen bonding between ether and water molecules is the reasoning behind this property and again gives us another Distinguishable factor between the two groups of molecules.



The shape of ether molecules is very similar to that of water molecules. This allows for the polarisation of the C-O bond.

Naming Ethers

Ethers are named as alkoxy derivatives of alkanes with the smaller alkoxy group being named as the substituent. Instead of naming an alkyl chain with the -yl ending we change it to -oxy. The longest alkyl group is used to name the parent alkane (2nd part of the name) The remainder of the molecule is therefore the alkoxy group.



Ethoxypentane.

Formula	Systematic Name
$\text{CH}_3 - \text{O} - \text{CH}_3$	methoxymethane
$\text{C}_2\text{H}_5 - \text{O} - \text{CH}_3$	methoxyethane
$\text{C}_3\text{H}_7 - \text{O} - \text{C}_2\text{H}_5$	ethoxypropane
$\text{C}_2\text{H}_5 - \text{O} - \text{C}_6\text{H}_{13}$	ethoxyhexane
$\text{C}_3\text{H}_7 - \text{O} - \text{C}_4\text{H}_9$	propoxybutane

Uses of Ethers

Ethers are relatively non-polar molecules as they have two alkyl groups arranged symmetrically round the oxygen atom. Ethers will, therefore, not dissolve ionic species as they are unable to solvate the ions effectively. However, ethers will be able to dissolve most non-polar solvents, including most organic compounds.

The use of ethers as solvents depends on several factors:-

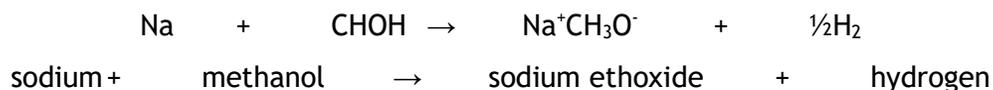
1. they possess little reactivity with potential solutes.
2. they dissolve many organic, but few inorganic (ionic) substances.
3. the small molecules are volatile allowing easy removal after use.
4. used for solvent extraction.

Ethers, however, have two major drawbacks as solvents:-

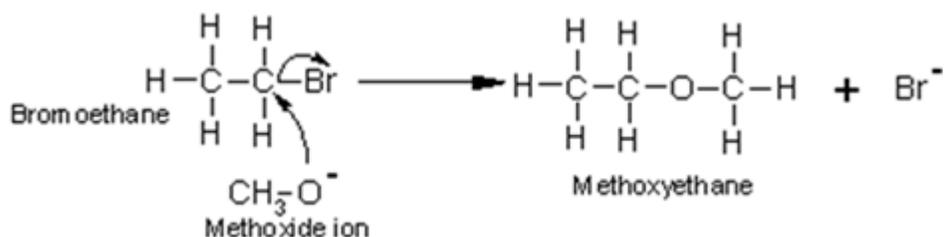
1. they form explosive mixtures with air .
2. they form explosive peroxides on long term storage.

Preparation of Ethers

Ethers can be prepared by the nucleophilic attack of an alkoxide ion on a halogenoalkane. When sodium (a reactive metal) a sodium alkoxide ion is formed.



The sodium methoxide is then dissolved in alcohol to yield the methoxide ion. It is this negatively charged methoxide ion which attacks the carbon atom with a slight positive charge in the monohaloalkane.



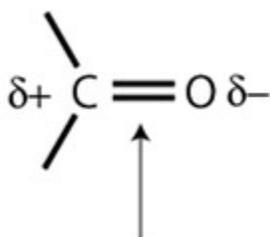
The product of the reaction is an ether along with the negatively charged halide ion which has been substituted.

The preparation of ether done under reflux with haloalkane and the alkoxide is an example of nucleophilic substitution.

Aldehydes and Ketones

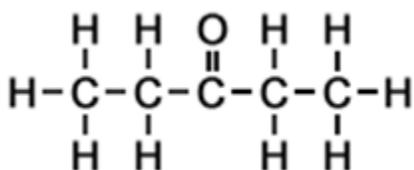
Aldehydes and ketones are organic compounds which contain the carbonyl C=O functional group.

Carbonyl group

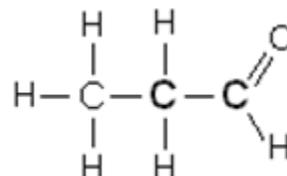


Polar Covalent Bond

These compounds we have met in higher chemistry. They are formed from the oxidation of an alcohol. The product of oxidation (either aldehyde or ketone) is Dependant on the type of alcohol oxidised.

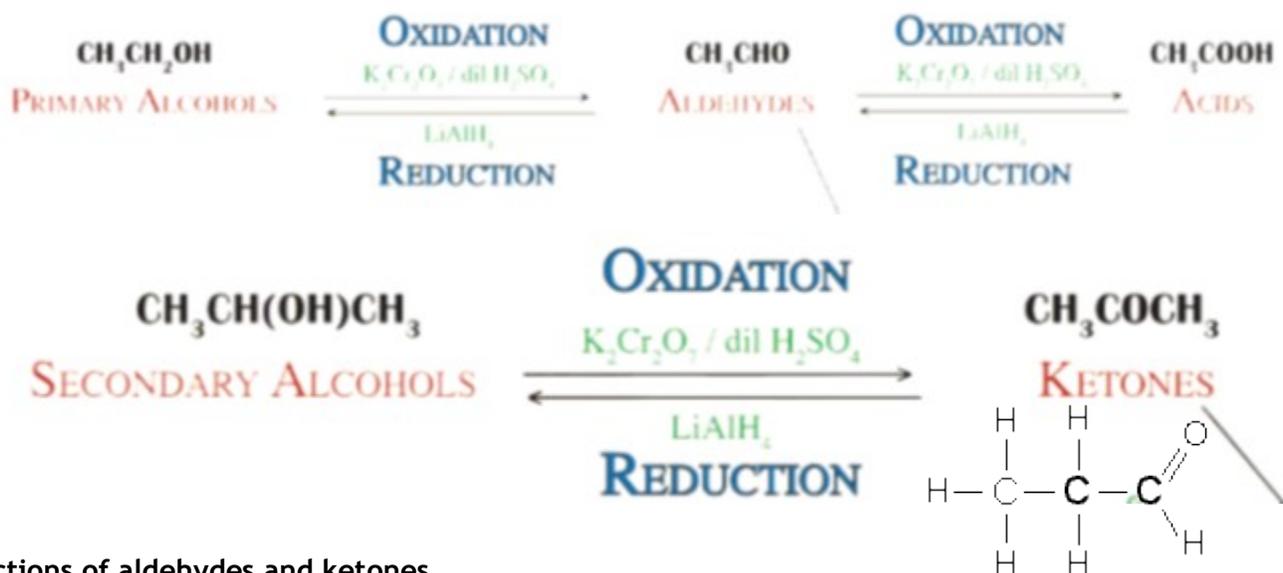


Pentan-3-one



propanal

Primary alcohols are oxidised to produce aldehydes whilst secondary alcohols are oxidised to produce ketones.



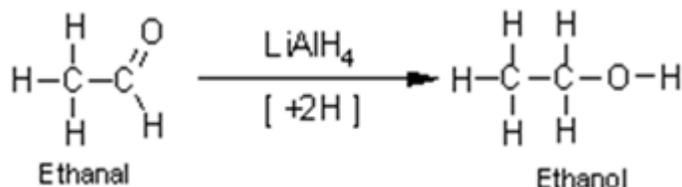
Reactions of aldehydes and ketones

Aldehydes and ketones can therefore be reduced to produce the corresponding alcohol from which it was initially derived.

The production of the aldehyde/ketone is performed using an oxidising agent

- Acidified dichromate—orange to green colour change
- Tollens reagent—silver mirror formed
- Benedicts reagent—blue to orange/red colour change

The reverse reaction which is termed reduction uses lithium aluminium hydride dissolved in ether as a reducing agent.



Carboxylic Acids

Carboxylic acids contain the carboxyl functional group



These are compounds which can be either solid or liquid at room temperature which reflects the high degree of hydrogen bonding present in the molecule.

As the carbon chain gets longer the hydrogen bonding does diminish and so the longer the carboxylic acid the lower the melting point. As the chain length of the carboxylic otherwise known as alcanoic acid increase the solubility also decreases due the diminishing hydrogen bonding.

Preparation of carboxylic acids

Carboxylic acids can be prepared in two ways

1. Oxidation of primary alcohols/aldehydes
2. Hydrolysing nitriles / esters / amides

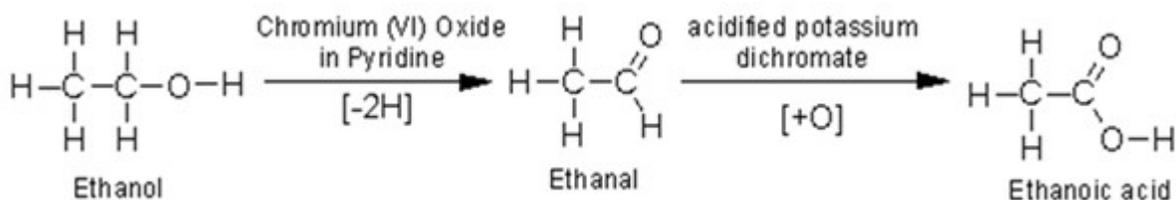
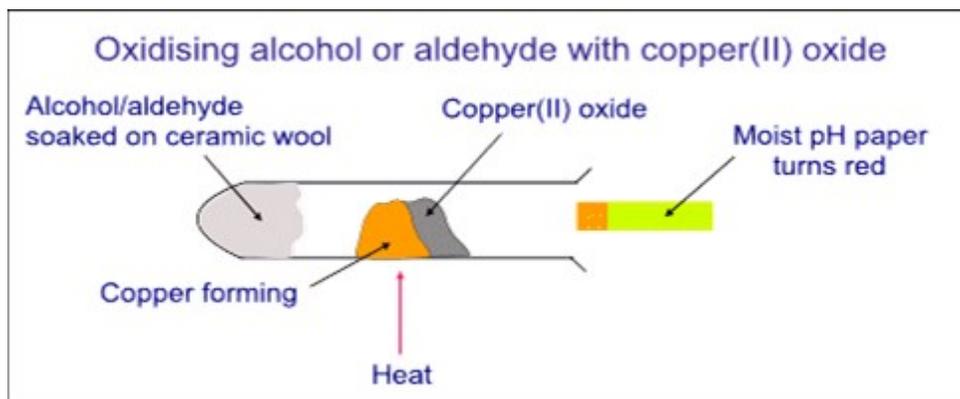
Reactions of carboxylic acids

These organic compounds can also undergo various reactions

1. Formation of salts by reactions with bases or metals
2. Condensation reactions with alcohols to produce esters in the presence of an acid catalyst
3. Reactions with amino groups to form an amide link

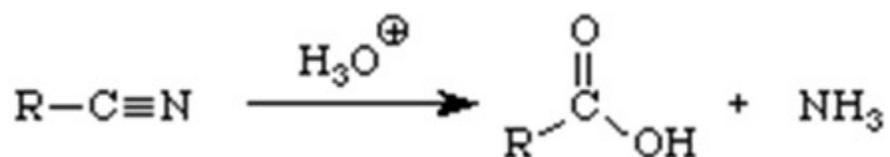
4. Reduction with lithium aluminium hydride to form primary alcohols.

