Raffles Institution
Year 5 H2 Chemistry 2017
Lecture Notes 9 – Introduction to Organic Chemistry

Lecturer: Mr Lee Chee Keong

Content:

- I. Empirical, molecular and structural formulae
- II. Functional groups and the naming of organic compounds
- III. Common terms for organic reactions and reactivities
- IV. Shapes of organic molecules; σ and π bonds
- V. Isomerism: *constitutional (structural); cis-trans; enantiomerism*

17
23 | 400
− 23
170
− 161
9

17 $\frac{9}{23}$

Learning Outcome

Candidates should be able to:

(a) interpret, and use the nomenclature, general formulae and displayed formulae of the following classes of compound:
  - (i) hydrocarbons (alkanes, alkenes and arenes)
  - (ii) halogen derivatives (halogenoalkanes and halogenoarenes)
  - (iii) hydroxyl compounds (alcohols and phenols)
  - (iv) carbonyl compounds (aldehydes and ketones)
  - (v) carboxylic acids and derivatives (acyl chlorides and esters)
  - (vi) nitrogen compounds (amines, amides, amino acids and nitriles)

(b) interpret, and use the following terminology associated with organic reactions:
  - (i) functional group
  - (ii) degree of substitution: primary, secondary, tertiary, quaternary
  - (iii) homolytic and heterolytic fission
  - (iv) carbocation
  - (v) free radical, initiation, propagation, termination
  - (vi) electrophile (Lewis acid), nucleophile (Lewis base)
  - (vii) addition, substitution, elimination, condensation, hydrolysis
  - (viii) oxidation and reduction

  [In equations for organic redox reactions, the symbols [O] and [H] are acceptable]

(c) interpret, and use the following terminology associated with organic reactivities:
  - (i) delocalisation
  - (ii) electronic effect (electron-donating and electron withdrawing effect)
  - (iii) steric effect (steric hindrance)

(d) describe sp^3 hybridisation, as in ethane molecule, sp^2 hybridisation, as in ethene and benzene molecules, and sp hybridisation, as in ethyne molecule

(e) explain the shapes of, and bond angles in, the ethane, ethene, benzene, and ethyne molecules in relation to σ and π carbon-carbon bonds

(f) predict the shapes of, and bond angles in, molecules analogous to those specified in (e)

(g) apply (b) and (c) to the understanding of mechanisms in terms of organic structure and bonding

(h) recognise that the mechanisms of polar reactions involve the flow of electrons from electron-rich to electron poor sites.

(i) describe constitutional (structural) isomerism

(j) describe *cis-trans* isomerism in alkenes, and explain its origin in terms of restricted rotation due to the presence of π bonds [use of E,Z nomenclature is **not** required]

(k) explain what is meant by a chiral centre

(l) deduce whether a given molecule is optically active based on the presence or absence of chiral centres and/or a plane of symmetry

(m) recognize that an optically active sample rotates plane-polarised light and contains chiral molecules

(n) recognize that enantiomers have identical physical properties except in the direction in which they rotate plane-polarised light [usage of the term diastereomers is not required.]

(o) recognize that enantiomers have identical chemical properties except in their interactions with another chiral molecule

(p) recognize that different stereoisomers exhibit different biological properties, for example in drug action

(q) deduce the possible isomers for an organic molecule of known molecular formulae

(r) identify chiral centres and/or *cis-trans* isomerism in a molecule of a given structural formula

Lecture Outline	**References**
1. Organic Chemistry and the Carbon Atom	Organic Chemistry by David Klein
2. Classification of Organic Compounds	A-Level Chemistry by Peter Cann & Peter Hughes
3. Formulae of Organic Compounds	Principles of Organic Chemistry by Peter R.S. Murray
4. IUPAC Nomenclature for Organic Compounds	An Introduction to Organic Chemistry by G.I. Brown
5. Terminology Associated with Organic Reactions	Chemistry in Context by Hill & Holman
6. Isomerism	http://www.chemguide.co.uk/orgmenu.html

1 Organic Chemistry and the Carbon Atom

1.1 Introduction

C

CARBON.

Electronic configuration: $1s^2 2s^2 2p^2$

Organic chemistry is the chemistry of the compounds of **carbon and hydrogen** (with the exception of CO, CO_2, CS_2 and various bicarbonates, carbonates, and cyanides which are considered to be inorganic). Many such compounds are found in living plants and animals, and that is the origin of the term "organic".

There are three important properties of carbon that enable it to form so many stable compounds.

- Carbon has a fully shared octet of electrons in its compounds.
- Carbon can form strong single, double and triple bonds with itself, or any other groups of atoms.
- Each carbon can form 4 covalent bonds, and thus a chain of carbon atoms can have many different groups attached to it and this leads to a wide diversity of compounds.

Organic compounds are relatively stable due to the:

- lack of lone pairs of electrons in the skeletal chains;
- inability of carbon to expand its valence shell to accommodate more than 8 electrons;
- presence of strong C–C and C–H bonds.

carbon has only 2 quantum shells

1.2 Oxidation number of C in compounds

average usually not that useful for a compound with more than 2C atoms

Recall

- Oxidation number of atoms in an element = 0.
- In a compound, the more electronegative atom is given a negative oxidation number.
- Sum of all oxidation numbers in a molecule = 0

Eg. Some common oxidation numbers

Atom	**O**	**H**	**F**
Oxidation number	−2 Except in peroxides, e.g. H_2O_2	+1 Except in metal hydrides, e.g. NaH	−1

How do we assign oxidation numbers from the structure of the compound?

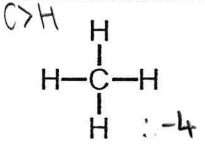
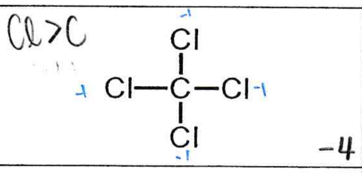
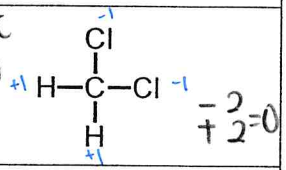
- Bonding electrons are assigned to the more electronegative atom.
- Thus for every bond, the more electronegative atom "gains" an electron and oxidation state decreases by −1.→ inverse r/s between electronegativity & oxidation state.←
- The less electronegative atom "loses" an electron and the oxidation state increases by +1.
- If a bond is formed between two atoms of the same element, then there is no "gain" or "loss" of electron.

F > O > N > Cl > Br > I > S > C > H

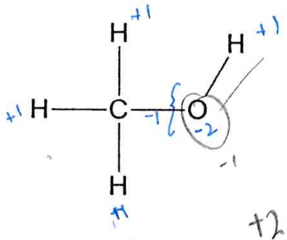
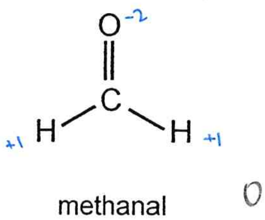
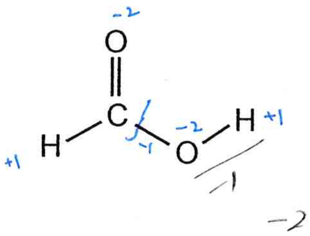
- Carbon is less electronegative than F, O, N, C*l*, Br, I, and S and more electronegative than H.
- This method is useful for any compound where an element occurs multiple times and would have different oxidation states.

Exercise 1

1. What is the oxidation number of carbon in each of the following compounds?

Compound	methane, CH_4	tetrachloromethane, CCl_4	dichloromethane, CH_2Cl_2
Structural Formula	C>H 	Cl>C 	Cl >C C >H 
Oxidation Number of Carbon	−4	+4	0

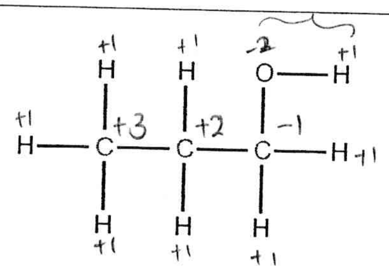
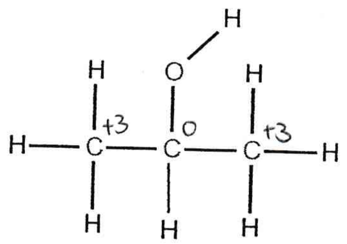
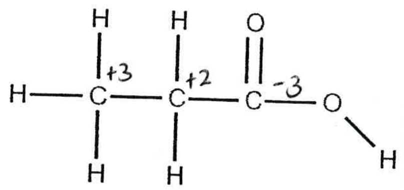
2. Calculate the oxidation number of carbon in methanol, methanal and methanoic acid. Hence, state the type of reaction undergone when methanol is converted to methanal and methanoic acid respectively. (modified from N09/III/2)

 methanol	 methanal	 methanoic acid
O.N. of C = +2	**O.N. of C =** 0	**O.N. of C =** +2

Type of reaction = oxidation.

electron with
vs

Determine the oxidation number of all carbon atom in the following compounds.

1.3 Bonding and Shapes in Organic Molecules *(This has been covered in Chemical Bonding 2.)*

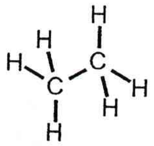
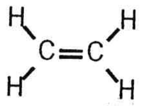
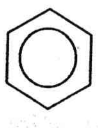
Learning outcome: Student should be able to:

☑ describe sp^3 hybridisation, as in ethane molecule, sp^2 hybridisation, as in ethene and benzene molecules, and sp hybridisation, as in ethyne molecule.
☑ explain the shapes of, and bond angles in, the ethane, ethene, benzene, and ethyne molecules in relation to σ and π carbon-carbon bonds.
☑ predict the shapes of, and bond angles in, molecules analogous to those specified above.

(a) Hybridisation helps to explain

- shape of the molecule
- bond angles and bond lengths in molecule

(b) Carbon typically shows three types of hybridisation:

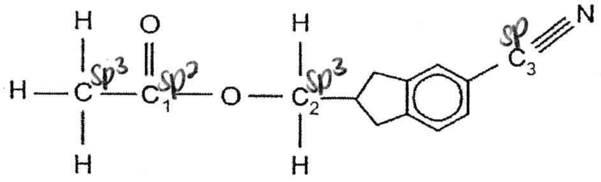
Compound	Type of Hybridisation	Type of C-C bond	Shape of molecule	Bond angle/ σ and π bonds in each C atom
ethane 	sp^3 4 regions of electron density	C–C	Tetrahedral around each C atom 4 bonds	109.5°/ 4 σ
ethene 	sp^2 3 regions of electron density	C=C (localised π bond)	Trigonal planar around each C atom 3 bonds.	120°/ 3 σ and 1 π
benzene 		Resonance hybrid, C⋯C (delocalised π bond) *(To be covered in detail in Arenes.)*		120°/ each C forms 3 σ bonds and has delocalisation of π electrons.
ethyne H—C≡C—H	sp 2 regions of electron density	C≡C	Linear around each C atom 2 bonds.	180°/ 2 σ and 2 π

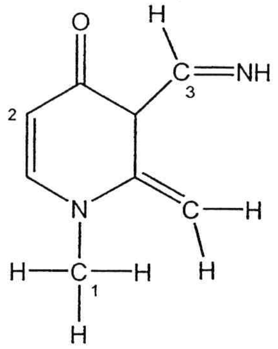
View animation on hybridisation:
http://www.mhhe.com/physsci/chemistry/essentialchemistry/flash/hybrv18.swf

degree of hybridisation inverse of # of bonds.

Exercise 2

Label the hybridisation state of each numbered C atoms in the following compounds.





