

2023 JC1 H2 CHEMISTRY (9729) ORGANIC CHEMISTRY

Topic 9: INTRODUCTION TO ORGANIC CHEMISTRY

Name:

Civics Group: _____

Introduction

Students 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 sp³ hybridisation, as in ethane molecule, sp² 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

<u>Isomerism</u>

Students should be able to:

- (a) describe constitutional (structural) isomerism
- (b) 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]

- (c) explain what is meant by a chiral centre
- (d) deduce whether a given molecule is chiral based on the presence or absence of chiral centres and/or a plane of symmetry
- (e) recognise that an optically active sample rotates plane-polarised light and contains chiral molecules
- (f) recognise 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]
- (g) recognise that enantiomers have identical chemical properties except in their interactions with another chiral molecule
- (h) recognise that different stereoisomers exhibit different biological properties, for example in drug action
- (i) deduce the possible isomers for an organic molecule of known molecular formula
- (j) identify chiral centres and/or *cis-trans* isomerism in a molecule of given structural formula

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1 Introduction

Organic chemistry, one of the major branches of chemistry, is concerned with

"the study of the *structure*, *properties*, *composition*, *reactions*, and *preparation* of **carboncontaining compounds**, which include not only hydrocarbons but also compounds with any number of other elements, such as hydrogen (most compounds contain at least one carbon– hydrogen bond), nitrogen, oxygen, halogens, phosphorus, silicon, and sulfur".

Carbon is special in that

- it has a strong tendency to form long chains and/or rings of carbon atoms due to the strength of the carbon–carbon bond
- it can form four bonds with its neighbouring atoms which allows for significant branching on carbon chains
- it forms strong π -bonds, making double and triple bonds possible within the structures

Hence, it can form a vast array of compounds, from the simple methane with one carbon atom, to the complex DNA with tens of billions of carbon atoms.

In the study of organic chemistry, we will make use of concepts that we have learnt in **Chemical Bonding** related to **covalent bonding** (e.g. sigma (σ) and pi (π) bonds, dative bonds, polarity of bonds and molecules) and **intermolecular forces** (e.g. instantaneous dipole-induced dipole interactions, permanent dipole-permanent dipole interactions, hydrogen bonds).

Before we go further into the topic, use Self Check 1A below to do a quick self-assessment of your grasp of these essential concepts.

(a)	A covalent bond is formed when electrons are shared between two atoms.				
(b)	σ bonds can be formed from either the head-on or side-on overlaps of orbitals.	True / False			
(c)	A double bond is composed of two π bonds.	True / False			
(d)	A dative bond is formed when one atom donates both electrons that are shared between two atoms.	True / False			
(e)	The donor atom in a dative bond has a filled orbital, while the acceptor atom has an accessible vacant orbital.	True / False			
(f)	CCl_4 is a polar molecule as the C-Cl bond is polar.	True / False			
(g)	The more polar a bond, the stronger the bond.	True / False			
(h)	CH ₃ CH ₂ OH forms intermolecular hydrogen bonds.	True / False			
(i)	CH ₃ CHO forms intermolecular hydrogen bonds.	True / False			

2 Representations in Organic Chemistry

LO (a) interpret, and use the nomenclature, general formulae and displayed formulae of hydrocarbons, halogen derivatives, hydroxyl compounds, carbonyl compounds, carboxylic acids and derivatives, nitrogen compounds

2.1 Formulae of Organic Compounds

We can show the elements present in an organic compound and their relative proportions in a few different ways.

The following different formulae are illustrated using lactic acid.

	type of formula	what it shows	representation of lactic acid
1	empirical formula	 shows the simplest ratio of the number of atoms of the elements present in one molecule of a compound order usually follows alphabetical order of symbols. However, for organic compounds, because carbon and hydrogen are always present, C is always cited first, H second and then the rest, in alphabetical order. 	
2	molecular formula	 shows the actual number of atoms of the elements present in one molecule 	$C_3H_6O_3$
3	constitutional formula	 shows how the constituent atoms of a molecule are joined together with minimal detail, using conventional groups, for an unambiguous structure 	
4	full structural or displayed formula	 detailed structure of molecule showing the relative position of atoms and the number of bonds between them 	
5	skeletal formula	 simplified representation of an organic formula derived from the structural formula by removing hydrogen atoms bonded to carbon atoms (and their associated bonds) and carbon atoms, leaving just the carbon–carbon bonds in the carbon skeleton and the associated functional groups 	
6	stereochemical formula	 shows spatial arrangement of bonds, atoms and groups in molecule in 3- dimension 	



Important concepts to remember:

- (i) I need to know the meanings of empirical, molecular, constitutional, full structural or displayed, and skeletal formulae.
- (ii) I need to know HOW TO DRAW full structural AND skeletal formulae.