Oxidation of primary alcohol or aldehyde



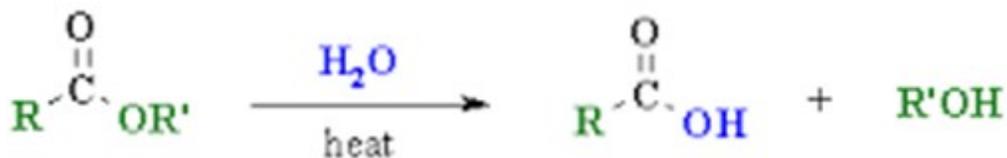
Hydrolysis of nitriles

Refluxing a nitrile with a strong acid or base brings about the hydrolysis of the nitrile and forms a carboxylic acid.



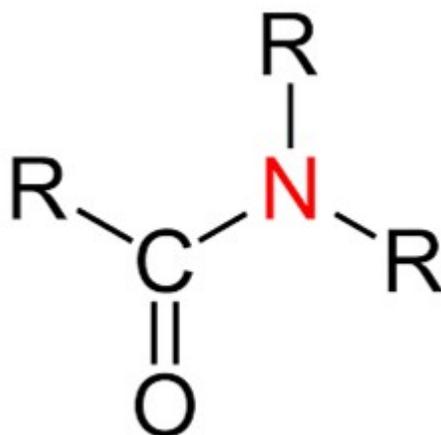
Hydrolysis of Esters

The hydrolysis of an ester carried out in an alkaline environment is another way to produce a carboxylic acid.



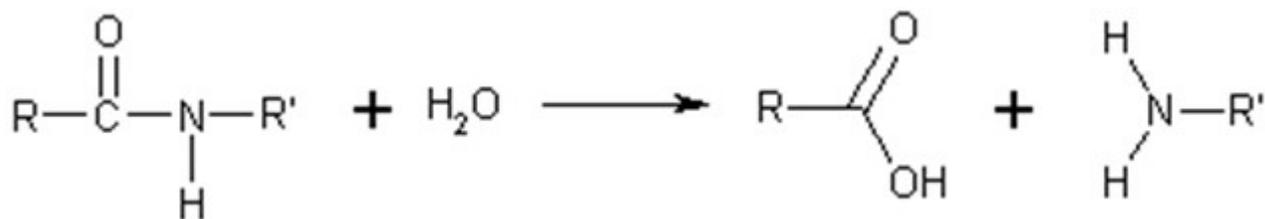
Hydrolysis of amides

An amide link is formed when a carboxylic acid is reacted with an amine yielding not only the amide but also 1 mole of water. The production of the amide is clearly a condensation reaction and so the reverse of this must be hydrolysis.



Hydrolysis of an amide would therefore produce the carboxylic acid along with the amine used to produce it.

The preparation of carboxylic acids is again another very important mechanism in organic chemistry which leads to many other reactions and therefore products.

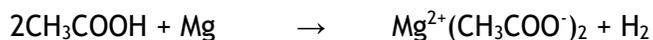


Reactions of carboxylic acids

Formation of salts from reactions with metals

Carboxylic acids remember are examples of weak acids—ones which will not fully dissociate— and so can undergo all the normal reactions of a dilute acid.

One of these could be the production of salts. A neutralisation reaction occurs between an acid and metal or base.

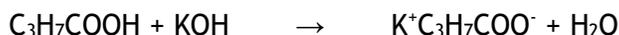


Above shows the reaction between magnesium and ethanoic acid to produce the salt magnesium ethanoate.

Carboxylic acid + Metal Carbonate

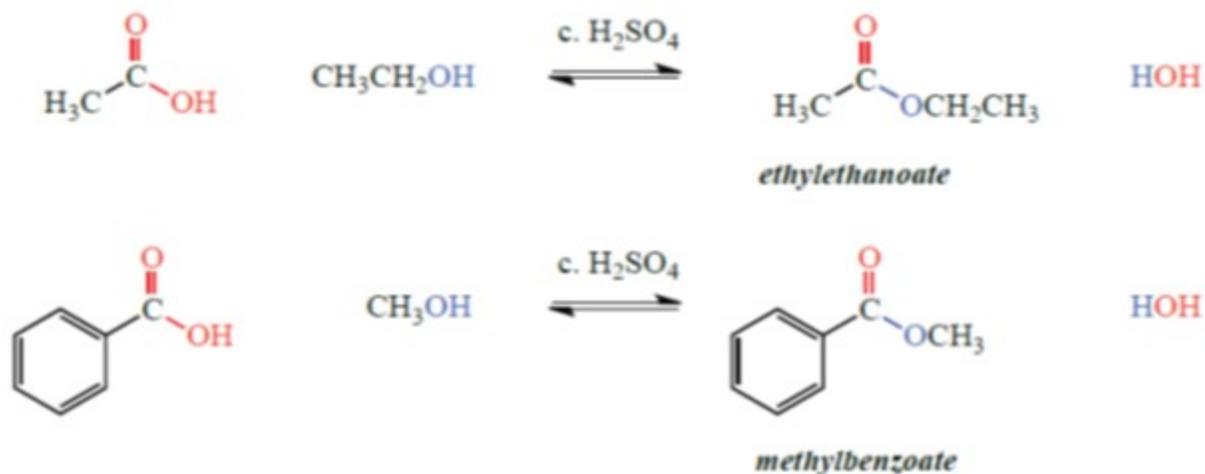


Carboxylic acid + Alkali



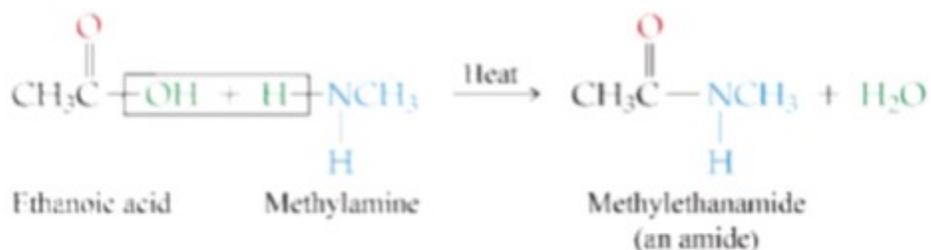
Condensation reactions

In organic chemistry the main reaction undergone by a carboxylic acid will be in the condensation in which an alcohol and acid join together producing an ester. An ester can be thought of as a derivative of an acid.

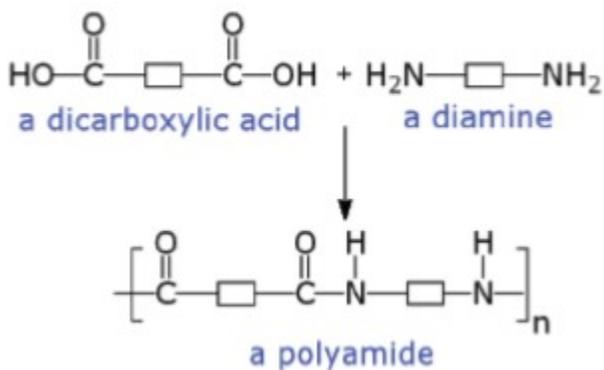


Reaction of carboxylic acid with amino group

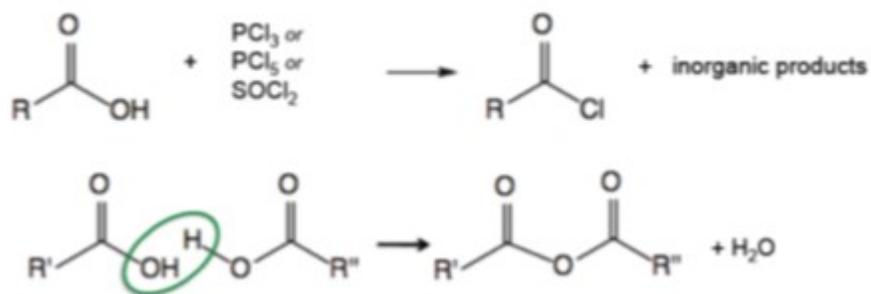
Another previously met reaction of acids is the reaction between the carboxyl group and an amine. This reaction involves the formation of an amide link which has previously been met at both higher and national five level. Again another condensation reaction in which the carboxylic acid reacts with the amino group to form an amide along with a water molecule. An amide can also be considered as a derivative of an acid.



An amide link is used in the manufacture of polymers as well as in polyamides more commonly known as proteins. In the case of proteins the amide link would more likely be known as the peptide link.



Two less familiar condensation reactions lead to less familiar products—an acid chloride and an anhydride. These products would normally be seen more as alternative reactants

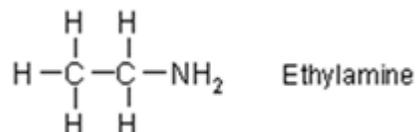


Amines

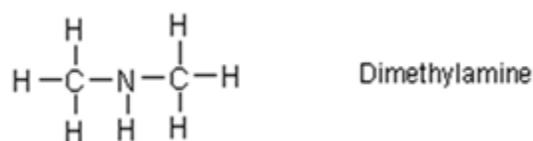
Amines are compounds related to ammonia (NH_3) in which one or more of the hydrogen atoms in the ammonia molecules are replaced by alkyl groups.

Amines can be classified as primary, secondary or tertiary.

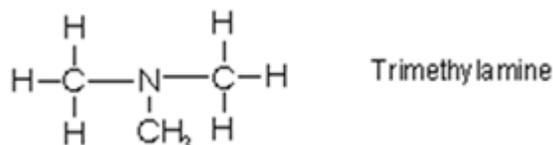
Primary amine general formula = RNH_2 e.g.



Secondary amine general formula = $(\text{R})_2\text{NH}$



Tertiary amine general formula = $(\text{R})_3\text{N}$

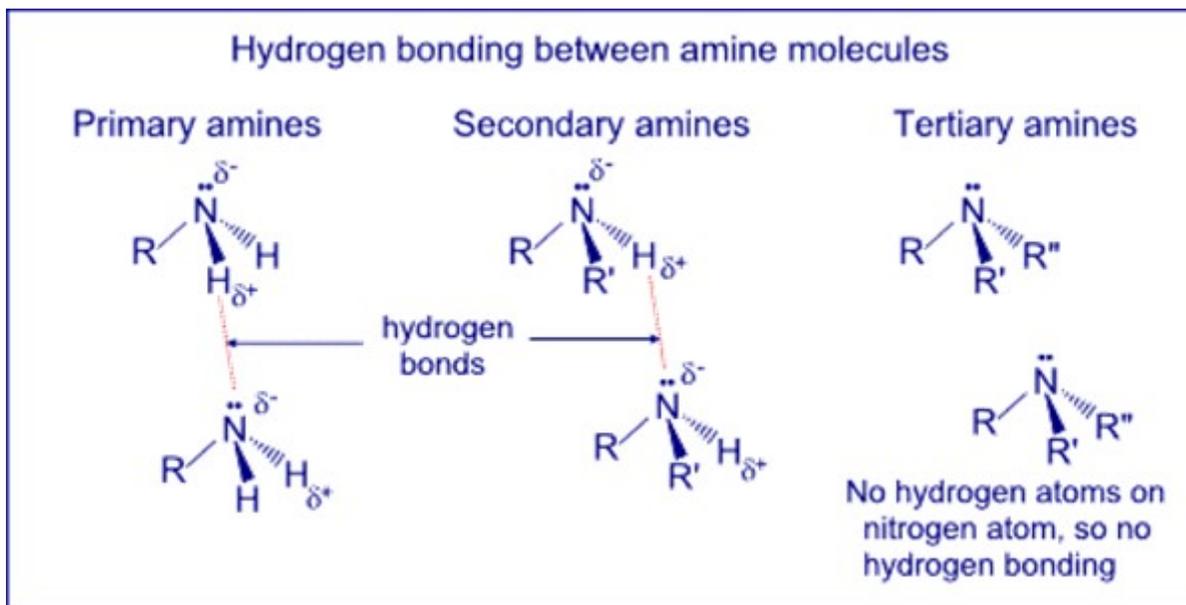


Properties of Amines

Primary and secondary amines generally have higher melting points and boiling points than that of tertiary amines of similar molecular mass due to the hydrogen bonding between the polar NH groups and water molecules. Primary and secondary amines will also have higher melting points and boiling points than alkanes with similar molecular masses for the same reason.