2 Classification of Organic Compounds

Learning outcome: Candidates should be able to:
☑ Interpret and use the following terminology associated with organic reactions: functional group

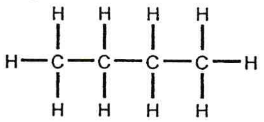
Organic compounds can be classified on the basis of the arrangement of the carbon skeleton:

HYDROCARBONS

Aliphatic hydrocarbons
- **open chains** of C atoms
- contain single or multiple C–C bonds

Straight chain hydrocarbons

e.g.



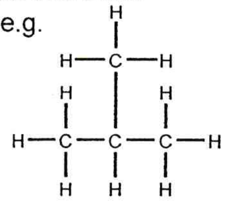
saturated

$H-C\equiv C-H$

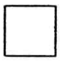
unsaturated

Branched chain hydrocarbons

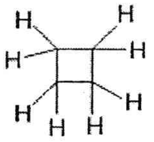
e.g.



Alicyclic hydrocarbons
- contain **closed ring** of C atoms
- contain single or multiple bonds
- H atoms are typically not shown in the structure

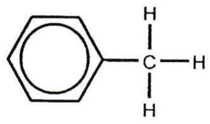
e.g.  is cyclobutane.

The hydrogens are typically **not** shown, like this:



Aromatic hydrocarbons
- contain benzene ring

e.g.



Since organic compounds may also contain elements other than H & C (e.g. N, O, S, P & the halogens), a more effective way of classifying them will be on the basis of **functional group** and **homologous series.**

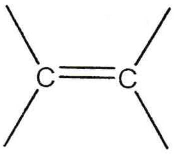
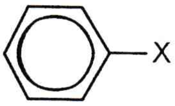
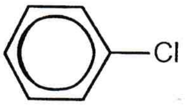
- A **functional group** is made up of an atom (e.g. C*l*) or group of atoms (e.g. –OH, –COOH) within the organic compound that is responsible for its **characteristic chemical properties.**
- A **homologous series** is a family of compounds having the **same functional group. Homologues** refer to the **members** in the same homologous series.

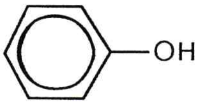
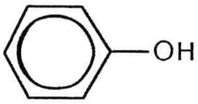
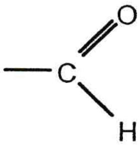
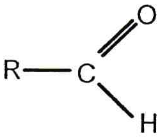
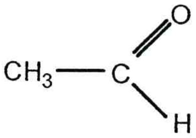
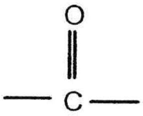
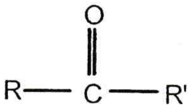
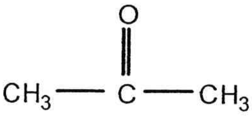
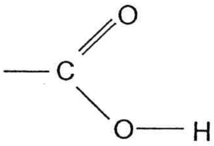
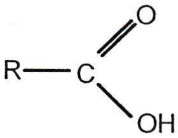
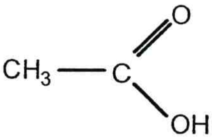
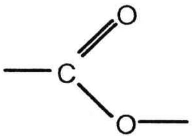
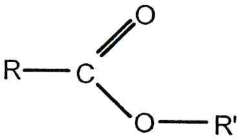
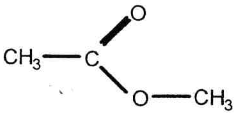
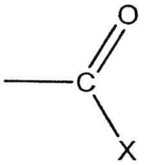
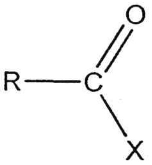
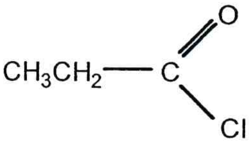
They have the following properties:
- ➢ can be represented by a general formula (e.g. Alkane general formula: C_nH_{2n+2})
- ➢ differs from the successive member by a methylene, $-CH_2-$, group.
- ➢ gradual change in physical properties such as boiling points ((mass/molecular size)
- ➢ similar chemical properties. ((electrons)) → types of reactions
- ➢ can be prepared by similar methods.

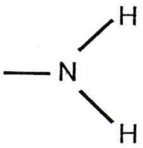
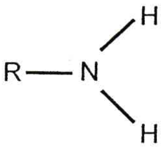
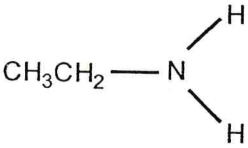
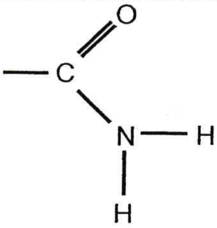
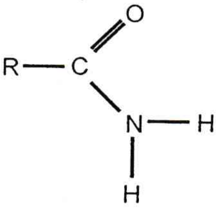
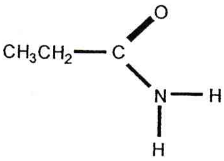
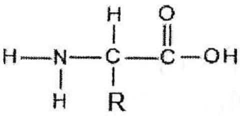
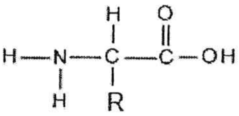
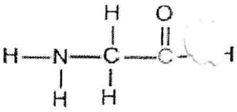
The first and simplest homologous series: Alkanes (General Formula : C_nH_{2n+2})

Molecular Formula	Structural Formula	Name	Boiling Point/ °C
CH_4	CH_4	Methane	–161
C_2H_6	CH_3CH_3	Ethane	–89
C_3H_8	$CH_3CH_2CH_3$	Propane	–44
C_4H_{10}	$CH_3(CH_2)_2CH_3$	Butane	–0.5

Some common homologous series are shown below. The name shows the functional group present in each of the homologous series (except for alkane which is not considered a functional group).

Classes of compounds	Homologous series	Structure of Functional group	General formula (R, R' = alkyl groups)*	Example
Hydrocarbons	alkane	–	C_nH_{2n+2}	Ethane CH_3CH_3
	alkene		C_nH_{2n}	ethene $CH_2{=}CH_2$
	alkyne	$-C\equiv C-$	C_nH_{2n-2}	ethyne $CH{\equiv}CH$
Halogen derivatives	halogenoalkane group 7.	–X (X= C*l*, Br, I)	RX (X= C*l*, Br, I)	**chloro**ethane $CH_3CH_2{-}Cl$
	halogenoarene group 7 + benzene ring	 –X (X= C*l*, Br, I)		**chlorobenzene** 

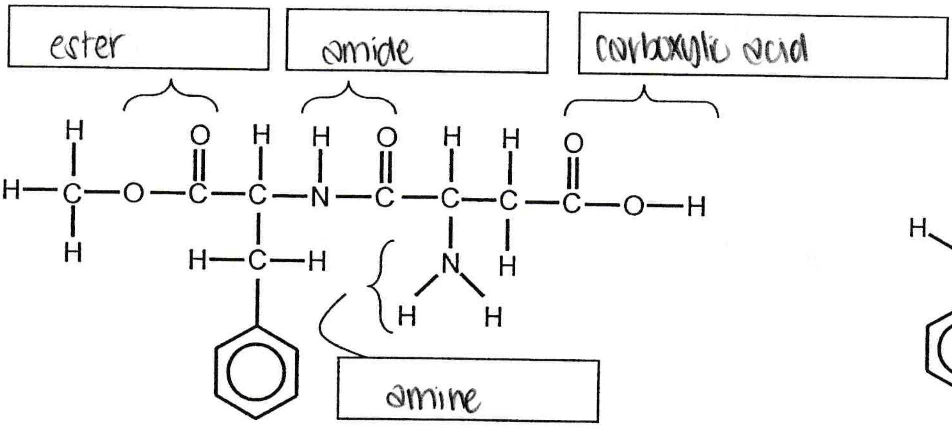
Classes of compounds	**Homologous series**	**Structure of functional group**	**General formula (R, R' = alkyl groups)***	**Example**
Hydroxyl compounds	alcohol	–OH	R–OH	ethan**ol** $CH_3CH_2–OH$
	phenol			**phenol** 
Carbonyl compounds	aldehyde carbon attached to hydrogen atom			ethan**al** 
	ketone			propan**one** 
Carboxylic acids and derivatives	carboxylic acid has -OH funct. group.			ethan**oic acid** 
	ester			methyl ethan**oate** 
	group 7. acyl halide X = C*l*, Br			propan**oyl** chloride 

Classes of compounds	Homologous series	Structure of functional group	General formula (R, R' = alkyl groups)*	Example
Nitrogen compounds	amine only nitrogen			ethylamine 
	amide			propanamide 
amine + -OH	-OH funct. grp. amino acid carboxylic acid.			
	nitrile	$-C{\equiv}N$	$R-C{\equiv}N$	propanenitrile CH_3CH_2-CN

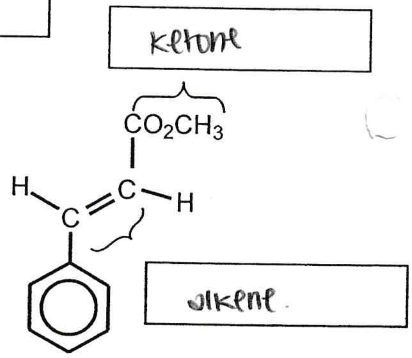
*R and R' are known as alkyl groups with the general formula C_nH_{2n+1}. Examples are methyl (CH_3-), ethyl (CH_3CH_2-), propyl ($CH_3CH_2CH_2-$) etc.

Exercise 3

Identify the functional groups present in the following compounds.



Aspartame



Methyl cinnamate

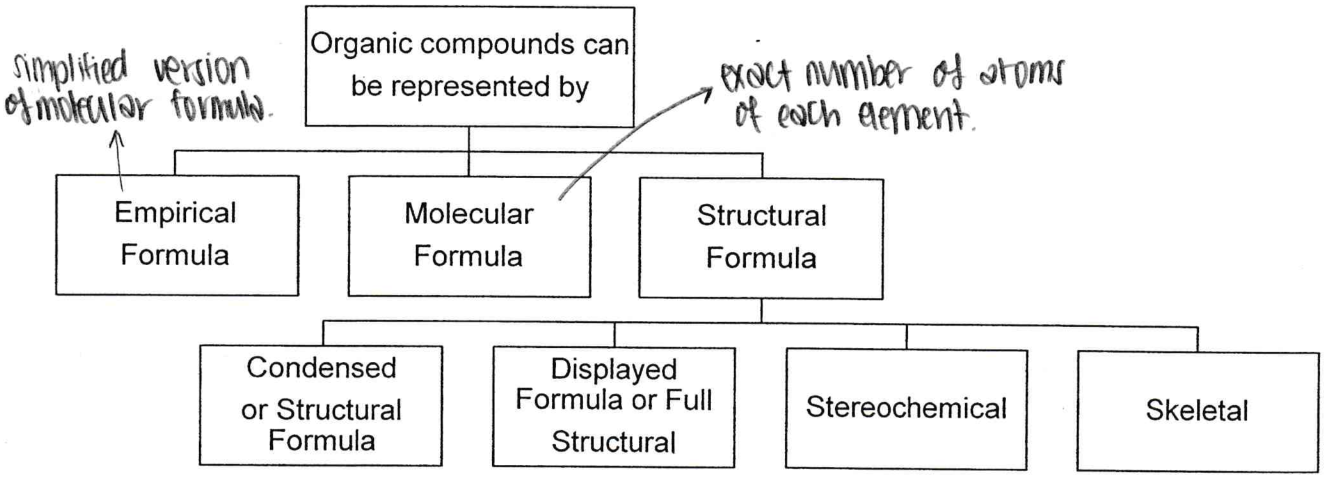
Note: Usually we do not label alkane and benzene functional groups.