3 Classification of Organic Compounds

LO (b) interpret, and use the following terminology associated with organic reactions:
 (i) functional group
 (ii) degree of substitution: primary, secondary, tertiary, quaternary

Organic compounds are thought of as consisting of a relatively **unreactive backbone**, *e.g.* a chain of sp³ hybridised carbon atoms, and one or several **functional groups**. Names of organic compounds are derived from the functional group(s) and main carbon chain.

3.1 Nature of structure

We can categorise organic compounds based on the nature of their carbon skeletons:

- saturated : compounds such as alkanes, whose molecules contain only single bonds, are referred to as saturated compounds because these compounds contain the maximum number of hydrogen atoms that the carbon compound can possess
- unsaturated : compounds with *multiple bonds*, such as alkenes, alkynes, and aromatic hydrocarbons, are said to be unsaturated because they possess fewer than the maximum number of hydrogen atoms, and are capable of reacting with hydrogen under the proper conditions
- aliphatic : acyclic (compounds with no ring of atoms) or cyclic (compounds containing ring of atoms), saturated or unsaturated carbon compounds, excluding aromatic compounds
- aromatic : a cyclically conjugated molecular entity with a stability (due to delocalisation of electrons) significantly greater than that of a hypothetical localised structure is said to possess aromatic character, i.e. containing benzene

3.2 Functional groups

The **functional group** is an atom, or a group of atoms that has similar chemical properties whenever it occurs in different compounds. It defines the characteristic **physical and chemical properties** of families of organic compounds.

The carbon atom on which the functional group is attached to is known as the **alpha** (α) **carbon**. The naming continues as beta (β), gamma (γ), delta (δ), ..., until the last carbon in the chain, which is termed the omega (ω) carbon.

A series of compounds with the **same functional group**, where each member differs from the next member by a **constant CH₂ unit** is called a **homologous series**. Members of a homologous series are called homologs.

All compounds in any one homologous series

- can be represented by a general formula
- have a relative molecular mass 14 (corresponding to one CH₂ unit) greater than the preceding compound in the series
- can be prepared by similar methods
- have similar chemical properties
- exhibit a regular gradation of physical properties (due to the increasing size of hydrocarbon chain)

Here are the common functional groups you will encounter:

Hydrocarbons (compounds that contain only carbon and hydrogen atoms)



Technically, alkanes do not have any functional group.

From the electrostatic potential maps for ethane, ethene, ethyne and benzene, it can be seen that ethane is **non-polar** (generally green), while there are regions of **higher electron density** (yellow \rightarrow red) in the other three due to the π **bond/system**.



This is generally true for alkanes in that the C—C and C—H bonds are **essentially** non-polar and hence they are unreactive towards polar (charged) reagents, and forms the **unreactive skeleton** of most organic compounds.

Carbon bonded to electronegative atoms

• **Single bond** (R is the carbon framework, typically an alkyl group; see 3.3)

Aliphatic		Aromatic	
Halogenoalkar	nes (X = F, C <i>1</i> , Br,	I) Halogenoarenes (X = F,	C <i>l</i> , Br, I)
RCH ₂ -X	primary (1°)	×	
R ₂ CH-X	secondary (2°)		
R ₃ C-X	tertiary (3°)		
Alcohols		Phenol	
RCH ₂ -OH	primary (1º)		
R ₂ CH- OH	secondary (2°)		
R ₃ C-OH	tertiary (3°)		
Amines		Phenylamine (Aniline)	
RNH	primary (1º)		
R ₂ NH	secondary (2°)	NH ₂	
R ₃ N	tertiary (3°)		
⊕ R₄ N	quaternary ammonium ion ((4°)	
R- 0 -R	R- SH	R- S -R R-	-NO ₂
Ether	Thiol	Sulfide (Thioether) Nitro c	ompound

• Double bond to oxygen



(Note: Both the R-groups for ketone, ester and acid anhydride may not be the same.)

• Triple bond to nitrogen

R−C≡N Nitrile

3.3 Alkyl and Aryl Groups

When a hydrogen atom is removed from an alkane, this gives an **alkyl group**. The symbol **R** is used to represent a general alkyl group (*i.e.* a methyl, ethyl, etc. group).