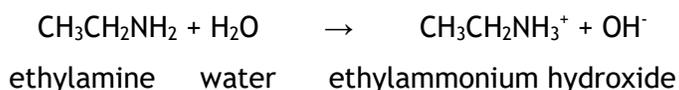
Alkane	Formula Mass	Boiling Point / °C	Amine	Formula Mass	Boiling Point / °C
ethane	30	-89	Methylamine (1°)	31	-7.5
propane	44	-42	Dimethylamine (2°)	45	7.4
butane	58	-1	Trimethylamine (3°)	59	3.5
butane	58	-1	Propylamine (1°)	59	48.6

Short chain primary and secondary amines are also water soluble due to again the hydrogen bonding between the polar NH group and the OH groups in water molecules. As seen previous the solubility decreases as the chain length increases.

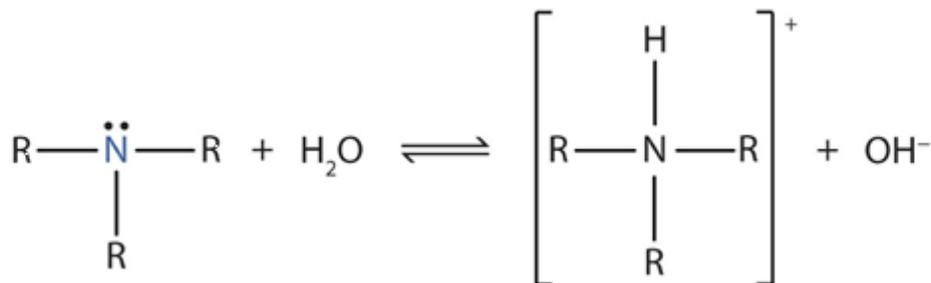


Remember no hydrogen bonding occurs in tertiary amines.

Amines can be termed as bases due to the lone pair on the nitrogen atom of the NH₂ group being able to accept a proton from a water molecule.

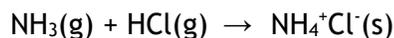


Note the ionisation of the base is incomplete therefore it can be said to be a weak base.

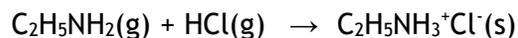


Reactions of Amines

Amines will react (just like ammonia) with acids to form salts:



ammonium chloride



ethylamine

ethylammonium chloride

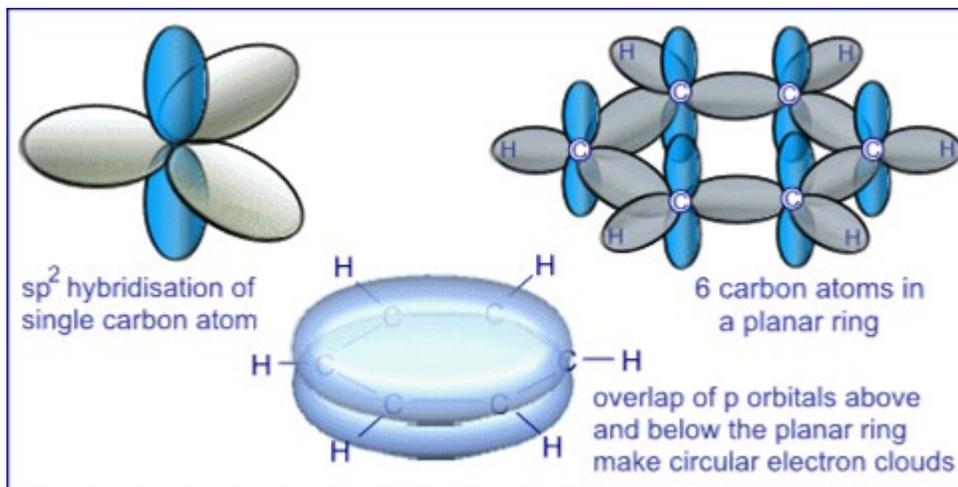
Aromatics

Aromatics are an enormous group of chemicals based on the benzene ring. This benzene ring is super important in advanced higher chemistry and gives any molecule it is attached to very distinctive properties.



Bonding in benzene can be described in terms of sp^2 hybridisation, sigma and pi bonds, and electron delocalisation.

Benzene's **stability** is due to the presence of **delocalised electrons**.



The lack of double bonds in the structure explains the **resistance** of benzene to undergo **addition reactions**.

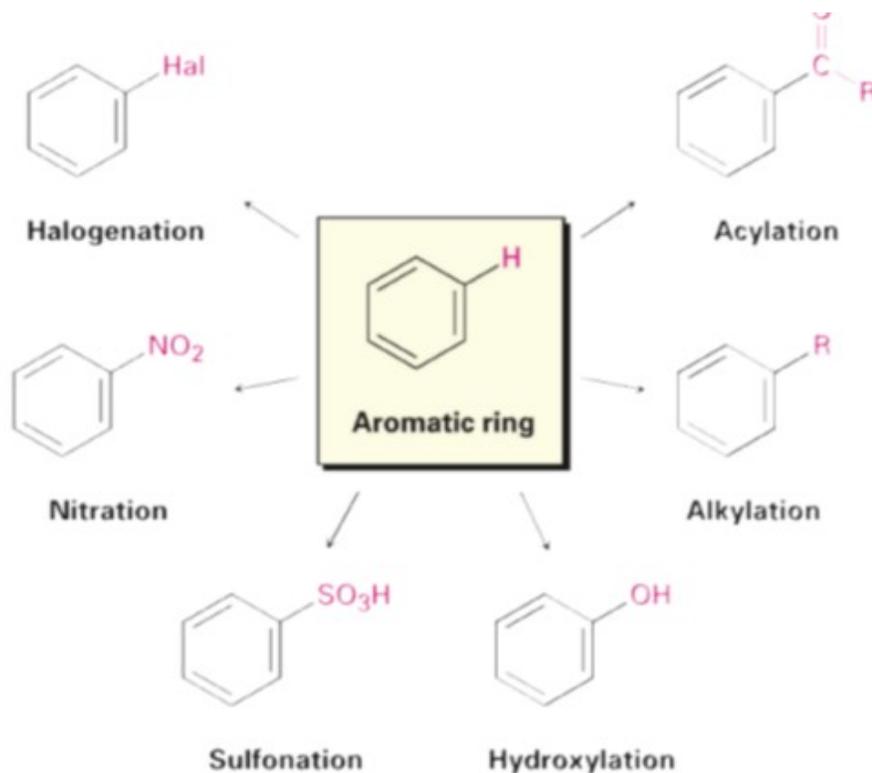
Note: The shape of a benzene molecule is: **PLANAR**

Reactions of Benzene

Most functional groups are introduced into the benzene ring by a substitution reaction. During the substitution reaction the pi cloud of electrons will be disturbed however in the final product it would be re-established.

Electrophilic substitution

Only four electrophilic substitution reactions need to be learnt for advanced higher chemistry however there can be many other products made in this way.



The region of high electron density in the delocalised electron cloud attracts Electrophiles to the benzene ring.

Remember– electrophiles are negative loving

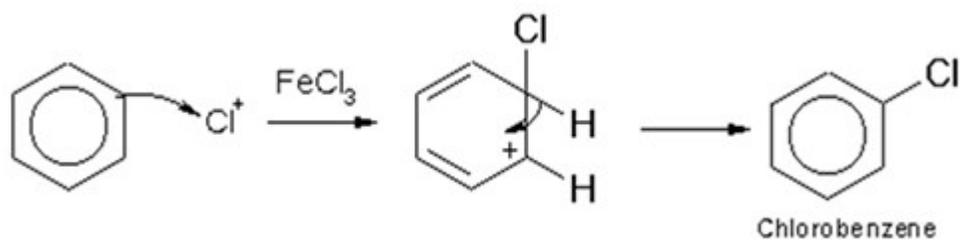
Reactions of benzene rings are in general substitution reactions.

- Chlorination of benzene
- Nitration of benzene
- Sulfonation of benzene
- Alkylation of benzene

Chlorination and Bromination:

Chlorobenzene or indeed bromobenzene can be produced by reacting chlorine or bromine with benzene in the presence of an iron(III) chloride catalyst or aluminium chloride catalyst.

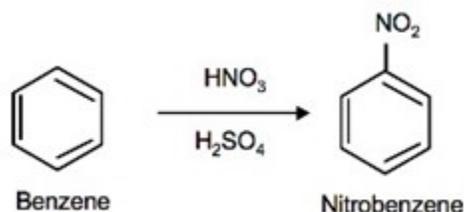
As the chlorine molecule approaches the benzene ring it becomes polarised by the delocalised electron cloud. The positively charged end of the chlorine molecule is now an electrophile and attacks the benzene ring.



Bromination would occur in a similar manner however instead of the chloride catalyst either Iron(II) bromide or aluminium bromide would be used.

Nitration of benzene

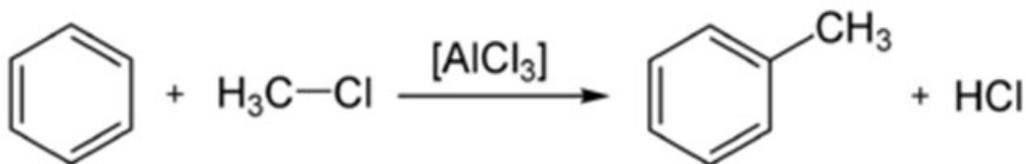
In nitration of benzene the electrophile is the nitronium ion. It is this ion which will attack the benzene ring to give a nitrobenzenium ion and then nitrobenzene.



Concentrated nitric and sulphuric acid produce the nitronium ion, NO_2^+ .

Alkylation of benzene

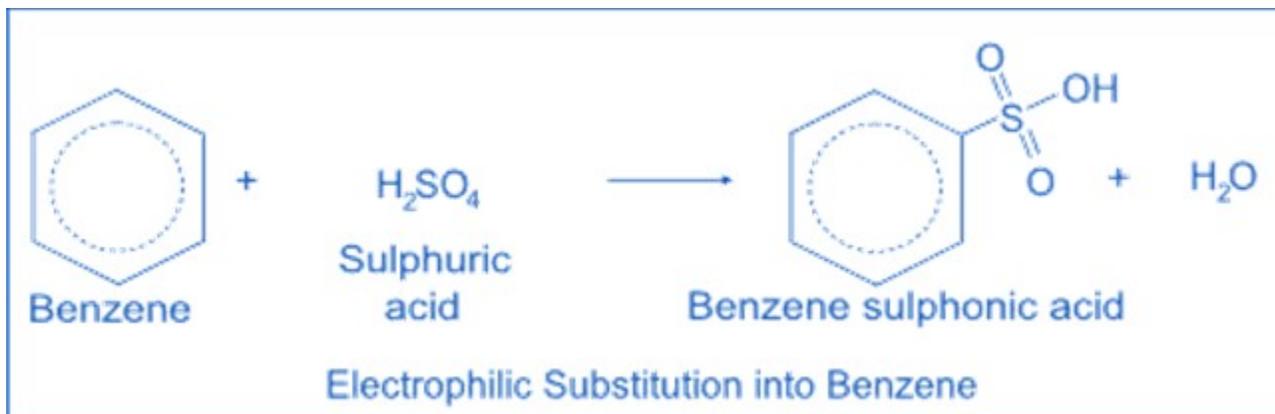
Alkylbenzenes can be formed by reacting benzene with a halogenoalkane with aluminium chloride acting as a catalyst.