3 Formulae of Organic Compounds

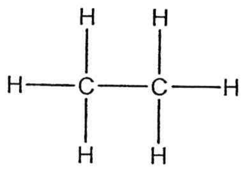
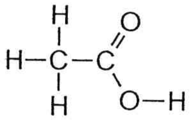
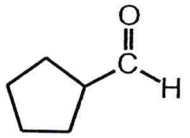
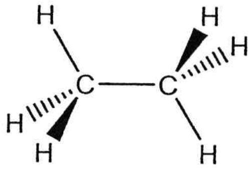
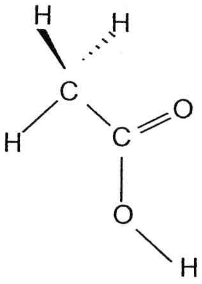
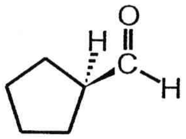
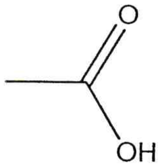
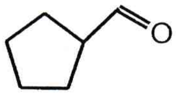
Learning outcome: Candidates should be able to:

☑ interpret and use the general formulae and displayed formulae of the following classes of compound: alkanes, alkenes and arenes, halogenoalkanes and halogenoarenes, alcohols and phenols, aldehydes and ketones, carboxylic acids, acyl chlorides and esters, amines, amides, amino acids and nitriles. *(Details will be covered in the respective functional group studies.)*

In candidates' answers, an acceptable response to a request for a structural formula will be to give the minimal detail, using conventional groups, for an unambiguous structure.
e.g. $CH_3CH_2CH_2OH$ for propan-1-ol, not C_3H_7OH.



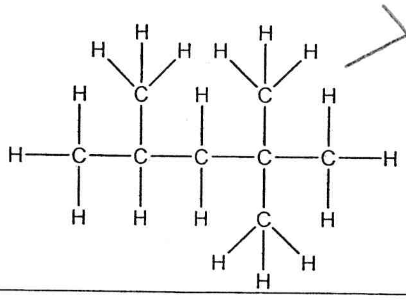
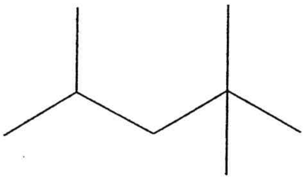
Type of Formula	Characteristics	Examples		
		Ethane	Ethanoic acid	Cyclopentane-carbaldehyde
Empirical	▪ Shows the **simplest ratio** of the different types of atoms in a molecule.	CH_3	CH_2O	$C_6H_{10}O$
Molecular	▪ Shows the **actual number** of each type of atom in a molecule. ▪ Integral multiple (n) of empirical formula. E.g. $(CH_2O)n$	C_2H_6	$C_2H_4O_2$	$C_6H_{10}O$

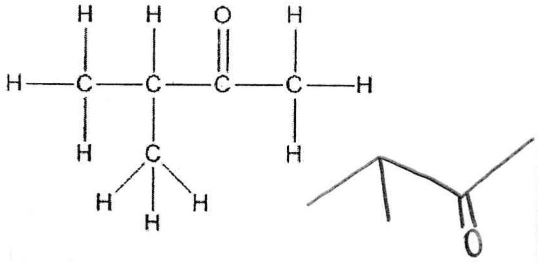
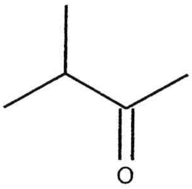
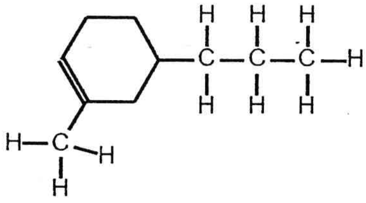
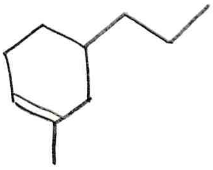
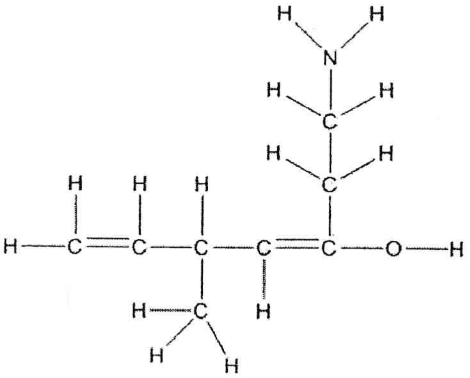
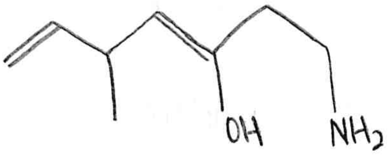
	Type of Formula	Characteristics	Examples		
			Ethane	Ethanoic acid	Cyclopentane-carbaldehyde
Structural	**Condensed Structural**	- Shows how groups of atoms are **sequentially** arranged.	CH_3CH_3	CH_3CO_2H	
	Displayed/ Full structural	- Shows how every atom in the molecule is bonded to other atoms and the number of bonds between them. - C and H in rings are not shown.			
	Stereochemical	- Shows spatial (3-dimensional) structure of a molecule. - Solid lines (——) represent bonds on the same plane as the paper. - Dashed line (·······) represent bonds receding into the paper. - Heavy wedged line (◀) represents bonds coming out of the paper.			
	Skeletal	- shows the carbon skeleton with any functional groups such as –OH or –Br. - Straight lines represent the C-C bonds. - C & H atoms are not explicitly shown.			

How to read and draw skeletal structures [only carbon & hydrogen atom attached not shown]

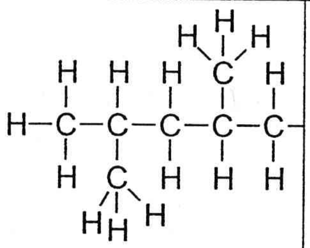
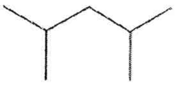
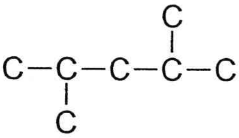
1. Carbon atoms in a straight chain are drawn in a zigzag format.
2. The end of every line represents a carbon atom.
3. Double bonds are shown with two lines, and triple bonds are shown with three lines.
4. Direction in which single bonds are drawn is irrelevant.
5. Hydrogen atoms attached to C atoms are not shown. The number of H atoms at each C may be inferred by the fact that each C atom must form 4 bonds.
6. Heteroatoms (atoms other than carbon and hydrogen) are drawn and any hydrogen atoms attached to a heteroatom is also drawn.

Exercise 4: Draw the skeletal formula of the compounds shown below.

Displayed Formula	Skeletal Formula
 	

Displayed Formula	**Skeletal Formula**
	
 (C and H in rings are not shown in displayed formula)	
	

- When drawing the structure of a molecule, ensure that the structure drawn is not ambiguous.

Acceptable			**Unacceptable**
	$(CH_3)_2CHCH_2CH(CH_3)_2$		

Acceptable	**Unacceptable**
$CH_3CH_2CH_2OH$	C_3H_7OH. C_3H_7– can either be $CH_3CH_2CH_2$– or $(CH_3)_2CH$–, so the formula C_3H_7OH can either be $CH_3CH_2CH_2OH$ or $(CH_3)_2CHOH$. (Ambiguous)

4 IUPAC Nomenclature for Organic Compounds

(This will be covered in greater detail in future lectures on each functional group.)

Learning outcome: Candidates should be able to:

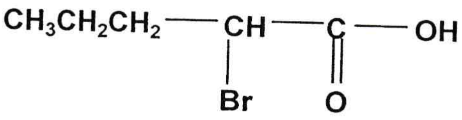
☑ interpret and use the nomenclature of the following classes of compound: alkanes, alkenes and arenes, halogenoalkanes and halogenoarenes, alcohols and phenols, aldehydes and ketones, carboxylic acids, acyl chlorides and esters, amines, amides, amino acids and nitriles.

The most common way to name organic compounds is to use the systematic naming developed by **IUPAC** (**I**nternational **U**nion of **P**ure & **A**pplied **C**hemistry).

Every name consists of a root, a suffix and one or more prefixes. → P comes before S in alphabetic order.

Prefix(es)	Root	Suffix
Denotes substituents / side groups	Denotes longest continuous carbon chain bearing the principal functional group	Denotes principal functional group

e.g.


$CH_3CH_2CH_2-CH(Br)-C(=O)-OH$

2-bromopentanoic acid

prefix	root	suffix
substituents / side groups (bromo) + #	longest continuous carbon chain bearing the principal functional group (pentan–)	principal functional group (–COOH: –oic acid)

(a) The Root

- In the aliphatic straight chain system, the name of the root takes its name according to the **number of C atoms in the longest continuous chain**.

meredith eats peanut butter, peter hates having oranges (n) durians

No. of C atoms	1	2	3	4	5	6	7	8	9	10
Root	meth-	eth-	prop-	but-	pent-	hex-	hept-	oct-	non-	dec-

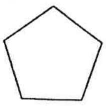
- For a **saturated** (→ single bond) hydrocarbon, the name of the root ends with **–an–**. For an **unsaturated** (→ not single bond) hydrocarbon with C=C bond, the name of the root ends with **–en–**; **unsaturated** hydrocarbon with C≡C bond, the name of the root ends with **–yn–**.

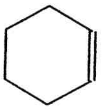
- For unsaturated hydrocarbon with C=C bond, the position of the double bond is denoted by the lowest carbon number possible.

$CH_3CH_2CH=CH_2$ but–1–ene

$CH_3CH=CHCH_3$ but–2–ene

- In an **alicyclic** system, the word **cyclo** is added to the front of the root corresponding to the same number of C atoms.

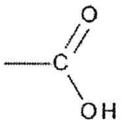
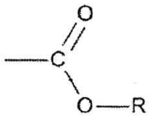
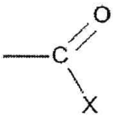
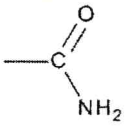
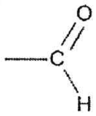
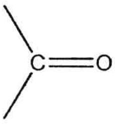
e.g. cyclopentane 

cyclohexene 

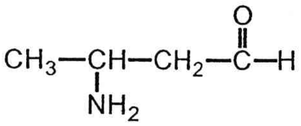
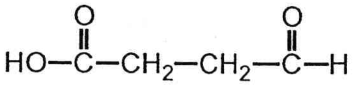
↱ end

(b) The Suffix

- Indicates what functional group is joined to the chain.

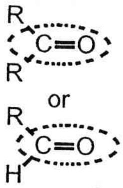
Formula of Functional Group	Functional Group	Suffix	Example
	carboxylic acid	**−oic acid**	$CH_3\mathbf{COOH}$ ethan**oic acid**
	ester	**alkyl.....oate**	$CH_3COO\mathbf{CH_2CH_3}$ **ethyl** ethan**oate**
 , X= Cl, Br, I	acid halide	**−oyl halide**	$CH_3\mathbf{COC}l$ ethan**oyl chloride**
	amide	**−amide**	$CH_3\,CH_2\,CH_2\mathbf{CONH_2}$ butan**amide**
$-C{\equiv}N$	nitrile	**−nitrile**	$CH_3\,CH_2CN$ propane**nitrile**
	aldehyde	**−al**	CH_3CHO ethan**al**
	ketone	**−one**	$CH_3\,CH_2CO\,CH_3$ butan**one**
$-OH$	alcohol	**−ol**	$CH_3\,CH_2\,CH_2OH$ propan**ol**
$-NH_2$	amine	**−amine**	$CH_3\,CH_2\,CH_2NH_2$ propan**amine**

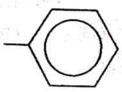
- When there is more than one functional group in the compound, the **functional group placed higher in the table** is listed as a **suffix** with everything else being a prefix, e.g.:

Compound	Name	Remarks
 $CH_3-CH(NH_2)-CH_2-C(=O)-H$	3-aminobutanal aldehyde > amine	$-CHO$ is found higher in the table than $-NH_2$ so the suffix is $-$al and $-NH_2$ is named as the prefix ‘amino’
 $HO-C(=O)-CH_2-CH_2-C(=O)-H$	4-oxobutanoic acid carboxylic acid > aldehyde	$-COOH$ is found higher in the table than $-CHO$ so the suffix is -oic acid and $-CHO$ is named as the prefix ‘oxo’

(c) The Prefix

- Denotes all other functional groups on the root.