Alkanes have the general formula, C_nH_{2n+2} . So the general formula for alkyl chains is C_nH_{2n+1} —.

alkane	alkyl group	bond-line	ball-and-stick model
CH ₃ —H methane	H₃C—⋚ methyl		° 🗶
CH ₃ CH ₂ —H ethane	CH₃CH₂—⋚ ethyl	- vvv	, Marco and a second se
CH ₃ CH ₂ CH ₂ —H propane	CH ₃ CH ₂ CH ₂ —§ propyl	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	
CH ₃ CH ₂ CH ₂ CH ₂ —H butane	$CH_3CH_2CH_2CH_2$	- Str	. So Star

FYI: Ball-and-Stick Model

• Displays both the three-dimensional position of the atoms and the bonds between them

Atoms are typically represented by spheres, bonds are represented by rods

Similarly, groups derived from arenes by removal of a hydrogen atom from an aromatic ring carbon atom are known as **aryl groups**. The symbol **Ar** is used to represent a general aryl group.

When a benzene ring is attached to some other group of atoms in a molecule, it is called a **phenyl group**, and it is represented in several ways:



3.4 Degree of Substitution

Degree of substitution in an organic molecule is based on the **number of carbon atom(s)** (generally also the **number of alkyl group(s)**) bonded to the atom of interest.

In the case of alkanes:







A secondary (or 2°) carbon is bonded to two other carbons



A tertiary (or 3°) carbon is bonded to three other carbons



A quaternary (or 4°) carbon is bonded to four other carbons

For **alcohols and halogenoalkanes**, this is based on the number of carbon atom(s) attached to the α -carbon; while for **amines and amides**, it is based on the number of carbon atom(s) attached to the **nitrogen atom**.

	Halogenoalkanes	Alcohols		Amines
primary (1º) secondary (2º) tertiary (3º)	RCH ₂ X R ₂ CHX R ₃ CX	RCH ₂ OH R ₂ CHOH R ₃ COH	primary (1°) secondary (2°) tertiary (3°) quaternary ammonium ion (4°)	RNH₂ R₂NH R₃N ⊕ R₄N

Important concepts to remember:

- (i) I need to know that if an organic molecule contains double (C=C, C=O, etc) or triple (C =C, C=N, etc) bond, it is unsaturated.
- (ii) I need to know that compounds having same functional group have similar chemical properties BUT different physical properties (such as melting and boiling points).
- (iii) I need to know the STRUCTURE of different functional groups and I MUST know how to identify them: Alkene, Alkyne, Halogenoalkanes, Alcohol, Phenol, Aldehyde, Ketone, Carboxylic acid, Amide, Ester and Ether.

Note: ether is not in H2 syllabus

- (iv) I need to know the meaning of primary (1°), secondary (2°) and tertiary (3°).
- (v) I need to know that alcohol and amine need to be labelled as 1°, 2° and 3°.



4 Organic Nomenclature

LO (a) interpret, and use the nomenclature, general formulae and displayed formulae of hydrocarbons, halogen derivatives, hydroxyl compounds, carbonyl compounds, carboxylic acids and derivatives, nitrogen compounds

The **IUPAC** (International Union of Pure and Applied Chemistry) name of an organic compound is composed of **three** parts.



There are **four** key steps in naming organic compounds.

1. Find the longest carbon chain and name this as an alkane. This is the parent name.

no. of carbons	alkane name	no. of carbons	alkane name
1	meth <i>ane</i>	7	hept <i>ane</i>
2	eth <i>ane</i>	8	oct <i>ane</i>
3	prop <i>ane</i>	9	non <i>ane</i>
4	but <i>ane</i>	10	dec <i>ane</i>
5	pent <i>ane</i>	11	undec <i>ane</i>
6	hex <i>ane</i>	12	dodec <i>ane</i>

Identify the <u>major functional group</u>. Replace –*ane* (in the alkane) with a <u>suffix</u> (see Table 4.1).

If there is **more than one functional group** present in the molecule, the one of **highest priority** as stated below is the **principal functional group**, and is named by the **suffix**. All other function group(s) are substituents, and will be named using the prefix(es).

Functional group priorities (Do NOT be stressed by the following!)carboxylic acid (RCO2H) > ester (RCO2R) > acid (acyl) chloride (RCOCl) >amide (RCONH2) > nitrile (RCN) > aldehyde (RCHO) > ketone (RCOR) >alcohol (ROH) > phenol (\bigcirc - OH) > amine (RNH2) > benzene (\bigcirc) >alkene (RCH=CHR) > alkyne (RC≡CR) > alkane (RH) > ether (ROR) >sulfide (RSR) > halogenoalkane (RX) > nitro compound (RNO2)

- 3. Number the atoms in the main chain. Begin at the end nearer the <u>major</u> functional group and give this the <u>lowest</u> number. For alkanes, begin at the end nearer the first branch point.
- 4. Identify the <u>substituents</u> (*e.g.* minor functional groups) on the main chain and their number. The substituent name and position is the <u>prefix</u> (see Table 4.1).