In this reaction, known as a Friedel-Craft's alkylation, the aluminium chloride generates a positive electrophilic substituting reagent (CH_2CH_3^+).

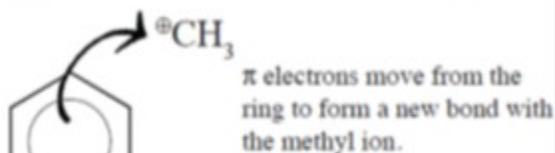
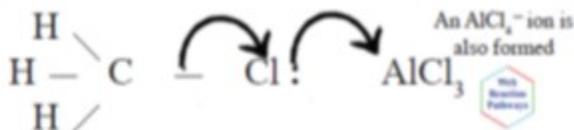
Sulfonation of benzene

Sulfonation involves the substitution of a hydrogen atom of the benzene ring for the sulfonic acid group. This is brought about by heating the benzene with a slight excess of concentrated sulfuric acid. The electrophile is the SO_3^- which even though is neutral acts as a powerful electrophile.



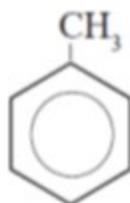
ALKYLATION - USING ALKYL HALIDES/ AlCl_3

The production of the *electrophile* requires the presence of AlCl_3 . (The Al make use of its empty 4^{th} orbital).



The positive charge is shared over the whole ring.

Electrons move from the C—H bond, a H^+ ion is *eliminated*.

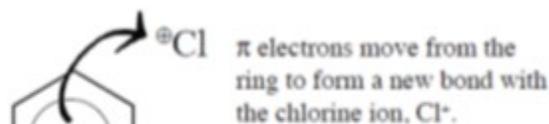


Overall, an alkyl group takes the place of a hydrogen atom, **SUBSTITUTION**.

The H^+ ion reacts with the AlCl_4^- to reform AlCl_3 and a molecule of HCl .

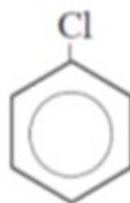
HALOGENATION - USING HALOGENS/ AlCl_3

The production of the *electrophile* is helped by the presence of AlCl_3 . The reaction would be very slow otherwise.



The positive charge is shared over the whole ring.

Electrons move from the C—H bond, a H^+ ion is *eliminated*.

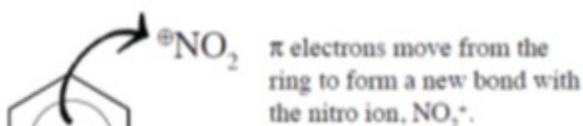


Overall, a halogen atom takes the place of a hydrogen atom, **SUBSTITUTION**.

The H^+ ion reacts with the AlCl_4^- to reform AlCl_3 and a molecule of HCl .

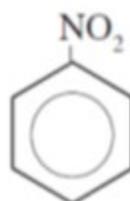
NITRATION - USING $\text{H}_2\text{SO}_4/\text{HNO}_3$

The production of the *electrophile*, NO_2^+ is a result of a reaction between these two strong acids.



The positive charge is shared over the whole ring.

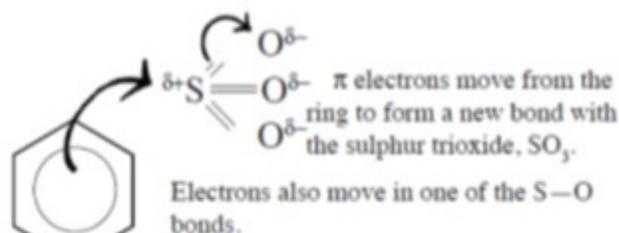
Electrons move from the C—H bond, a H^+ ion is *eliminated*.



Overall, a nitro group takes the place of a hydrogen atom, **SUBSTITUTION**.

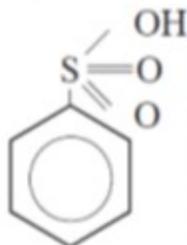
SULPHONATION - USING $\text{H}_2\text{SO}_4/\text{SO}_3$

The *electrophile* is a molecule of SO_3 . The 3 oxygen atoms are more electronegative; a large δ^+ forms on the sulphur.



The positive charge is shared over the whole ring.

Electrons move from the C—H bond, a H^+ ion is *eliminated*.



The H^+ ion that is eliminated from the benzene ring attaches itself to the oxygen ion.

Overall, a HSO_3 group takes the place of a hydrogen atom, **SUBSTITUTION**.

Phenol and Phenylamine

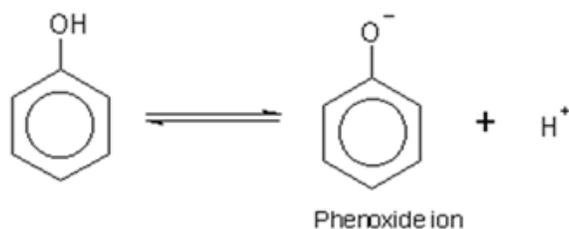
Phenol is an aromatic compound with the structure.



The phenol compound contains the hydroxyl group which is common to alcohols however it is this which changes the properties of the benzene ring.

Phenol acts as a weak acid due to the attached OH group. The electron withdrawing nature of benzene means that the polarity of the OH group is increased which causes a very limited ionisation when phenol is dissolved in water.

Phenol is the only alcohol to show acidic properties.



The phenol itself has to lose the hydrogen of the OH group to exhibit the acidic properties. Though the ionisation is so weak that the phenol does not react with carbonates to give off carbon dioxide—as phenol is even weaker than carbonic acid.

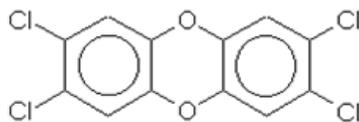
The ability of the negative charge on the phenoxide ion to be shared with the delocalised electrons in the benzene ring makes its formation possible.

Other aromatic compounds

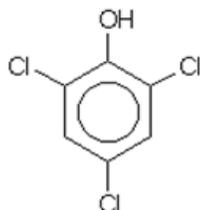
There are a large number of substituted benzene compounds which are used in the manufacture of a large number of consumer products. We can also get compounds which contain more than one benzene ring in the structure. (There is no need to remember these structures.)



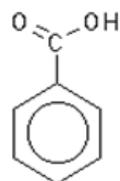
Naphthalene



2,3,7,8-tetrachlorodibenzodioxin
2,3,7,8-TCDD



Trichlorophenol



Benzoic acid

Synthetic Routes

The starting point in planning a synthesis is to examine the final product of the synthesis. This is called the target compound. By looking at the functional groups and structure of the target molecule, chemists can work backwards, through a logical sequence of reactions, until a suitable starting compound is found. The synthetic route to the target compound can involve many steps and can take years to achieve the synthesis of the target molecule.

(c) Stereochemistry

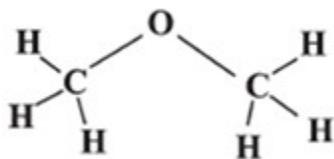
(i) Stereoisomerism

Isomerism is an interesting and important feature of organic chemistry. Isomerism occurs whenever there is more than one way to organise a given number of atoms into a molecule.

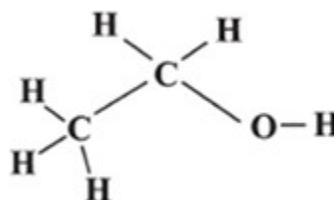
The definition of isomer is - "compounds with the same molecular formula but a different structural formula"

In structural isomerism, the molecules differ in terms of the order in which the atoms are joined together.

For example 2 possible isomers with molecular formula C_2H_6O



Methoxymethane



ethanol

In methoxymethane, the oxygen atom lies between the two carbon atoms whereas in ethanol the two carbon atoms are bonded together with the oxygen at the end. Clearly, the two substances belong to different homologous series and will have very different chemical and physical properties.

In stereoisomers, the molecules differ only in the orientation of the atoms in space. They have identical formulae and the atoms are bonded together in the same order. However, because the arrangements of the atoms in space is different, the molecules are non-superimposable.

Non superimposable just means that no matter how hard you try it is impossible to superimpose the image of one molecule on top of the other.

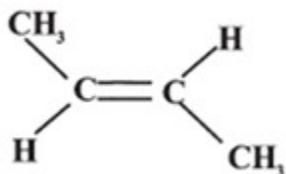
There are two different types of stereoisomerism - **geometric** and **optical**.

Geometric Isomerism

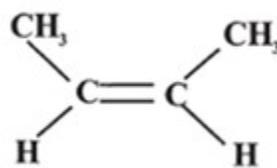
Geometric isomerism is one type of stereoisomerism and generally arises because of the lack of free rotation around a double bond, especially a carbon-carbon double bond. Rotation around a double bond may be restricted as the π bond would have to be broken.

Also, if both carbon atoms of the double bond each carry a single substituent, then two isomers will exist, one with the substituents on the same side of the double bond and the other with the substituents on the opposite sides.

e.g. But-2-ene



trans-but-2-ene



cis-but-2-ene

If the substituents are on opposite sides of the double bond, the isomer is called the *trans*-isomer whereas if the substituents are on the same side it is called the *cis*-isomer. Structure (a) is the *trans* isomer as both the methyl groups are on opposite sides from one another whilst structure (b) is the *cis*-isomer as both methyl groups are on the same side.

Geometric isomers are different compounds and so have distinct physical properties. The boiling points of the two different isomers of but-2-ene show great difference.

Isomer	Boiling Point / °C	Melting Point / °C
<i>trans</i> -but-2-ene	-106	+4
<i>cis</i> -but-2-ene	-139	+1

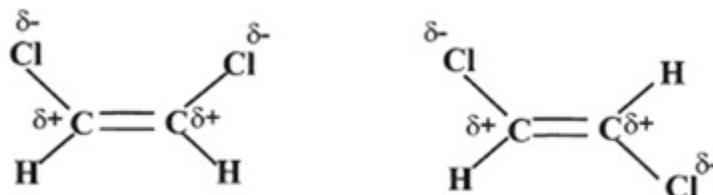
The differences in melting points can be explained in terms of the differences in the shapes of their molecules. It appears likely that molecules of the *trans* isomers can pack more closely together in the solid state than the *cis* isomers. This close packing will therefore increase the van der Waals' forces between the molecules and so increase the melting point.

Geometric Isomers

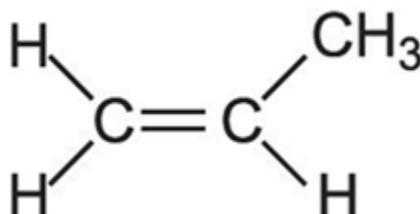
In both geometric isomers of 1,2-dichloroethane the Cl-Cl bonds are polar. In the *cis*- isomer both bonds lie on the same side of the double bond and so the molecule itself will be polar. However, because of the symmetry of the *trans*- isomer, the polarities of the bonds cancel each other out and so the molecule itself is non-polar. As a result of these extra polar-polar attractions between the molecules of the *cis* -isomer, the *cis*-isomer has a higher boiling point than the *trans* -isomer.