	Substituent Group	Prefix
Nitrile	$-C\equiv N$	cyano-
aldehyde & ketone		oxo-
alcohol	$-OH$	hydroxy-
amine	$-NH_2$	amino-
ester	$-OR$	alkoxy-
halogens	$-Br$	bromo-
	$-Cl$	chloro-
	$-F$	fluoro-

Substituent Group	Prefix
$-I$	iodo-
$-NO_2$	nitro-
$-C_6H_5$ or 	phenyl-
$-C_nH_{2n+1}$	alkyl-
$-CH_3$	methyl-
$-CH_2CH_3$	ethyl-
$-(CH_2)_2CH_3$	propyl-
$-(CH_2)_3CH_3$	butyl-

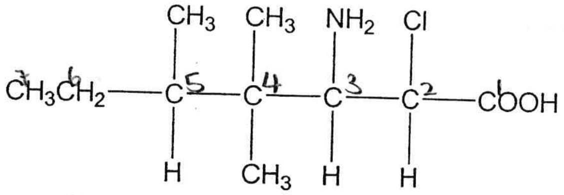
Arabic Numerals

Arabic numerals are used in the name to indicate the positions of attachment of substituents, multiple C to C bonds and/ or principal functional group. These numbers are called **positional numbers.**

Steps to take in naming compounds

e.g.

Compound A $CH_3CH_2CH(CH_3)C(CH_3)_2CH(NH_2)CH(Cl)CO_2H$



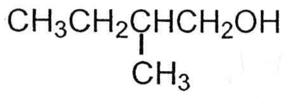
$$\overset{7}{C}H_3\overset{6}{C}H_2-\underset{H}{\overset{CH_3}{C^5}}-\underset{CH_3}{\overset{CH_3}{C^4}}-\underset{H}{\overset{NH_2}{C^3}}-\underset{H}{\overset{Cl}{C^2}}-\overset{1}{C}OOH$$

1. *Suffix* and *Root* (i) Identify the principal functional group (ii) Select the longest continuous C chain containing the principal functional group. Count the number of C atoms.	(i) principal functional group: **$-CO_2H$** ***suffix:*** ' **-oic acid** ' (ii) number of C in parent chain: 7 ***root:*** ' **heptan–** ' (all single bonds in the carbon chain)
2. *Prefixes* Identify all remaining functional groups, showing as the *prefixes.*	others: CH_3, NH_2, Cl functional groups ***prefixes***: ' **methyl** ', '**amino**' and '**chloro**'
3. *Prefixes* Number the C atoms in the main chain from one end such that (i) the lowest number is given to the group cited as the *suffix*, then (ii) the lowest possible individual numbers to the groups cited as *prefixes.*	(i) position of principal functional group: on **C 1** (ii) position of the amino functional group: on **C 3** (iii) position of the chloroalkane functional group: on **C 2** (iv) position of the 3 methyl substituents: two on **C 4** and one on **C 5**

4. String *prefixes* together. ▪ If same substituent appears more than once, indicate using di-, tri-, tetra- etc. ▪ The appropriate positional number is still required even if the groups are connected to the same carbon on the main chain. ▪ Different prefixes are listed in alphabetical order. Multiplying prefixes (e.g. di, tri) does not affect the alphabetical order. ▪ Commas(,) are used to separate numbers and hyphens(–) to separate numbers and words.	**3-amino-2-chloro-4,4,5-trimethyl** 1-chloro-2-amino-3,3,4-trimethylheptanoic acid 2-chloro-3-amino-4,4,5-trimethylheptanoic acid. 3-amino-2-chloro-4,4,5-trimethylheptanoic acid.
5. String *prefixes, root* and *suffix*	IUPAC nomenclature for compound A is **3-amino-2-chloro-4,4,5-trimethylheptanoic acid**

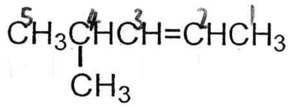
Exercise 5

Give the IUPAC names of the following compounds:



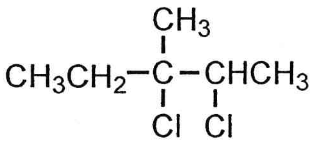
$\mathrm{CH_3CH_2\underset{CH_3}{\underset{|}{C}}HCH_2OH}$

2-methylbutanol



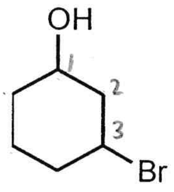
$\mathrm{\overset{5}{C}H_3\underset{CH_3}{\underset{|}{\overset{4}{C}}}H\overset{3}{C}H=\overset{2}{C}H\overset{1}{C}H_3}$

4-methylpent-2-ene



$\mathrm{CH_3CH_2-\underset{Cl}{\underset{|}{\overset{CH_3}{\overset{|}{C}}}}-\underset{Cl}{\underset{|}{C}}HCH_3}$

2,3-dichloro-3-methylpentane



3-bromo-cyclohexol

5 Terminology Associated with Organic Reactions

Learning outcome: Candidates should be able to:

☑ interpret and use the following terminology associated with organic reactions: degree of substitution: primary, secondary, tertiary, quaternary, homolytic and heterolytic fission, carbocation, free radical, initiation, propagation, termination, electrophile (Lewis acid), nucleophile (Lewis base), addition, substitution, elimination, condensation, hydrolysis, oxidation and reduction. [In equations for organic redox reactions, the symbols **[O]** and **[H]** are acceptable.]

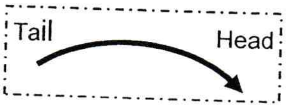
☑ recognise that the mechanisms of polar reactions involve the flow of electrons from electron-rich to electron poor sites.

→ endothermic
heat absorbed

→ exothermic
heat released

5.1 Mechanisms

- Organic reactions involve breaking and forming covalent bonds.
- Every reaction involves the **flow of electron density from electron–rich to electron–poor sites**. Electrons move to break bonds and form new bonds.
- **Mechanisms** illustrate how the electrons move during a reaction.
- Curved arrows are used to show the actual movement of electrons.
- **Tail**: shows **where the electrons are coming from (bond pair or lone pair)**
- **Head**: shows **where the electrons are going**.
- Mechanisms are proposed to be consistent with the reaction stoichiometry, the rate equation and with all other available experimental data.



5.2 Types of Bond Fission (Bond cleavage)

There are 2 ways in which a covalent bond can break.

→ one e⁻ to each atom (evenly distributed)

(a) Homolytic Fission

- The breaking of a covalent bond such that one electron goes to each of the atoms, forming **free radicals**.

(free radicals)

↷ indicates the movement of **one** electron only
half arrow

bond breaks, one electron goes to each atom

E.g.

→ two e⁻ to one atom (unevenly distributed)

(b) Heterolytic Fission

- The breaking of a covalent bond such that both the electrons go to the same atom, forming **positive and negative ions**.

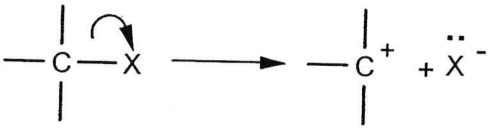
↶ indicates the movement of **a pair** of electrons

- There are 2 ways how this can occur:

  (1) Both electrons go to the leaving group. This occurs when carbon is **less** electronegative than X. The positively charged carbon ion formed is called **carbocation**.

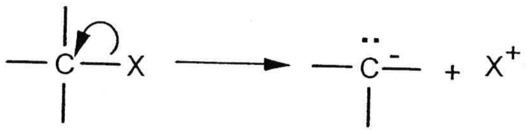
→ ability to draw e⁻ to itself

+ve



  (2) Both electrons go to carbon. This occurs when carbon is **more** electronegative than *X*. The negatively charged carbon ion formed is called **carbanion.**

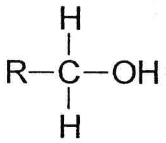
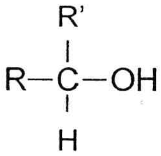
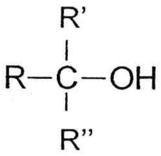
negative.

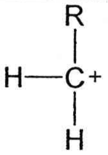
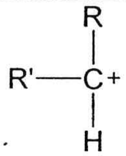
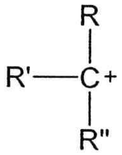


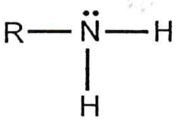
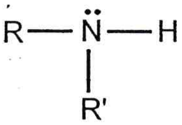
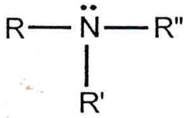
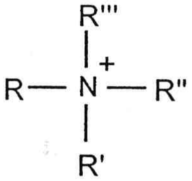
↳ # hydrogen atoms attached — inversely related to — degree of substitution.

5.3 Degree of substitution

- The degree of substitution of an atom in an organic compound is determined by the number of alkyl or aryl groups bonded to it.
- Organic compounds with different degrees of substitution may undergo different reactions.

Type of alcohol	Primary (1°)	Secondary (2°)	Tertiary (3°)
Number of R groups bonded to carbon bearing the –OH group	1	2	3
Structure	 $\mathrm{R-\underset{H}{\overset{H}{C}}-OH}$	 $\mathrm{R-\underset{H}{\overset{R'}{C}}-OH}$	 $\mathrm{R-\underset{R''}{\overset{R'}{C}}-OH}$

Type of carbocation	Primary (1°)	Secondary (2°)	Tertiary (3°)
Number of R groups bonded to carbon bearing the positive charge	1	2	3
Structure	 $\mathrm{H-\underset{H}{\overset{R}{C^+}}}$	 $\mathrm{R'-\underset{H}{\overset{R}{C^+}}}$	 $\mathrm{R'-\underset{R''}{\overset{R}{C^+}}}$

Type of amine	Primary (1°)	Secondary (2°)	Tertiary (3°)	Quaternary (4°)
Number of R groups bonded to nitrogen	1	2	3	4
Structure	 $\mathrm{R-\underset{H}{\ddot{N}}-H}$	 $\mathrm{R-\underset{R'}{\ddot{N}}-H}$	 $\mathrm{R-\underset{R'}{\ddot{N}}-R''}$	 $\mathrm{R-\underset{R'}{\overset{R'''}{N^+}}-R''}$

↑ substituted => degree

5.4 Types of organic species

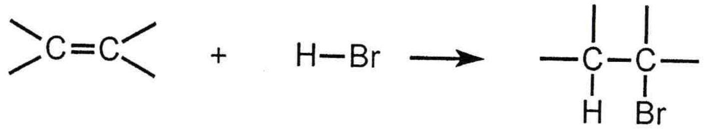
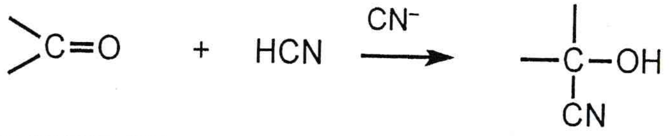
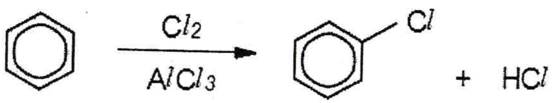
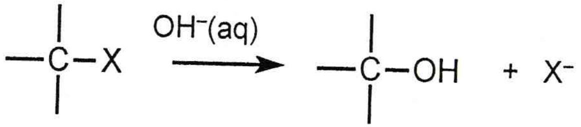
Species	Defined as	Characteristics
Electrophile +ve cation attracted to electrons	Electron pair acceptor (Lewis acid)	▪ **electron-deficient** species (e.g. HBr, Br^+, NO_2^+). ▪ attracted to regions of negative charge or regions of electron rich sites (δ– sign) in a molecule. ▪ may possess an empty orbital to accept an electron pair.
Nucleophile -ve anion not attracted	Electron pair donor (Lewis base)	▪ **electron-rich** species (e.g. OH^-, CN^-, NH_3, H_2O) ▪ attracted to regions of positive charge or regions of electron deficient sites (δ+ sign) in a molecule ▪ possess at least one lone pair of electrons
Free radical		▪ contains an **unpaired electron** formed from the homolytic fission of a covalent bond (e.g. $C\ell\bullet$) ▪ electrically neutral.