The names of two or more different substituents should be included in **alphabetical order** in the prefix (*e.g.* hydroxy before methyl). If two substituents happen to be on the **same carbon**, they are given the **same number**.

A **multiplier** is used in the prefix or suffix to indicate the presence of two or more of the minor or major functional groups (or substituents).

number	multiplier	number	multiplier
1*	mono-	6	hexa-
2	di-	7	hepta-
3	tri-	8	octa-
4	tetra-	9	nona-
5	penta-	10	deca-

* The multiplier 'mono-' for one substituent is seldom used in the actual naming, but rather, is used in comparison to molecules with more than one substituent.



Write the IUPAC name of the following compounds.



 Table 4.1: Prefixes and suffixes of functional groups

class of compound	structure of functional group	prefix (minor functional group)	suffix (major functional group)
alkane	_	alkyl-	-ane
alkene)c=c	alkenyl-	-ene
alkyne	—c≡c—	alkynyl-	-yne
arene		phenyl-	-benzene
	RCH ₂ –X primary (1°)	fluoro-	alkyl fluoride
halogenoalkane	R ₂ CH–X secondary (2 ⁰)	chloro-	alkyl chloride
nalogenoaikane	R ₃ C–X tertiary (3⁰)	bromo-	alkyl bromide
	where X = F, C <i>l</i> , Br, I	iodo-	alkyl iodide
	×	fluoro-	aryl fluoride
hologonoorono		chloro-	aryl chloride
nalogenoarene		bromo-	aryl bromide
	where X = F, C <i>l</i> , Br, I	iodo-	aryl iodide
	RCH ₂ –OH primary (1º)		
alcohol	R ₂ CH–OH secondary (2 ⁰)	hydroxy-	-ol
	R ₃ C–OH tertiary (3⁰)		
phenol	ОН	(hydroxyphenyl)-	-phenol
aldehyde	R H	formyl-	-al

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class of compound structure of functional group		prefix (minor functional group)	suffix (major functional group)
ketone	O II R ^C R	oxo- (=O) or alkanoyl (–C(=O)R)	-one
amine	RNH₂ primary (1º) R₂NH secondary (2º) R₃N tertiary (3º) R₄N⁺ quaternary (4º)	amino-	-amine
phenylamine	NH ₂	N-phenylamino-	-phenylamine
amide	$\begin{array}{ccc} O & NH_2 : \text{primary amide} \\ \parallel & NHR : \text{secondary amide} \\ R & NR_2 & NR_2 : \text{tertiary amide} \end{array}$	carboxamido- or carbamoyl-	-amide
nitro compound	R-NO ₂	nitro-	-
nitrile	R−C≡N	cyano-	-nitrile
carboxylic acid	R ^C OH	carboxy-	-oic acid
acid(acyl) halide	$R^{-C} X$ where X = C <i>l</i> , Br	carbonohalidoyl-	-oyl chloride -oyl bromide
ester		alkanoyloxy (RCOO–) or alkoxycarbonyl (ROCO–)	alkyl alkanoate
ether	R ^{∕O} ∕R	alkoxy-	alkyl ether

4.1 Special cases

Alkenes and alkynes

The position of the double or triple bond is indicated by the number of the <u>lowest</u> carbon atom in the alkene or alkyne.

Aromatics

Monosubstituted benzene derivatives are usually named after benzene (C_6H_6), although some nonsystematic or common names (in brackets) are still used.



Х	name
CH₃	methylbenzene (toluene)
$CH=CH_2$	ethenylbenzene (styrene)
ОН	hydroxybenzene (phenol)
NH ₂	aminobenzene (aniline)
CN	cyanobenzene (benzonitrile)

The word benzene comes first when functional groups of higher priority (than benzene) are on the ring

۱	Х	name
۱	CHO	benzenecarboxaldehyde (benzaldehyde)
	CO ₂ H	benzenecarboyxlic acid (benzoic acid)

Disubstituted derivatives are sometimes named using the prefixes ortho- (or positions 2- and 6-), meta- (or positions 3- and 5-) and para- (or position 4-).

For trisubstituted derivatives, the **lowest** possible numbers are used and the prefixes are arranged alphabetically.