Isomer	Boiling Point / °C	Melting Point / °C
--------	--------------------	--------------------

cis-dichloroethene	-80	+60
trans-dichloroethene	-50	+48



So, geometric isomerism can occur in organic compounds which contain a C=C double bond. However, in addition to the double bond the molecule must also have two different groups attached to each of the carbon atoms of the double bond. Propene for example would not display geometric isomerism as it has two identical hydrogen atoms attached to one of the carbon atoms of the double bond.



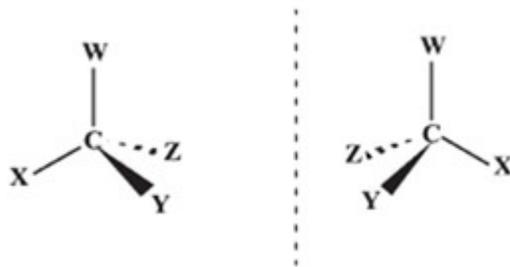
Although, geometric isomerism is most common in compounds which contain a C=C double bond, it can also arise in saturated rings where rotation about the C-C single bond is restricted.

Optical Isomerism

This type of stereoisomerism occurs whenever a molecule contains a tetrahedral carbon atom that has four different groups attached.

Molecules which contain a tetrahedral carbon atom with four different groups are called chiral molecules. These molecules shown above have two possible arrangements. They differ only in that one is a mirror image of the other. Such isomers are known as enantiomers. It is impossible to exactly superimpose the structure of one enantiomer on top of the other.

The two enantiomers are said to be asymmetric which means they have no centre of symmetry, plane of symmetry or axis of symmetry. The relationship between these two enantiomers is a bit like the relationship between your two hands, which are also mirror images and cannot be superimposed on each other. A right handed glove does not fit a left hand and is said to be chiral.



Unlike geometric isomers, optical isomers or enantiomers have identical physical properties except that they have an opposite effect on plane polarised light. For this reason, it is said that they are optically active. They also have identical chemical properties except when reactions are carried out in a chiral (asymmetric) environment.

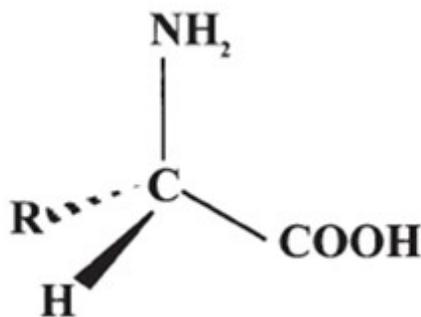
A beam of light consists of an infinite number of waves vibrating in all planes perpendicular to the direction in which the light travels. If this beam of light is passed through a polariser (such as the polaroid film in polaroid sunglasses) all the vibrations are cut out except those in one plane. The light emerging from the polariser is plane-polarised light.

When plane-polarised light is passed through a solution containing an optical isomer the plane of the polarised light is rotated through a certain angle. If this solution is replaced by an equimolar solution of the other optical isomer it too will rotate the plane of polarised light by the same angle but in the opposite direction. Substances that can rotate a plane polarised light are said to be optically active.

An equimolar mixture of the two optical isomers would have no effect on plane-polarised light since the rotational effect of one would cancel out the opposite rotational effect of the other. This mixture is said to be optically inactive and is known as a racemic mixture.

Chirality is extremely important in biological systems. Enzymes are complex proteins that are condensation polymers built up from monomers known as 2-amino acids or α -amino acids.

The α -amino acids are chiral as can be seen in the diagram and therefore there will be two optical isomers for every amino acid found in proteins.



Since the monomer units are chiral, it follows that the enzymes themselves will be chiral. If the substrate molecule on which an enzyme works is chiral, then only one of the optical isomers of the substrate will fit the enzyme's active site. Therefore, the other isomer will not be biologically active.

In general, if a naturally occurring molecule can exhibit optical isomerism, only one of the optical isomers is usually present in the biological system.

(d) Experimental determination of structure

In organic chemistry not only are we able to synthesise products used to meet market demands but also we can verify that the correct chemical structure has actually been synthesised.

There are various methods used to determine the chemical structure of compounds such as

- Elemental microanalysis
- Mass spectroscopy
- Infrared spectroscopy
- Proton NMR spectroscopy
- UV/Vis spectroscopy

Elemental Microanalysis otherwise known as combustion analysis is used to determine the masses of elements in a sample of an organic compound in order to determine its empirical formula. The compounds dealt with will normally contain carbon, hydrogen, sulphur and nitrogen.

Empirical formula shows the simplest whole number ratio of different atoms in the compound.

Ethane C_2H_6 has a C:H ratio of 1:3 therefore its empirical formula would be CH_3 .

In combustion analysis a tiny sample of compound is burned in an excess of oxygen which ensures that the products of the combustion reaction are carbon dioxide, nitrogen dioxide, sulfur dioxide and water.

The mixture of gases is then carried in a stream of helium over heated copper which reduces the nitrous oxides produced to nitrogen.

The quantities of each of the products of combustion are then determined by infrared detectors, absorbed in anhydrous magnesium chlorate and measurements of thermal conductivity.

Knowing the masses of CO_2 , SO_2 , H_2O and nitrogen makes it very easy to calculate the masses of carbon, hydrogen, sulphur and nitrogen in the compound and therefore its empirical formula.

(i) Empirical Formula

Example 1

A hydrocarbon was found to contain 4.5 g of carbon and 1.5 g of hydrogen. Calculate the empirical formula of the hydrocarbon?

Element	C	H
Mass	4.5 g	1.5
Divide by atomic mass	$\frac{4.5}{12}$	$\frac{1.5}{1}$
	= 0.375	1.5
Divide to give whole numbers	$\frac{0.375}{0.375}$	$\frac{1.5}{0.375}$
	= 1	4

Empirical Formula: CH₄.

Example 2

Analysis of an alcohol shows it to contain 37.5% carbon and 12.5% hydrogen. What is the empirical formula?

Element	C	H	O
% by mass	37.5	12.5	50
Divide by atomic mass	$\frac{37.5}{12}$	$\frac{12.5}{1}$	$\frac{50}{16}$
	= 3.125	12.5	3.125
Divide to give whole numbers	$\frac{3.125}{3.125}$	$\frac{12.5}{3.125}$	$\frac{3.125}{3.125}$
	= 1	4	1

Empirical Formula: CH₄O

Example 3

5.0 g of aluminium was burned in oxygen producing 9.45 g of aluminium oxide. Calculate the empirical formula.

Element	Al	O
Mass	5 g	4.45 g
Divide by atomic mass	$\frac{5}{27}$	$\frac{4.45}{16}$
	= 0.185	0.278
Divide to give whole numbers	$\frac{0.185}{0.185}$	$\frac{0.278}{0.185}$
	= 1	1.5
Scale-up (x2)	2	3

Empirical Formula: Al₂O₃

Mass Spectrometry

Mass spectrometry is a technique used to determine the accurate molecular mass and structural features of a compound.

The sample is vapourised and then ionised by being bombarded with electrons in the ionisation chamber.

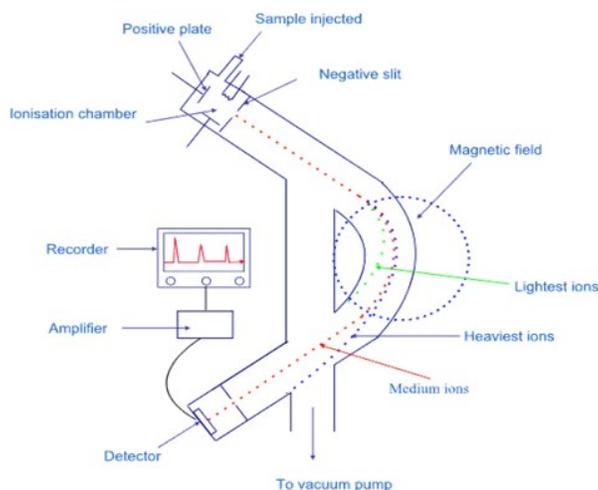
The sample molecules then break up into smaller fragments (Fragmentation)

The parent ion and ion fragments are:

1. accelerated by an electric field and then
2. deflected by a magnetic field

Ions with lower m/z (mass/charge) ratio are deflected more than ions with higher m/z ratio.

A mass spectrum (specific to each organic substance) is obtained.



When the organic molecules are bombarded with energetic electrons, the following occurs:
an electron can be removed to form a positively charged molecular ion,



Parent ion: is the initial molecular ion that is produced

e.g. butane (C_4H_{10}) parent ion = ($C_4H_{10}^{+}$)

Fragmentation:

This causes molecules to break into pieces which also become molecular ions.

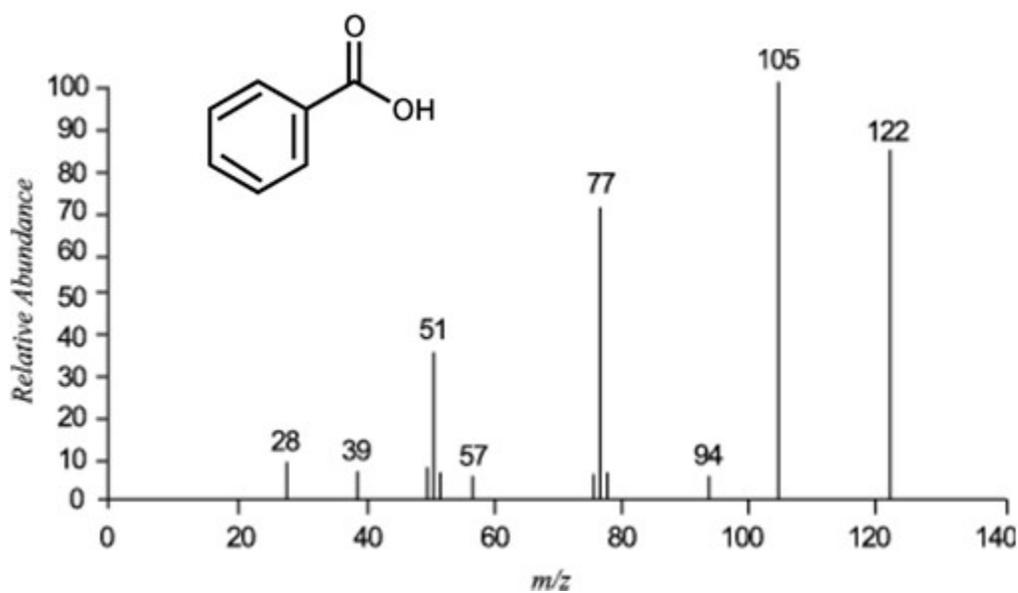
e.g. fragments of butane could be:

molecular ion	Mass/charge(m/z)
---------------	----------------------

$C_4H_9^+$	$\frac{57}{1} = 57$
$C_3H_6^+$	$\frac{42}{1} = 42$
CH_3^+	$\frac{15}{1} = 15$

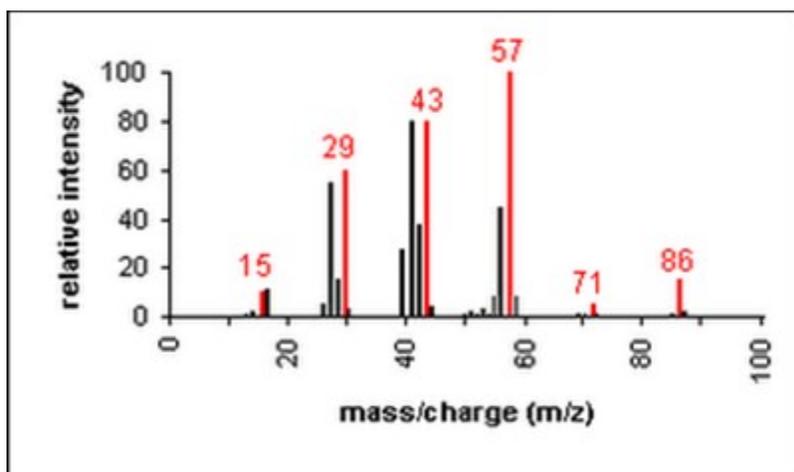
Examples of Mass Spectra

Benzoic Acid



- The peak with the highest m/z value is often the molecular ion:
 - $C_6H_5COOH^+ = 122$
- The most abundant peak is called the base peak and is assigned an abundance of 100%:
 - $C_6H_5CO^+ = 105$
- Other abundances are given smaller percentages, relative to the base peak:
 - $C_6H_5^+ = 77$

Hexane



Mass /amu	Fragment
86	C ₆ H ₁₄ ⁺ (molecular ion)
71	C ₅ H ₁₁ ⁺
15	CH ₃ ⁺

Infrared spectroscopy

Infra-red spectroscopy can be used to identify certain functional groups in an organic compound.