6 membered rings
↳ cis

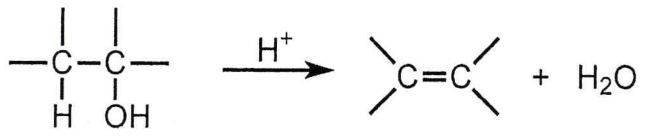
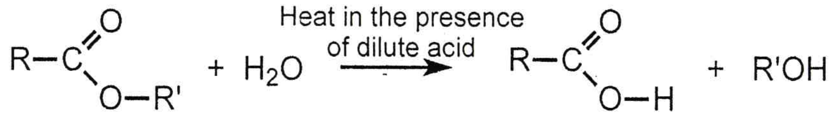
↑ ring strain } hard to get trans

8 membered + above
↳ trans possible
↗ more flexible

5.5 Types of organic reactions *(Details of the mechanisms will be done in topics related to the functional groups.)*

	Types of reaction	**Examples**
Addition →Not single bond - only occurs when there is unsaturation in the reactant molecules. - 2 substances react to give a single product. - a π bond is broken to form two σ bonds. - the σ bond remains unbroken	**Electrophilic Addition** - in alkenes ↳double bond	
	Nucleophilic Addition - in aldehydes and ketones ↳ $\underset{H}{\underset{\mid}{C}}=O$ ↳ $\underset{R}{\underset{\mid}{C}}=O$	
Substitution - 1 atom or a group of atoms is replaced by another atom or group of atoms. - 2 substances react to give 2 products.	**Free Radical Substitution** - in alkanes ↳single bond.	$CH_4 + Cl_2 \xrightarrow{\text{uv light}} CH_3Cl + HCl$
	Electrophilic substitution - in arenes ↳benzene ring	
	Nucleophilic substitution - in halogenoalkanes ↳group 7.	

5.5 Types of organic reactions *(Details of the mechanisms will be done in topics related to the functional groups.)*

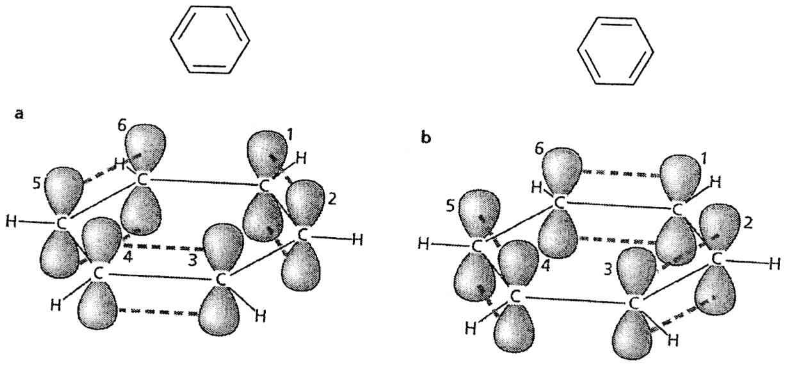
Types of reaction	Examples
Elimination ■ Involves removal of atoms or groups of atoms from adjacent carbon atoms to form multiple bonds.	
Hydrolysis → addition of water, H_2O ■ A reaction in which water is used to break a bond in a molecule.	
Condensation → removal of water, H_2O ■ Two molecules react together to form a bigger molecule with the elimination of small molecules such as H_2O or HCl.	
Oxidation +O / −H / −e⁻ ■ the addition of oxygen from oxidising agent; or ■ hydrogen is removed from the molecule; or ■ loss of electrons; or increase in oxidation number	$CH_3CHO + [O] \longrightarrow CH_3COOH$ [In equations for organic redox reactions, the symbols [O] and [H] are accepted.]
Reduction −O / +H / +e⁻ ■ the removal of oxygen; or ■ hydrogen is added to the molecule; or ■ gain of electrons; or ■ decrease in oxidation number	$CH_3CN + 4[H] \longrightarrow CH_3CH_2NH_2$
Rearrangement • Involves migration of an atom or groups of atoms from one site to another within the same molecule.	 $R-\underset{Cl}{CH}-CH=CH_2 \longrightarrow R-CH=CH-\underset{Cl}{CH_2}$

6 Terminology Associated with Organic Reactivities

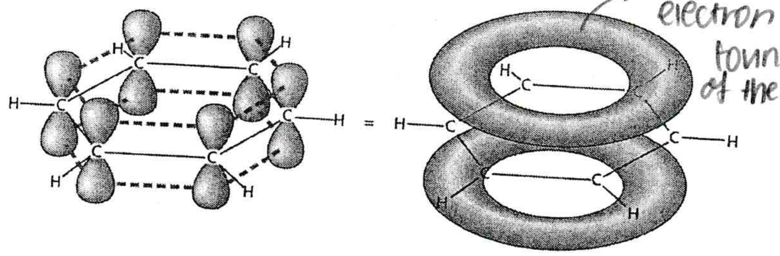
Learning outcome: Candidates should be able to interpret, and use the following terminology associated with organic reactivities: delocalisation, electronic effect (electron-donating and electron withdrawing effect) and steric effect (steric hindrance).

6.1 Delocalisation (resonance ≠ hybridisation)

- Just as two p orbitals can overlap sideways to form a π bond, two or more π bonds can overlap with each other to produce a more extensive π bond.
- For example, benzene, C_6H_6, is a planar, six-membered ring of sp^2-hybridised carbon atoms. The unhybridised p orbitals of the carbon atoms could overlap as shown to produce three C=C bonds between atoms 1 and 2, 3 and 4, and 5 and 6 of the ring. Overlap to produce double bonds between atoms 2 and 3, 4 and 5, and 6 and 1 of the ring are just as likely to occur.



- Thus, all six p orbitals overlap with one another to produce a set of six **delocalised π electrons**:



region of space an electron can be found 90% of the time.

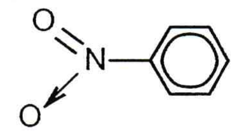
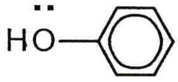
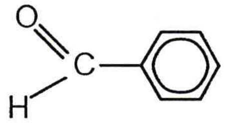
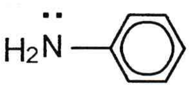
- These six electrons are said to participate in **resonance**. All six C-C bonds have the **same bond energy** and **same length**.

Bond	Bond energy / kJ mol^{-1}	Bond length / nm
C – C	350	0.154
C = C	610	0.134
C ⎓ C (benzene)	520	0.139

↓ e^-

6.2 Electronic Effect

- An atom or a group of atoms is said to be an **electron-withdrawing** substituent if it **decreases the electron density** in the compound. It is said to be an **electron-donating** substituent if it **increases the electron density** in the compound. ↑e^-
- Such electronic effect is either due to the:
  - donation or withdrawal of electrons through σ **bonds** due to the electronegativity difference between atoms;
  - delocalisation of lone pair of electrons on the atom adjacent to the benzene ring into the π **electron cloud** of benzene;
  - delocalisation of π **electron cloud** of benzene onto the substituent.
- Some examples of such substituents in benzene are shown:

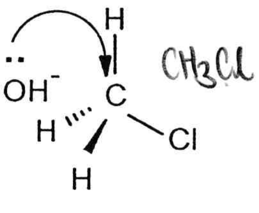
Electron-withdrawing	Electron-donating
	
	

6.3 Steric Effect (Steric Hindrance) ↓ or prevent reaction

- **Steric hindrance** occurs when the presence of a substituent hinders the approach of an attacking reactant and either **prevents** a reaction from taking place or **lowers the reactivity** of a particular site within a molecule.

  For example, CH_3Cl and $(CH_3)_3CCl$ undergo different mechanisms when reacting with OH^-.

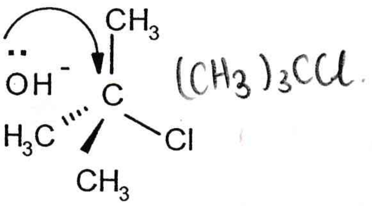
Nucleophilic attack of C by OH^- possible



-CH_3 group is larger than H

-CH_3 groups hinder the nucleophilic attack of C by OH^-.

Reaction proceeds by a different mechanism.



The three methyl groups in $(CH_3)_3CCl$ hinder the approach of a nucleophile towards the electron deficient carbon. Steric hindrance causes the reaction to proceed by a different mechanism.

7 Isomerism in Organic Compounds

Learning outcome: Candidates should be able to:
☑ describe constitutional (structural) isomerism
☑ deduce the possible isomers for an organic molecule of known molecular formula

Isomerism refers to the existence of two or more compounds with the **same molecular formula** but **different arrangement of the atoms** in their molecules. These compounds are known as **isomers**.

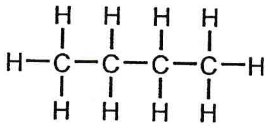
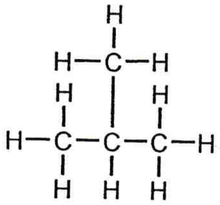
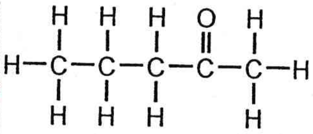
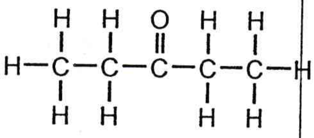
ISOMERISM

- **CONSTITUTIONAL ISOMERISM**
  STRUCTURAL FORMULA DIFF
  (same molecular formula; different structural formula)
  - **Chain Isomerism**
    - Different arrangement of C atoms
  - **Positional Isomerism**
    - Different positions of the same functional group
  - **Functional Group Isomerism**
    - Different functional groups
- **STEREOISOMERISM**
  ORIENTATION IN SPACE DIFF
  (same molecular formula; same structural formula, different arrangement in space)
  - ***Cis-trans* Isomerism**
    - Restricted rotation and 2 different groups attached to each C of double bond or C atoms in ring structure
  - **Enantiomerism**
    - Non-superimposable mirror image

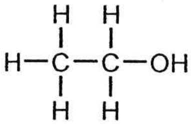
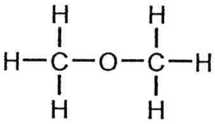
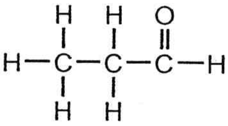
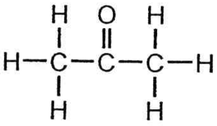
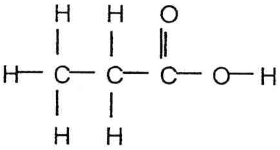
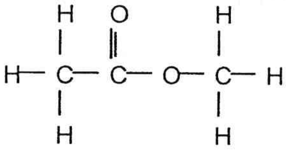
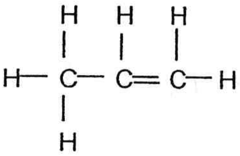
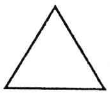
7.1 Constitutional (Structural) Isomerism

Constitutional (Structural) isomers have the **same molecular formula** but **different structural formula** i.e. different arrangement of atoms.