Infra-red radiation causes parts of a molecule to vibrate (stretch and/or bend) and matches the natural vibration frequency of the bonds.

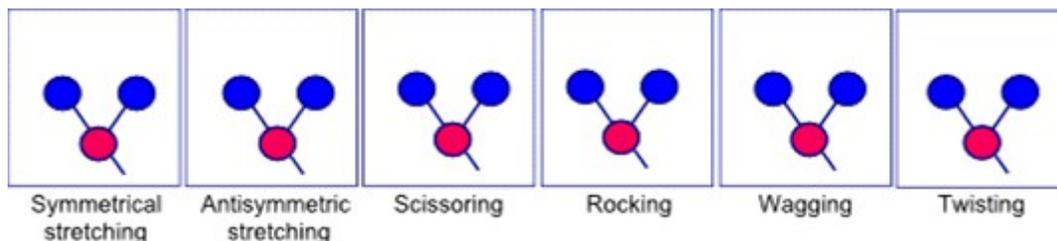
The wavelengths which are absorbed will depend on the type of chemical bond and the groups or atoms at the ends of these bonds.

Absorptions are measured in terms of wavenumber.

Wavenumber is the reciprocal of wavelength and is often used as the energy unit (x-axis) in infrared spectra.

$$\frac{1}{\lambda} (\lambda \text{ in cm}) = \text{cm}^{-1}$$

These bends and stretches are shown below.

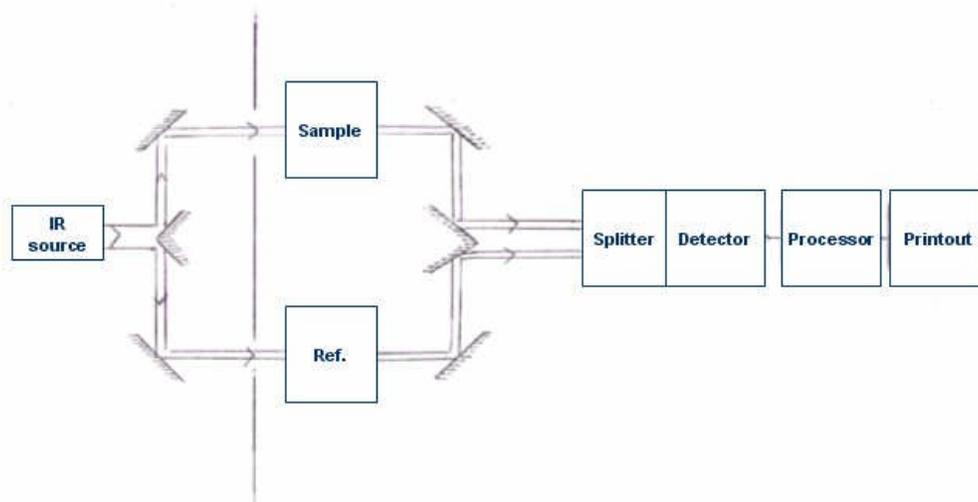


The **data book** (page 14) shows the wavenumber of the stretches and bends of particular bonds.

IR Spectrometer

An infra-red spectrometer passes radiation through a sample of the organic compound and then to a detector.

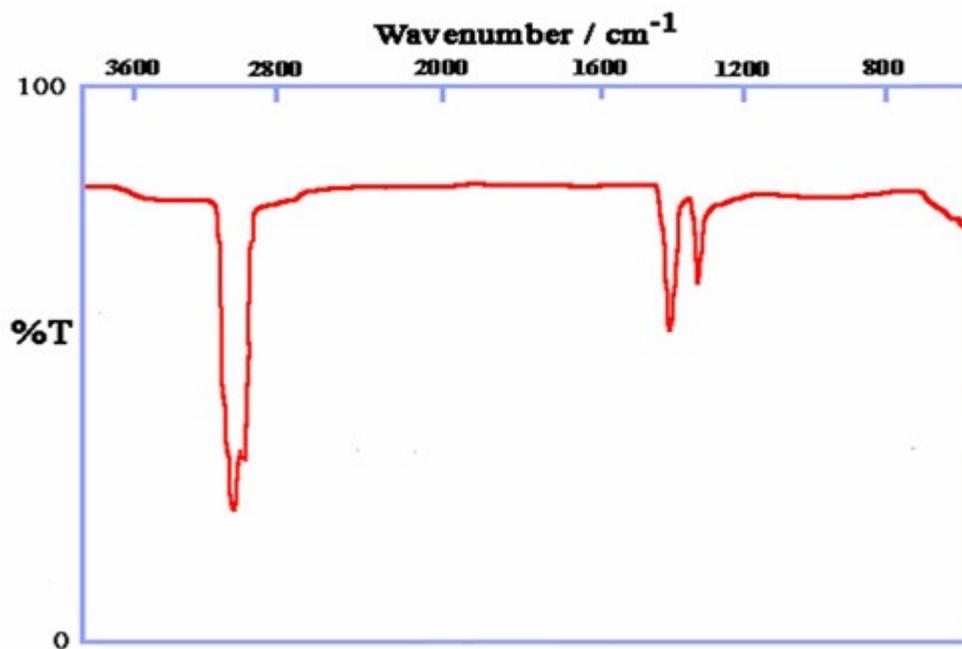
An identical beam is passed through a reference blank cell and the detector compares the intensities of radiation through the sample and reference cell.



Where groups absorb, infra-red radiation transmittance will be lower, and a trough is seen in the spectrum. The main use of IR spectra, which can be obtained quickly and cheaply, is to identify the presence of functional groups and the carbon backbone type in unknown organic compounds.

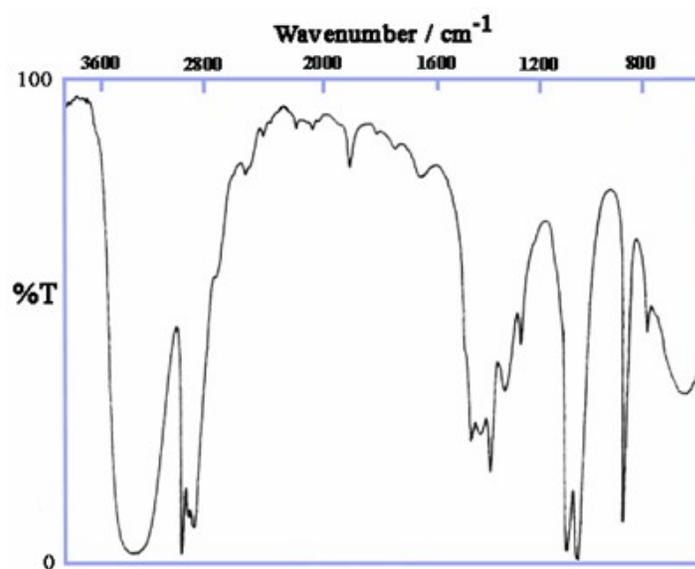
IR Spectra

Paraffin—mixture of alkanes



- C-H stretch at 2930 cm⁻¹
- asymmetric stretch at 2880 cm⁻¹

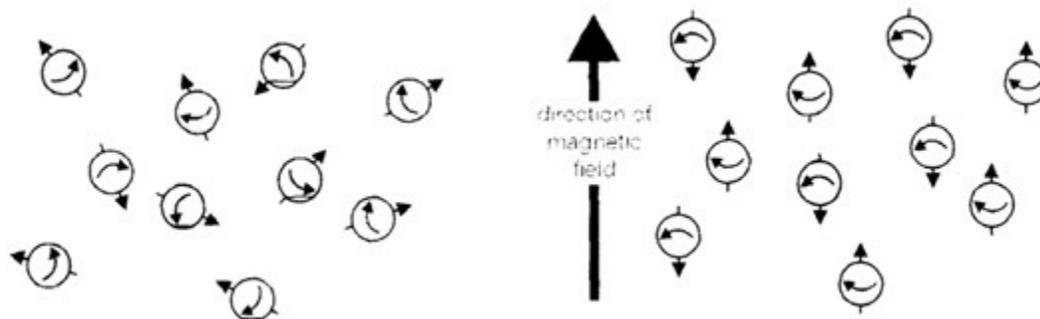
Ethanol



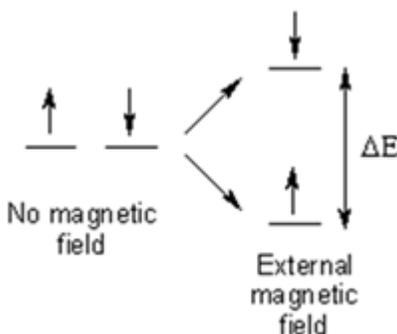
- O - H stretch in the region 3570 - 3200 cm⁻¹

Proton NMR Spectroscopy

Like electrons protons also possess a property known as spin. Because of this property the nuclei of the hydrogen atoms behave like tiny magnets. When these nuclei are placed in a magnetic field the nuclei align themselves with the field—just as a compass needle aligns itself with the Earth’s magnetic field. Energy is required to change the alignment of the hydrogen nuclei with the magnetic field—the nuclei can be pushed from one alignment to another by energy supplied by the radio waves.

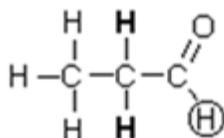


The energy difference between the aligned state and the non-aligned state depends on the environment that the nucleus is in.—the electrons in the surrounding atoms shield the nucleus from the magnetic field. When a hydrogen atom in a molecule absorbs radio waves as it flips between states, the frequency of the radio waves producing these flips tells us a great deal of information about the position of hydrogen atoms in a molecule.



Interpreting NMR Spectra

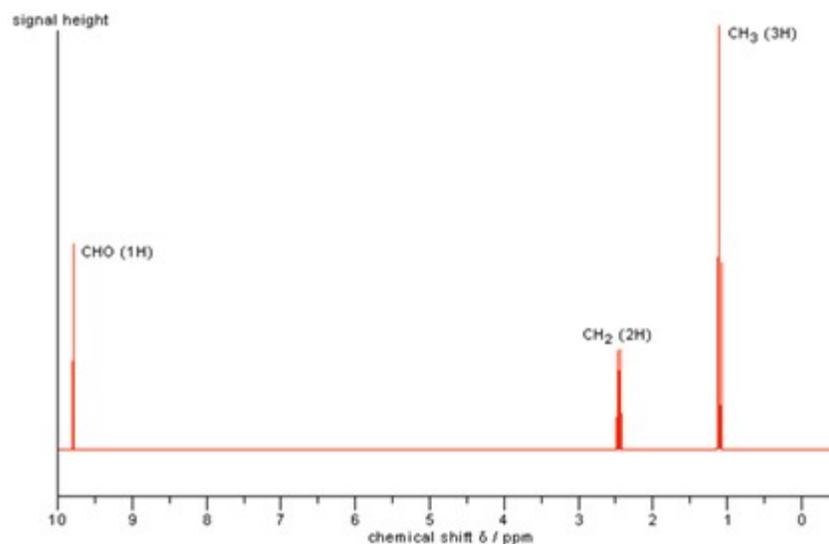
The compound, propanal, has hydrogen atom in three different environments.