Three main types of constitutional isomers:

Isomers	**Examples**
(1) **Chain Isomers** ▪ differ in the arrangement of carbon atoms in the chain. Carbon atoms may be arranged in **straight** chain or **branched** chain. ▪ Same functional groups, thus similar chemical properties but different physical properties.	 Butane C_4H_{10} (b.p. -0.5°C)  2-Methylpropane C_4H_{10} (b.p. -11.7°C)
(2) **Positional Isomers** ▪ **same** homologous series with the **functional group** located at **different positions** on the same carbon skeleton	 pentan-2-one  pentan-3-one
(3) **Functional Group Isomers** ▪ **different functional groups**, thus different chemical and physical properties.	See examples on next page.

Examples of functional group isomers

(1) Alcohol and ether with general formula $C_nH_{2n+2}O$	(2) Aldehyde and ketone with general formula $C_nH_{2n}O$
e.g.  Ethanol C_2H_5OH (b.p. 78.5°C)  Dimethylether CH_3OCH_3 (b.p. -23°C)	e.g.  Propanal CH_3CH_2CHO (b.p. 49°C)  Propanone CH_3COCH_3 (b.p. 56.5°C)
(3) Carboxylic acid and ester with general formula $C_nH_{2n}O_2$ e.g.  propanoic acid  methyl ethanoate	(4) Alkene and cycloalkane with general formula C_nH_{2n}  propene  cyclopropane

Exercise 6

1. Draw all the constitutional isomers of the organic compounds with molecular formula, $C_4H_{10}O$.

Constitutional isomers of alcohol:

Constitutional isomers of ether:

Systematic way of drawing structural isomers:

1. Identify functional groups e.g. alcohol and ether.
2. For one functional group, identify the longest chain, and draw all positional isomers.
3. Branch the chain and draw all positional isomers.
4. Repeat steps 2 and 3 for the other functional group.

7.2 Stereoisomerism

Learning outcome: Candidates should be able to:

☑ describe *cis-trans* isomerism in alkenes, and explain its origin in terms of restricted rotation due to the presence of π bonds
☑ explain what is meant by a chiral centre
☑ deduce whether a given molecule is chiral based on the presence or absence of chiral centres and / or a plane of symmetry
☑ recognise that an optically active sample rotates plane-polarised light and contains chiral molecules
☑ recognise that enantiomers have identical physical properties except in the direction in which they rotate plane-polarised light
☑ recognise that enantiomers have identical chemical properties except in their interaction with another chiral molecule
☑ recognise that different stereoisomers exhibit different biological properties, for example in drug action
☑ identify chiral centres and/ or *cis-trans* isomerism in a molecule of a given structural formula

- Refers to the existence of two or more compounds with the **same molecular formula and structural formula** but **different spatial arrangement of atoms**.

- There are two types of stereoisomerism:
  (i) *Cis-trans* Isomerism
  (ii) Enantiomerism

7.2.1 *Cis-Trans* Isomerism

- The following 2 conditions must be met in order for *cis-trans* isomerism to exist:

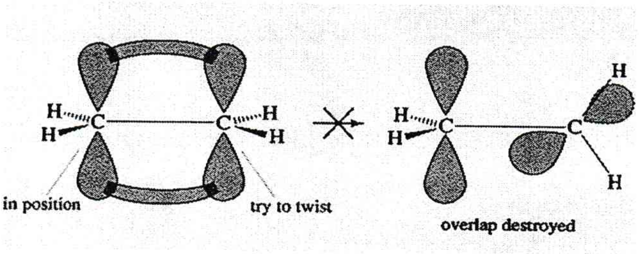
1: **Restricted rotation** about a bond either by the presence of:
   (i) a double bond (C=C, C=N or N=N); or
   (ii) a ring structure

2: For an alkene, each carbon atom in double bond must have two different groups attached to it. For a cyclic compound, two or more of the carbon atoms in the ring have **two different groups** attached to them

→ restricts free rotation.

(a) Alkenes

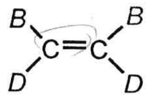
In alkenes, the C=C bond cannot undergo free rotation unless one of the bonds in the C=C bond is broken.



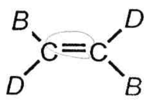
Thus, there is restricted rotation across a C=C bond. (There would be restricted rotation across other double bonds such as N=N or C=N)

If each of the carbon in C=C bond has two different groups attached, two stereoisomers are possible:
- A ***cis***-isomer has the two identical groups on the **same side** of the double bond.
- A ***trans***-isomer has the two identical groups on the **opposite sides** of the double bond.

opposite
↓
trans.

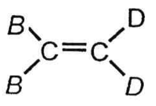


cis-isomer



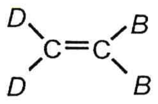
trans-isomer

Since bond rotation cannot occur at the C=C bond, the two molecules cannot interconvert spontaneously, i.e. they are two distinct compounds.



J

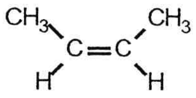
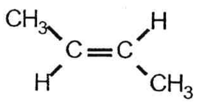
and



K

J and **K** are **identical, NO** *cis-trans* isomerism. (One of C atoms of the double bond is bonded to **two identical groups**).

- *Cis-trans* isomers generally have **similar** (but not identical) **chemical properties**; they react with the same reagents, but at different rates. They have **different physical properties** e.g:

Compound	*cis*–but–2–ene	*trans*–but–2–ene
Structure		
Boiling point / °C	3.72	0.88
Melting point/ °C	–138.9	–105.5

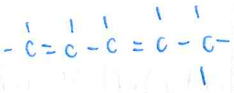
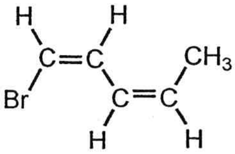
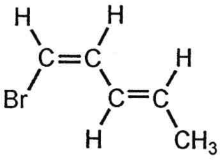
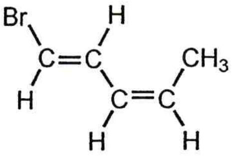
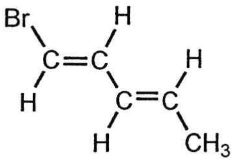
Compared to the *trans* isomer, *cis*-but-2-ene has a: → identical groups on the same side

- **higher boiling point** because of its slightly **higher polarity** (the molecule has a very slight net dipole moment compared to the trans-isomer) → identical groups on the same side
- **lower melting point** because of it fits into a crystalline lattice more poorly. ↳ unbalanced / horizontally unsymmetrical.

- If the number of such C=C bonds in a compound is ***n***, the maximum number of *cis-trans* isomers for the compound is $\boxed{2^n}$.

Exercise 7

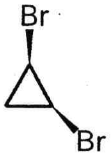
State the number of *cis–trans* isomers for (a) penta–1,3–diene, CH_2=CHCH=CHCH_3 and (b) 1–bromopenta–1,3–diene, BrCH=CHCH=CHCH_3

Compound	(a) penta–1,3–diene, CH_2=CHCH=CHCH_3	(b) 1–bromopenta–1,3–diene, BrCH=CHCH=CHCH_3
Number of C=C bonds that give rise to *cis–trans* isomerism	1	2
Number of *cis–trans* isomers	$2^1 = 2$	$2^2 = 4$
Structure of isomers		 cis,cis-1-bromopenta-1,3-diene  cis,trans-1-bromopenta-1,3-diene  trans,cis-1-bromopenta-1,3-diene  trans,trans-1-bromopenta-1,3-diene

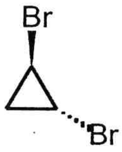
(b) Cyclic compounds

As ring structures also prevent free rotation, *cis-trans* isomers of ring compounds are possible.

E.g 1



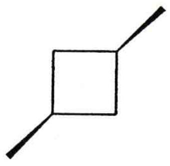
cis-1,2-dibromocyclopropane



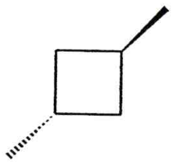
trans-1,2-dibromocyclopropane

E.g 2

entgagen – opp side
E/Z
zusammen – same side



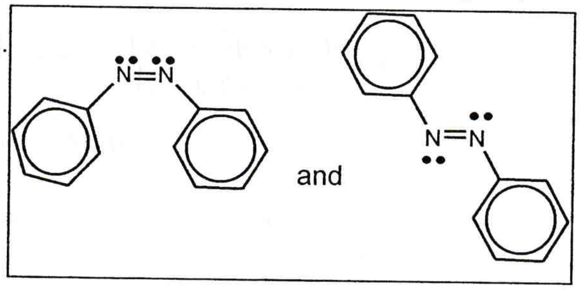
cis-1,3-dimethylcyclobutane

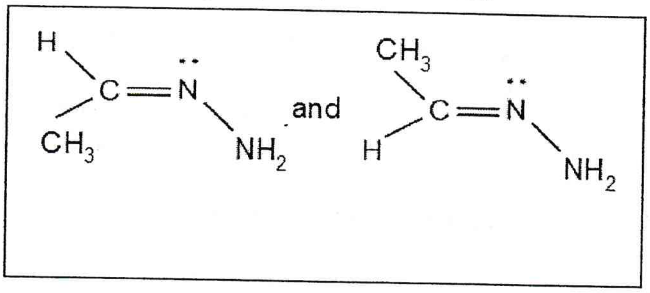


trans-1,3-dimethylcyclobutane

(c) Molecules containing a nitrogen-nitrogen (N=N) or carbon-nitrogen (C=N) double bond

e.g.

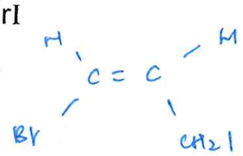




Exercise 8

Which molecules have isomers that exhibit *cis-trans* isomerism?

I	II	III	IV
C_3H_6BrI	C_3H_5I	$C_3H_4I_2$	C_3H_4BrI
✗	✓	✓	✓



A I, II and III only
B II, III and IV only
C II and IV only
D III and IV only

B C

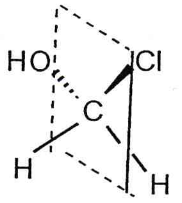
[N2005/I/21]

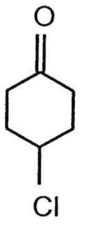
7.2.2 Enantiomerism

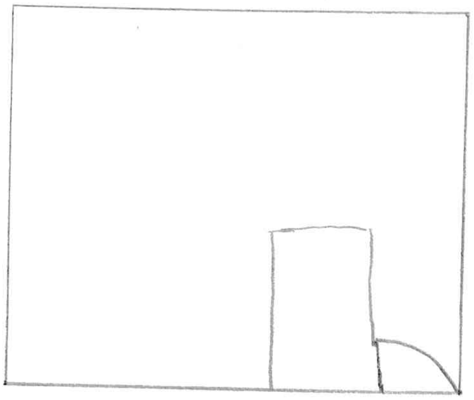
- Enantiomerism refers to the existence of compounds with the **same molecular and structural formulae** but with **different spatial arrangements of atoms.**
- A compound displays enantiomerism if
  - It forms a **non-superimposable mirror image;**
  - It **does not have a plane of symmetry** and;
  - It usually contains one or more **chiral** centres. (attached to 4 diff groups)

7.2.2. (A) Plane of Symmetry

- A molecule with a **plane of symmetry** forms a **superimposable mirror image**. It does not exhibit **enantiomerism**. Some examples of such molecules are shown below:



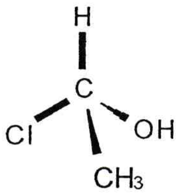


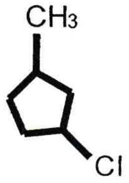


7.2.2 (B) Chiral Carbon

single bond

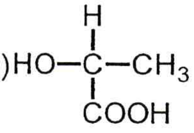
- A chiral carbon is **sp^3 hybridised** and has **four different groups** attached to it.
- A molecule containing at least one **chiral carbon** forms **non-superimposable mirror images**, provided there is **no plane of symmetry**. Such chiral molecules exhibit **enantiomerism**. (*Refer to 7.2.2.(F) Meso compound.*)
- Some examples of such molecules are shown below:

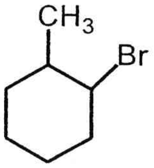


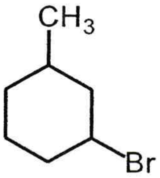


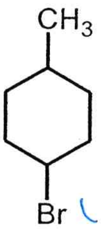
Exercise 9:

For the following compounds, mark the chiral carbon with an asterisk (*)

(a)

$\mathrm{HO{-}C(H)(COOH){-}CH_3}$

(b)


(c)


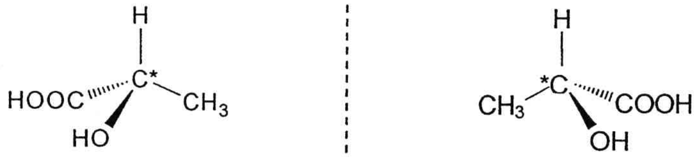
(d)


no chial carbons

left and right are same ∴ plane of symmetry.

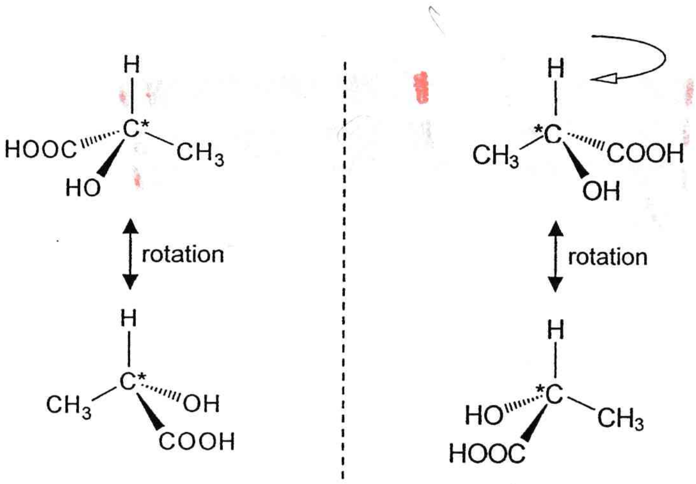
7.2.2 (C) Enantiomers

- Consider lactic acid, $CH_3CH(OH)COOH$, which has **1 chiral carbon** and **no plane of symmetry**.
- Lactic acid has two enantiomers:



(+)-lactic acid Mirror plane (–)-lactic acid

They are mirror images which are non-superimposable. A pair of stereoisomers which are **non-superimposable mirror images** are also called **enantiomers**. The two enantiomers of lactic acid are two different compounds.



(+)-Lactic acid mirror plane (-)-Lactic acid

Regardless of how you flip or rotate a molecule of (+)-Lactic acid, you will never be able to obtain the structure of a molecule of (-)-Lactic acid and vice versa.

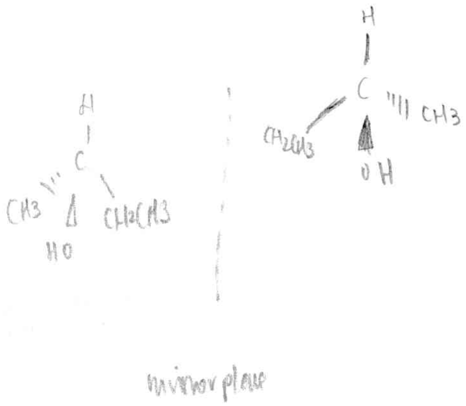
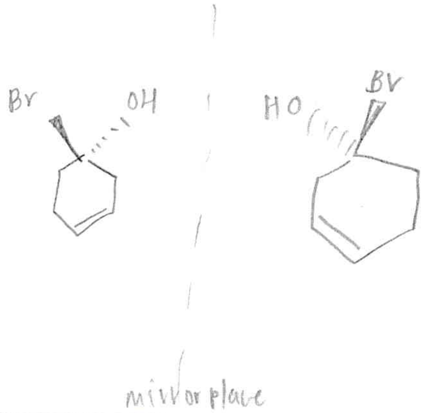
Compare and contrast the properties of the enantiomers:

Properties	**Characteristics**
Physical properties	Identical except that they rotate the plane of plane-polarised light in equal but opposite directions.
Chemical properties	Identical except in their interaction with another chiral molecule.
Biological properties	Different biological properties e.g. drug action

Exercise 10

Draw the enantiomers of

no cis-trans

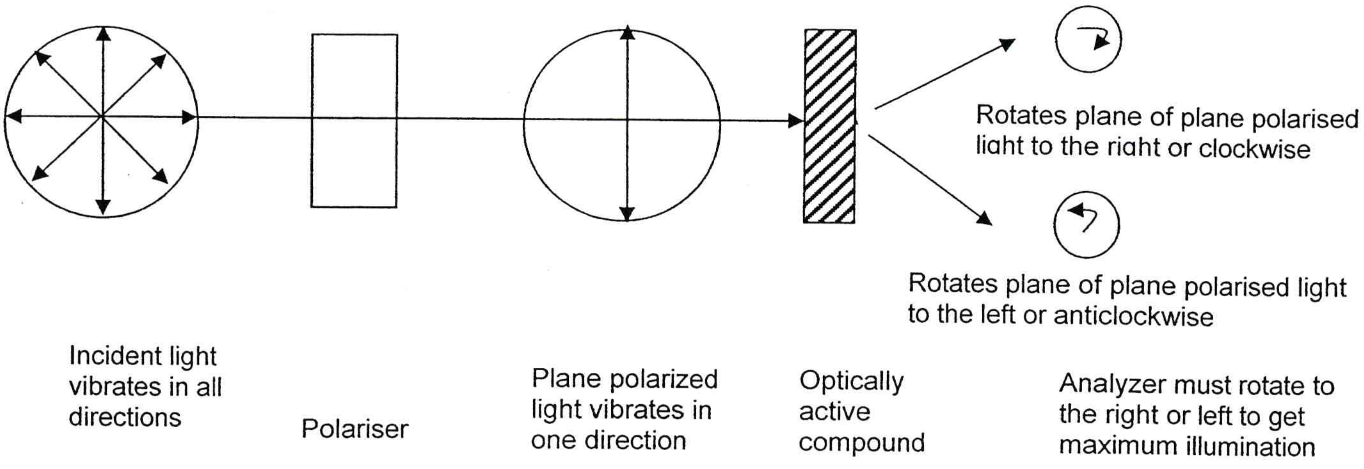
(a) butan-2-ol, $CH_3CH(OH)CH_2CH_3$	**(b)** 1-bromocyclohex-3-en-1-ol
	

(Note: when drawing structures of optical isomers, use " ⋯⋯ " and " ◀ " to show spatial 3-dimensional structure of a molecule)

7.2.2 (D) Rotation of plane-polarised light and optical activity

- Enantiomers differ in their rotation of the plane of plane-polarised light.

Samples containing:	**Rotation of plane-polarised light**	**Optical Activity**
(+)-lactic acid	Rotates the plane of plane-polarised light clockwise	Optically active
(–)-lactic acid	Rotates the plane of plane-polarised light with the same angle but anti-clockwise	Optically active
equal proportions of (+)-lactic acid and (–)-lactic acid (**racemic mixture**)	The rotating power of one enantiomer exactly cancels that of the other. ∴Does not rotate the plane of plane-polarised light.	Not optically active

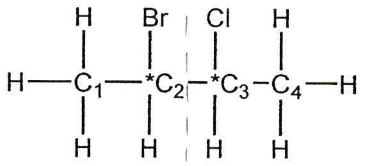


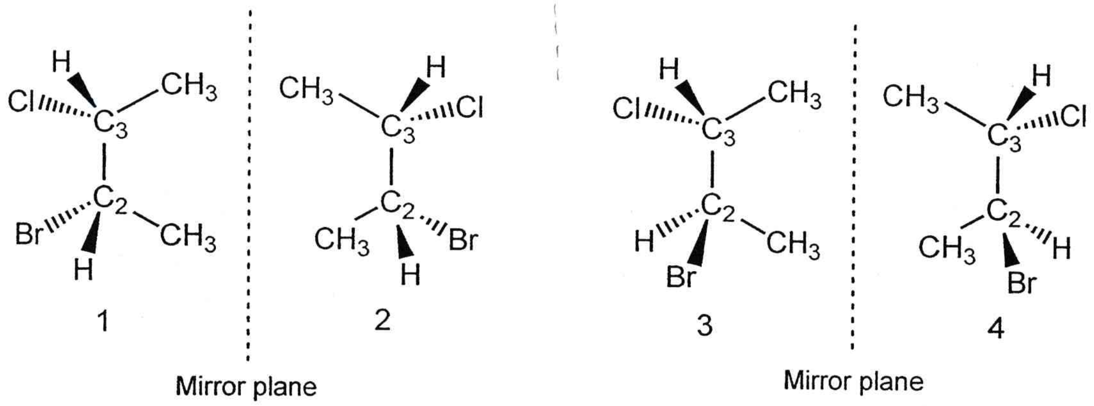
7.2.2 (E) Molecules with more than one chiral centres

→ same as cis-trans

- In general, a molecule with ***n*** chiral centers has a **maximum** of **2^n stereoisomers.**

Example: 2-bromo-3-chlorobutane: 2 chiral centers giving a total of 2^2 = 4 stereoisomers





Isomers **1** and **2** are **non-superimposable mirror images** of one another and so they are a pair of **enantiomers.**

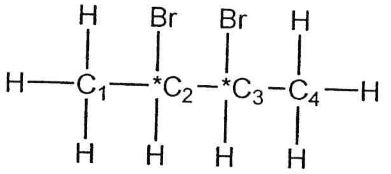
Isomers **3** and **4** are **non-superimposable mirror images** of one another and so they are a pair of **enantiomers.**

Isomers **1** (or **2**) and **3** (or **4**) are stereoisomers which are not mirror images of one another. Stereoisomers which are not mirror images are called diastereomers.