This molecule produces three sets of peaks in the nmr spectrum.

- Three hydrogen atoms in the CH₃ group.
- Two hydrogens in the CH₂ group

- A hydrogen atom in the CHO group



The CH_3 peak has three times the area of the CHO peak as there are three hydrogen atoms in an identical environment compared to the one hydrogen atom in the CHO environment. Information on chemical shifts is given in data book (p16).

Proton NMR spectra

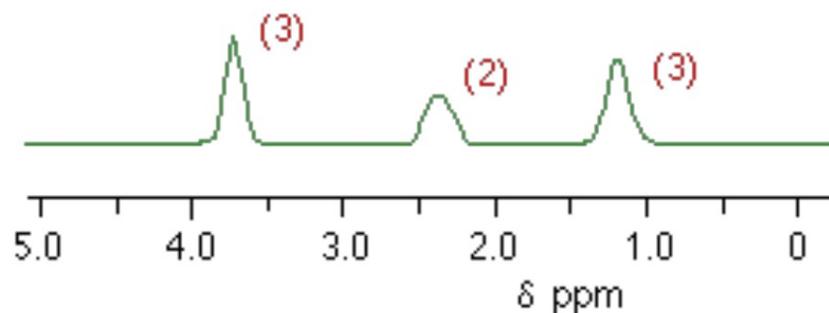
To run an NMR, we dissolve the compound being analysed in a solvent which contains no hydrogens. The solvent used will normally have Deuterium 2H replacing the H in the molecule CDCl_3 or CD_3COCD_3 so that the solvent will not produce peaks in the spectra.

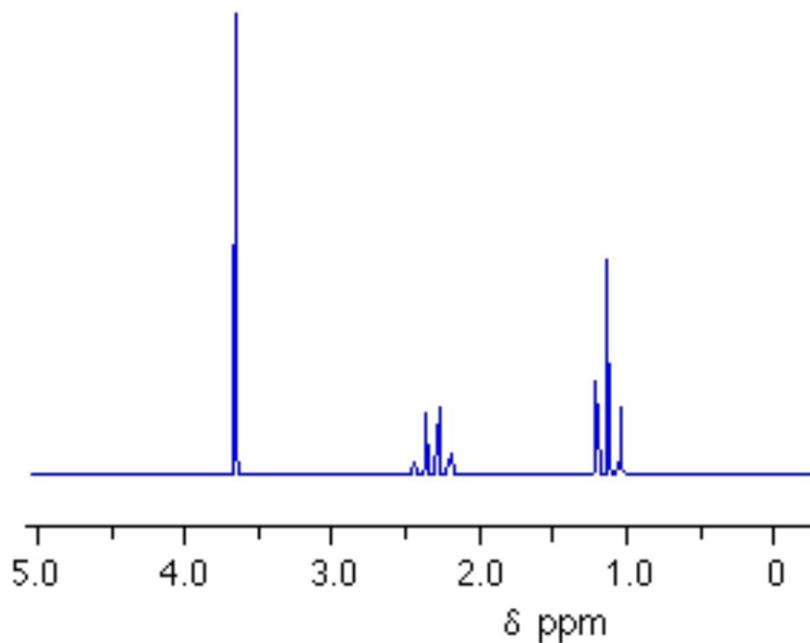
The compound tetramethylsilane (TMS) is normally added as a standard, with its chemical shift taken as zero.

High resolution versus low resolution spectra

Close examination of the spectrum above will confirm that each peak has a number of sub-peaks. This is due to a phenomenon called “coupling”.

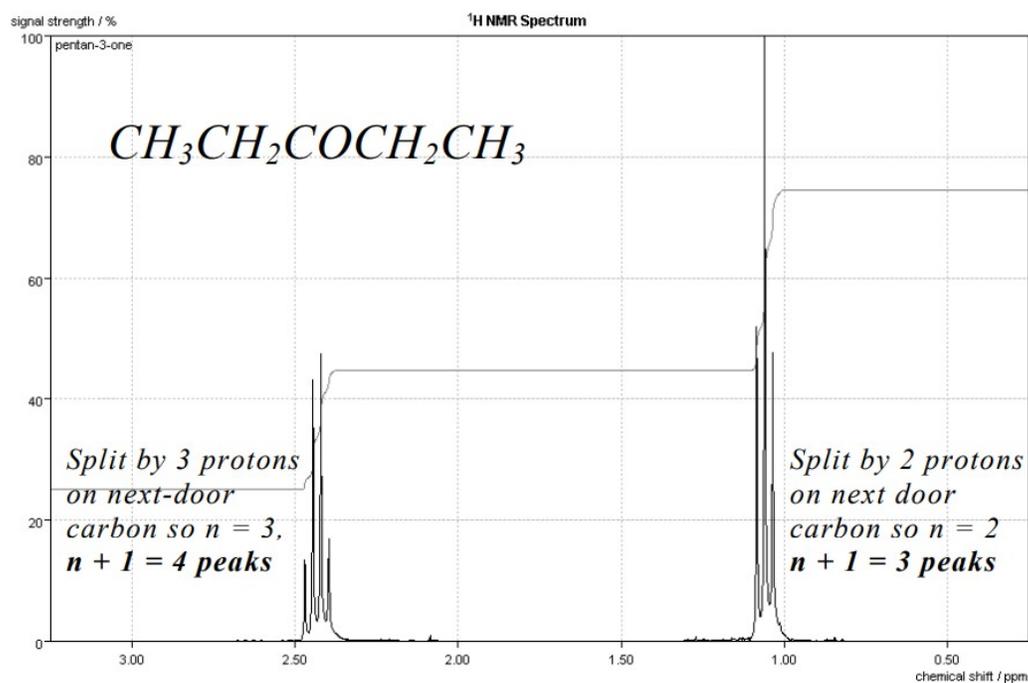
Compare the low- and high-resolution spectra for methyl propanoate below.





Under higher resolution, the peak arising from a particular hydrogen atom may be split into a double, triple or multiple peak. This provides a great deal of information about the structure of the molecule. The hydrogens on the neighbouring carbon atoms cause the splitting of peaks. The splitting follow a simple 'n + 1' rule, where a peak is split into a 'doublet' if there is one adjacent hydrogen, a 'triplet' if two adjacent hydrogens and so on.

e.g.



Not only can we tell how many different environments, and how many hydrogens are in each environment, we can also tell how many hydrogen are on the adjacent carbons. This is usually enough to help confirm the structure of a molecule

Magnetic resonance imaging MRI

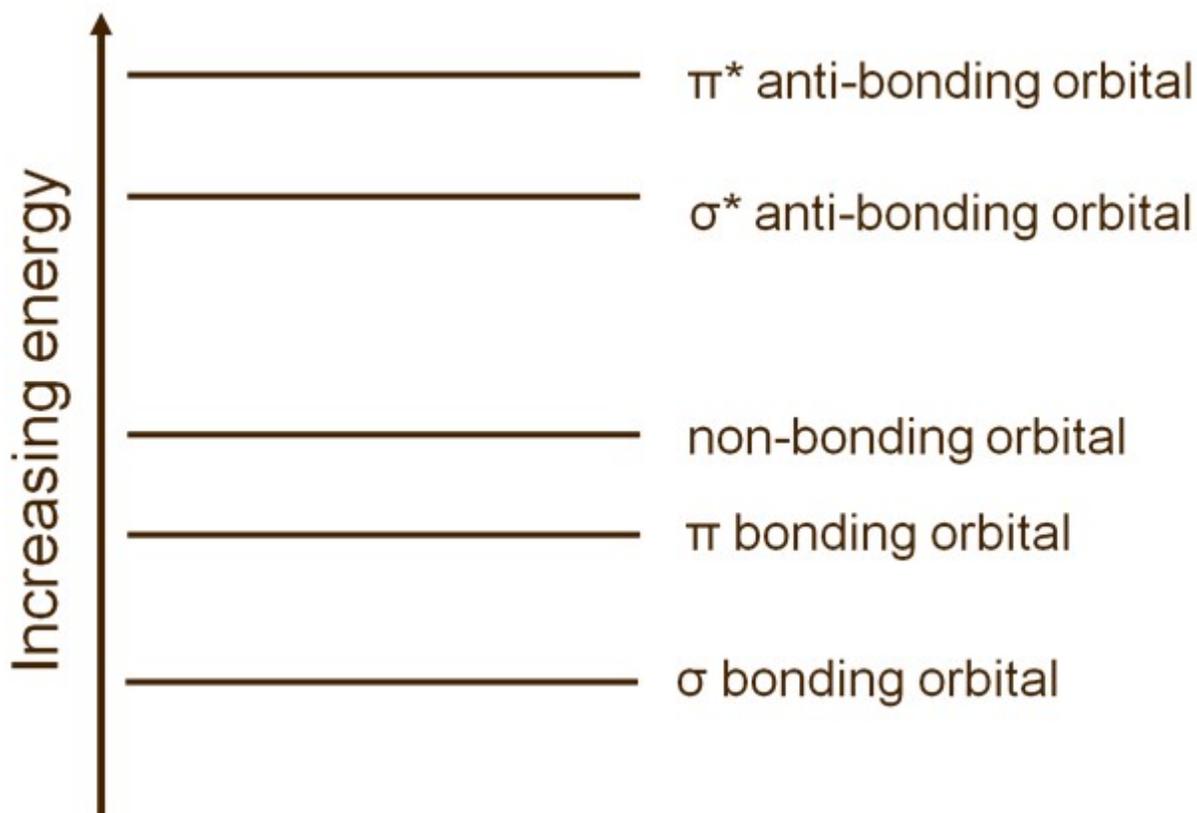
Nuclear magnetic resonance is the principle behind Magnetic resonance imaging. This is used to produce an image of the bodies internal organs and structures.

UV/Vis Spectroscopy

While many chemical compounds are coloured because they absorb visible light, most organic molecules appear colourless.

Energy from photons is used to promote electrons from bonding or non-bonding orbitals into the higher energy anti-bonding orbitals.

The σ^* and π^* anti-bonding orbitals are normally empty.



The σ and π bonding orbitals contain normal bonding pairs of electrons. The non-bonding orbital contains lone pairs of electrons.

Several transitions are possible, each with an electron being excited from a full orbital into an empty one.

Organic compounds that contain only σ bonds are colourless.

Molecules and Colour

The σ bonding orbital is the highest occupied molecular orbital (HOMO), and the lowest unoccupied molecular orbital (LUMO) is the σ^* anti-bonding orbital.

Excitations of electrons in compounds containing simple π bonds still involve a large transition to promote an electron from HOMO (π bonding orbital) to LUMO (σ^* anti-bonding orbital), and thus these compounds also absorb in the UV region of the spectrum.

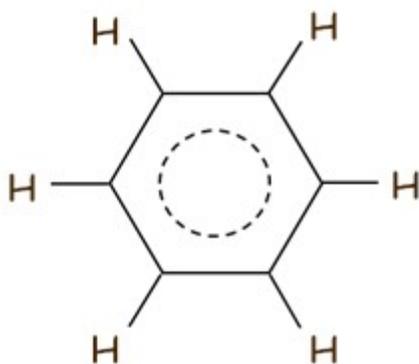
While these organic compounds do absorb light, the energy transitions involved in promoting an electron from σ to σ^* are very large.

These absorptions correspond to the UV part of the spectrum.

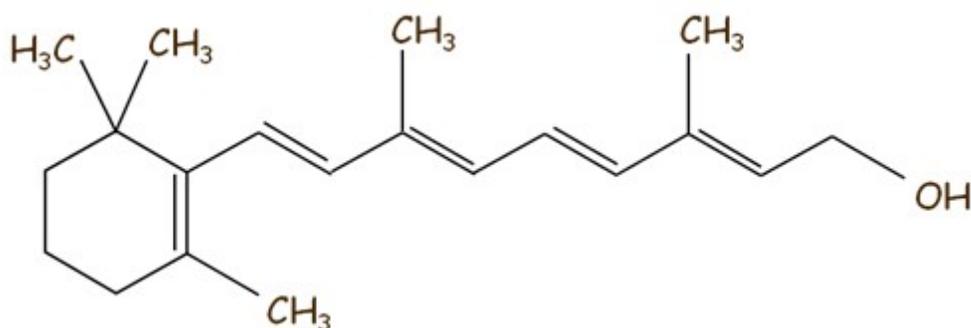
Conjugated system

Organic molecules that are coloured contain delocalised electrons spread over a number of atoms. These molecules are known as conjugated systems.

Previously we have considered conjugation in small molecules such as benzene.



For bonds to be conjugated in long carbon chains, alternating double and single bonds must be present. Vitamin A contains a long chain of alternating σ and π bonds.



The molecular orbital contains delocalised electrons which stretch along the length of the conjugated system.

The greater the number of atoms spanned by the delocalised electrons, the smaller the energy gap will be between the delocalised orbital and the next unoccupied orbital.

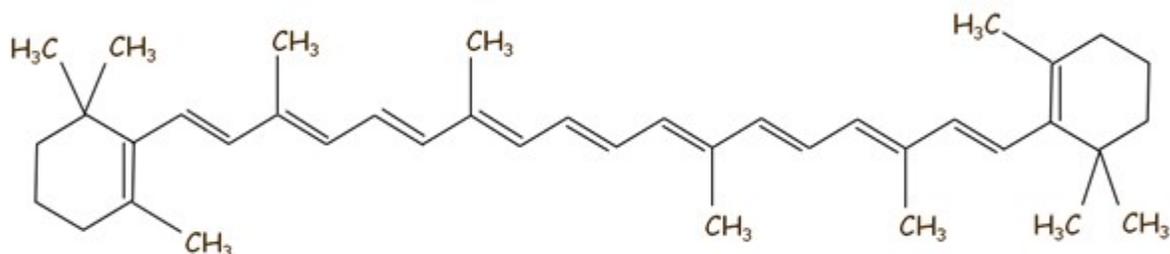
Exciting the delocalised electrons will therefore require less energy. If this falls within the visible part of the electromagnetic spectrum this will result in the compounds appearing coloured.

Chromophore

A chromophore is a group of atoms within a molecule that is responsible for its colour.

Coloured compounds arise because visible light is absorbed by the electrons in the chromophore, which are then promoted to a higher energy molecular orbital.

By comparing chromophores, we can find out about the energy of light that is being absorbed.



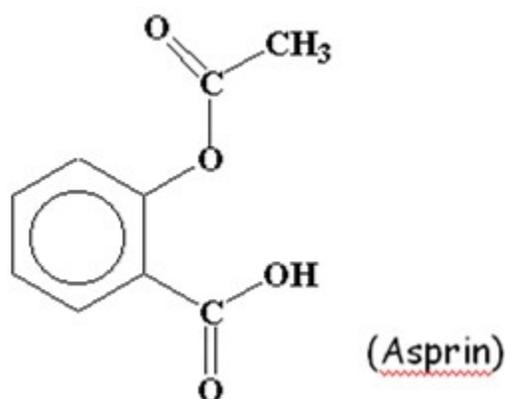
β -carotene is found in carrots, sweet potatoes and apricots. It has a conjugated system that spreads over eleven carbon-to-carbon double bonds. Light can be absorbed when electrons in a chromophore are promoted from one molecular orbital to another. If the chromophore absorbs the light of one colour the compound will exhibit the complementary colour. β -carotene gives colour to the above fruits and vegetables. It appears orange.

(e) Pharmaceutical chemistry.

Drugs are the active ingredients in medicines that alter the biochemical processes in the body and so affect the way in which your body works. Drugs which have a beneficial effect are called medicines. The study of drugs and their actions on the body is called pharmacology.

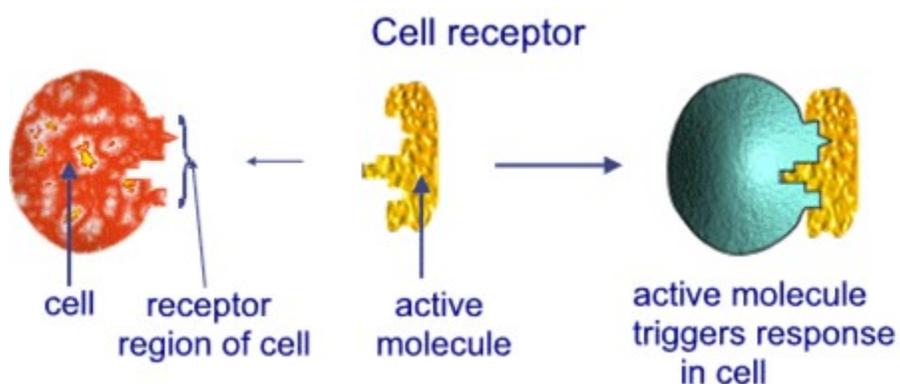
The first medicines were plant brews, the active compounds in plant extracts were identified. Development of these extracts has led to other medicines.

Aspirin (which is related to salicylin, extracted from willow bark) was developed this way.



Most medicines work by binding to RECEPTORS.

Receptors are usually PROTEIN molecules that are either on the surface of cells where they interact with small biologically active molecules or are enzymes that catalyse chemical reactions (catalytic receptors).



Pharmacophore

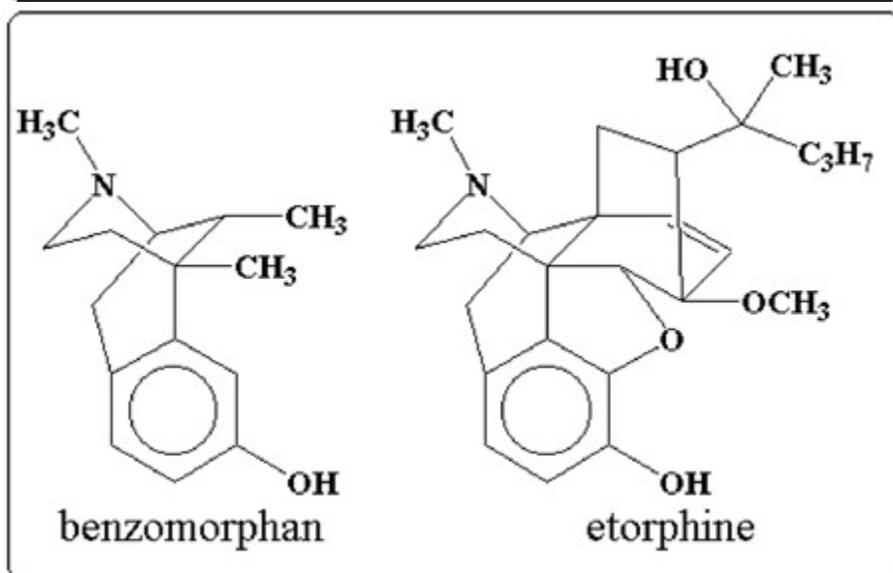
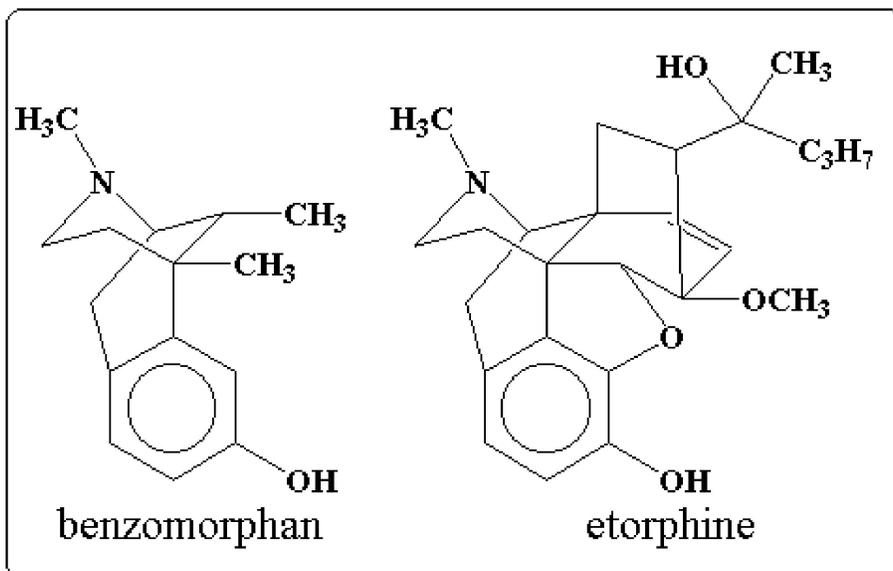
The structural fragment of the molecule which confers pharmacological activity on it is called the PHARMACOPHORE.

The shape of the pharmacophore complements that of the receptor site, allowing it to fit into the receptor.

The functional groups on both are correctly positioned to interact and bind the medicine to the receptor. By comparing the structures of medicines with similar pharmacological activity, the pharmacophore can be identified.

e.g.

morphine (highly addictive)



When the shape, dimensions and functional groups present have been identified, the pharmacophore can be cropped, added to and manipulated by chemists to produce compounds which are still analgesic but less addictive

Agonists and Antagonists

There are two types of drugs :

AGONISTS: which mimic the response of the body's active molecule

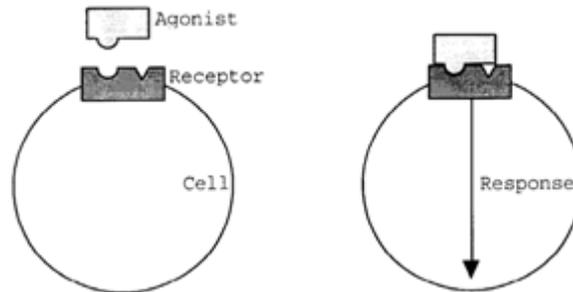
e.g. salbutamol

AND

ANTAGONISTS: which block the effect of the body's active molecule

e.g. anti-histamines, β -blockers

The agonist binds with the receptor and brings about changes which leads to the same pharmacological response as the natural substrate. Agonists are used in medicine to enhance the response produced by a natural substance. The agonist can act by having a higher concentration than the natural substrate, or by having a longer lifetime in the body and, hence having a greater effect.



An antagonist has a structure very similar to the pharmacophore which enables it to fit the receptor site. However, as it does not possess the actual structural fragment needed to trigger the normal pharmacological effect. As it is bound to the receptor site it prevents the normal substrate binding and hence blocks the normal pharmacological effect. Antagonists are normally used as medicines to stop or control an unwanted pharmacological effect.

If the antagonist binds to the active site of an enzyme and blocks the active site, it is known as an inhibitor.