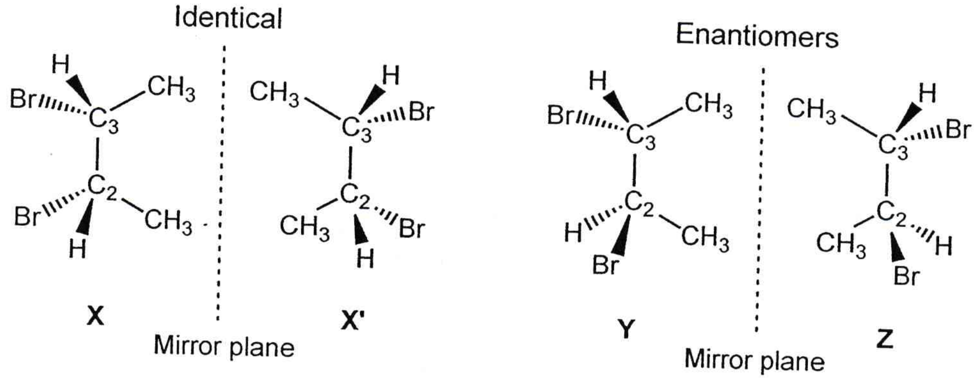
7.2.2. (F) Meso Compound

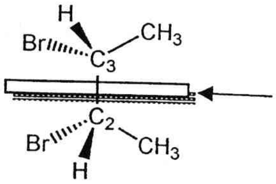
- A **meso compound:**
  - is one whose molecules are **superimposable on their mirror images** even though they contain **chiral centres.**
  - contains a **plane of symmetry.**
  - is **optically inactive.**

Example: 2,3-dibromobutane only has **3** stereoisomers. Why is that so?



$$H-\underset{H}{\overset{H}{C_1}}-\underset{H}{\overset{Br}{{}^*C_2}}-\underset{H}{\overset{Br}{{}^*C_3}}-\underset{H}{\overset{H}{C_4}}-H$$





X and its mirror image, X', are identical.
It is a **meso compound**.

mirror images w/o plone of symmetry

Exercise 11

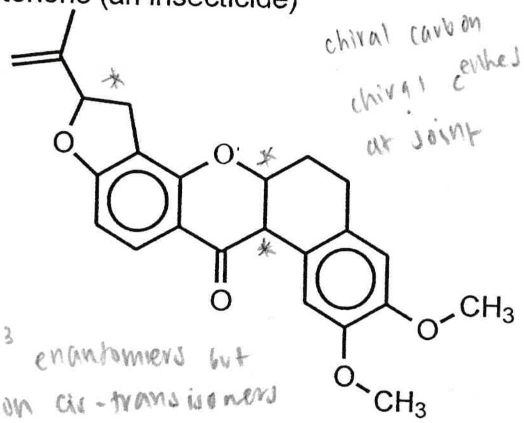
Draw the stereoisomers of 1,3-dimethylcyclopentane and state which stereoisomer is optically active.

- **Note**: If a molecule has **x** chiral centres and **y** double bonds that give rise to cis-trans isomerism, the **maximum** number of stereoisomers it can form is $2^{(x+y)}$.

Exercise 12

For the two molecules below, mark any chiral carbon present with an asterisk (*) and state the number of stereoisomers each molecule can form.

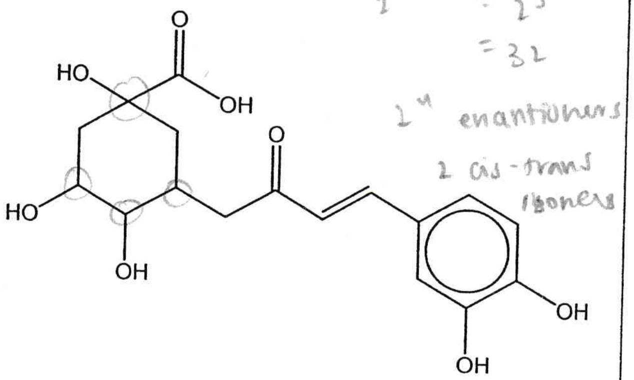
(a) rotenone (an insecticide)



chiral carbon
chiral carbons at joint

2^3 enantiomers but non cis-trans isomers

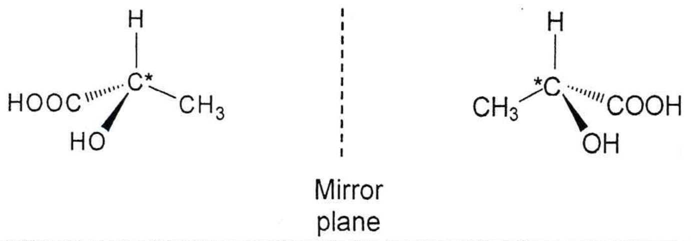
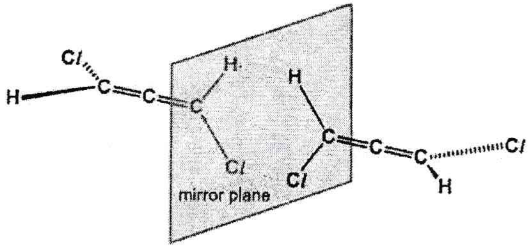
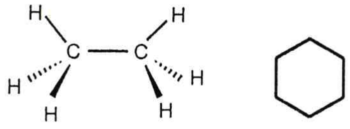
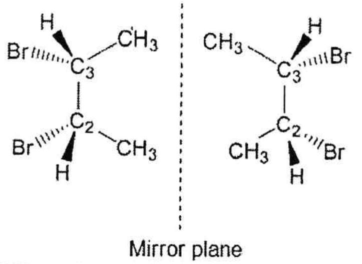
(b) Chlorogenic acid (occurs naturally in coffee and an edible species of bamboo)



$2^{4+1} = 2^5 = 32$

2^4 enantiomers
2 cis-trans isomers

Considerations for the existence of enantiomerism in a molecule

Mirror image	Plane of Symmetry	Chiral Centre	Example
Non-superimposable (exhibits enantiomerism)	No	Yes	
Non-superimposable (exhibits enantiomerism)	No	No	
Superimposable (No enantiomerism)	Yes	No	
Superimposable (No enantiomerism)	Yes	Yes	

Examples of the importance of enantiomerism in biological systems

The small difference in the arrangement of atoms between the (+) and the (-)–isomers may seem unimportant to you but to the cells of a living organism the difference is critical. Cells can recognise the difference and often can use only one of the enantiomer.

E.g.

- (+)-lactic acid is found in living muscle and (-)-lactic acid, in sour milk.
- The proteins in our bodies are built up from only one enantiomer of each amino acid. These are the (-)–enantiomers.
- Enantiomers can interact differently with the chiral taste buds on your tongue. (+)–amino acids all taste sweet; (-)–amino acids are often tasteless or bitter.
- Enantiomers can smell different. E.g. one enantiomer of limonene smells of oranges, the other of lemons.
- Yeast can ferment (+)–glucose to produce alcohol but not (-)–glucose.

Different stereoisomers have different biological properties, e.g. in drug action. Very often, only one enantiomer of the drug works as a medicine, while the other form is useless or less effective or may even cause serious side effect.

E.g.

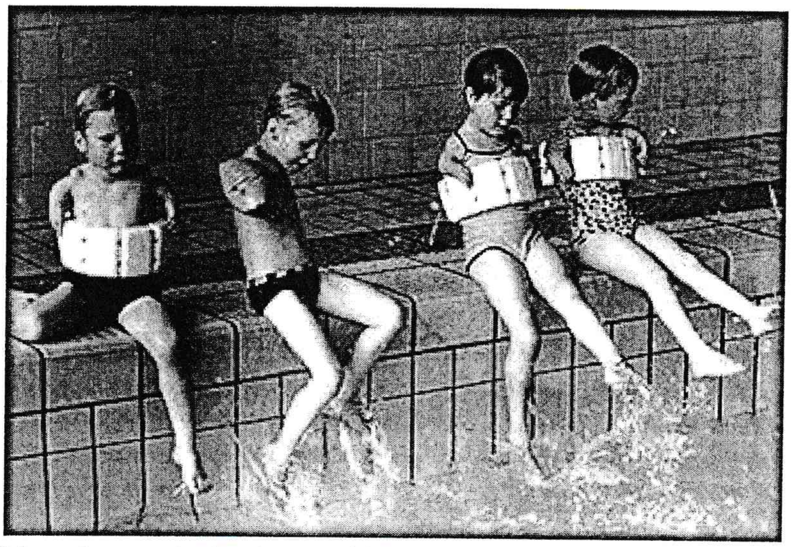
- (+)–thalidomide has sedative properties while (-)–thalidomide is a potent mutagen (it causes gene mutation which leads to deformed offspring).
- One enantiomer of ethambutol fights tuberculosis, the other causes blindness.
- Penicillin works by breaking peptide links which involve (+)–alanine. These occur in the cell walls of bacteria but not in humans. When its cell wall is broken, the bacteria is killed. So penicillin is very effective in killing bacteria but cannot have the same effect on us because we do not use (+)–alanine.
- (-)-ibuprofen is potent as a painkiller while (+)-ibuprofen is ineffective (and also harmless).
- (-)–dopa is widely used for its potent activity against Parkinson's disease while (+)–dopa has no biological effect.

Hence, research is carried out to synthesise 'chiral drugs' which contains only one enantiomeric form- both for efficiency and for protection against possible side effects of its mirror image form.

Thalidomide disaster: Why stereochemical considerations are so important in drug design

Thalidomide first appeared in Germany on 1st October 1957. It was marketed as a sedative with apparently remarkably few side effects. The Drug Company who developed it believed it was so safe it was suitable for prescribing to pregnant women to help combat morning sickness.

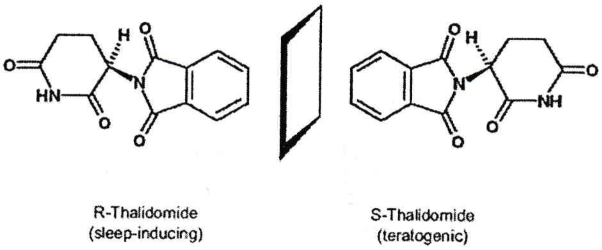
It was quickly being prescribed to thousands of women and spread to most corners of the globe. Nobody had any idea of what was to follow. Drug testing procedures were far more relaxed at that time, and although tests had taken place on thalidomide, they didn't reveal any of its tetragenic (roughly meaning causing malformations) properties. In most countries, drug companies were not required to submit testing results to the appropriate government agencies. The tests on thalidomide were conducted on rodents which metabolise the drug in a different way to humans. Later tests on rabbits and monkeys produced the same horrific side effects as in humans.



Towards the end of the fifties, children began to be born with shocking disabilities. It was not immediately obvious what the cause of this was. Probably the most renowned is *Pharcomelia*, the name given to the flipper-like limbs which appeared on the children of women who took thalidomide. Babies affected by this tragedy were given the name *'Thalidomide Babies'*.

Pictured right are some of babies born with the flipper-like limbs. Remarkably, many of the children involved have gone on to lead successful and fulfilling lives.

Thalidomide has just one chiral atom and so exists as two enantiomers. The diagram to the right shows the molecule without hydrogens. Notice that two of the groups attached to the chiral centre are part of the same ring structure. They are classified as two different groups since moving around from the chiral centre, the order of atoms is different each way. It is said the chiral atom has two different views around the ring.



R-Thalidomide (sleep-inducing) S-Thalidomide (teratogenic)

The Reality of Enantiomerism in Thalidomide

Laboratory tests after the thalidomide disaster showed that in some animals the 'S' enantiomer was tetragenic but the 'R' isomer was an effective sedative. It is now known that even when a stereoselective sample of thalidomide (only one of the enantiomers) is administered at the pH in the body, it can cause racemising. Both enantiomers are formed in a roughly equal mix in the blood. So, even if a drug of only the 'R' isomer had been created and administered, the disaster would not have been averted. *(http://www.chm.bris.ac.uk/motm/thalidomide/first.html)*