<u>Esters</u>

These are named in two parts. The first part represents the $\underline{R^1 \text{ group attached to oxygen}}$ (Note: This R^1 group comes from the alcohol). The second represent the $\underline{R^2CO_2}$ (Note: R^2 group comes from the carboxylic acid) portion which is named as an alkanoate (*i.e.* the suffix is –oate). A space separates the two parts of the name.



Important concepts to remember:

- (i) During the naming of an organic molecule:
 - Find the longest carbon chain that contains the functional group with the highest priority.
 - The "parent" will carry the suffix of the functional group with the highest priority.
 - The suffix will be numbered with the smallest number.
 - The substituents will then be the prefix with the lowest numbering, arranging in alphabetical order.
- (ii) For A-level, please be assured that examiner won't ask you to name very big and complex molecules. Usually it will be simple molecule. Most importantly, you need to be able to identify the different functional groups stated in the last section's "Important concepts to remember".

5 Bonding in Carbon Compounds

- LO (d) describe sp³ hybridisation, as in ethane molecule, sp² 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 carboncarbon bonds
 - (f) predict the shapes of, and bond angles in, molecules analogous to those specified in (e)

The electronic configuration of carbon is $1s^2 2s^2 2p^2$. Carbon has four valence electrons and can form four bonds to neighbouring atoms (*i.e.* tetravalent).

The **formation of covalent bonds** with other atoms require **unpaired electrons**. In its ground state, a carbon atom only has two unpaired electrons in its 2p orbitals, making it seem as if it can only form two bonds. However, it is possible to excite the carbon atom such that one of the paired electrons in the 2s orbital is **promoted** to the vacant 2p orbital:



In this way, the carbon atom now has **four unpaired electrons**, which makes it possible for it to form four bonds with other atoms or groups. The large amount of energy produced by forming these two extra bonds considerably outweighs that required (\approx 406 kJ mol⁻¹) for the unpairing of the 2s² electrons, followed by the 2s \rightarrow 2p promotion.

5.1 Hybridisation

The unpaired electrons available in a carbon atom for bonding are in **one 2s** and **three 2p** orbitals. If these orbitals are used for bonding, we will expect two kinds of bonds to be formed – one non-directed bond (due to the spherical 2s orbital), and three directed bonds at right angles to one another (due to the three 2p orbitals). However, we know that this is not the case. For example, the four C–H bonds in methane are known to be **identical** and **arranged symmetrically** (tetrahedrally) at an angle of 109.5°.



In 1931, Linus Pauling explained this by showing mathematically that the 2s and three 2p atomic orbitals combine or **hybridise** to form four new identical atomic orbitals capable of forming stronger bonds. This is the concept of **hybridisation**.



Making Thinking Visible

- **Q:** Hmm...so the carbon atom in an organic molecule actually undergoes hybridisation process?
- A: Hybridisation is **not a physical phenomenon**, meaning, the atom "is not aware of it". It is a mathematical operation that is created by scientists to describe the bonding in a molecule. The purpose for this creation is to explain the observations that was made.
- Q: Will we be asked to predict the hybridisation state of any other atom at A-level?
- A: Might be! If it does, it will be limited only to 4 regions of electron densities. Most of the time, you only need to be able to predict the hybridisation state of a carbon atom in an organic molecule.
 You will not be asked to explain the hybridisation state at all!

In organic chemistry, the most common types of hybridisation for carbon are **sp**³ (as in ethane), **sp**² (as in ethene and benzene) and **sp** (as in ethyne).

	sp ³ hybridisation	sp ² hybridisation	sp hybridisation
when does it occur	when carbon forms <u>four σ bonds</u>	when carbon forms three σ bonds and one π bond	when carbon forms two σ bonds and two π bonds
orbitals hybridised	<u>one</u> s orbital <u>three</u> p orbitals	<u>one</u> s orbital <u>two</u> p orbitals	<u>one</u> s orbital <u>one</u> p orbital
number of hybrid orbitals formed	four sp ³ hybrid orbitals \bigcirc sppppsp ³ sp ³ sp ³ sp ³ sp ³	three sp ² hybrid orbitals Image: spin spin spin spin spin spin spin spin	two sp hybrid orbitals \searrow \bigcirc \bigcirc \bigcirc s p sp sp
orientation of orbitals	 the four sp³ hybrid orbitals point to the corners of a <u>tetrahedron (109.5^o bond angle)</u>. 	 the three sp² hybrid orbitals point to the corners of a triangle (120° bond angle). the remaining unhybridised p orbital is perpendicular to the sp² plane. 	 the two sp hybrid orbitals point in the <u>opposite directions (180° bond angle)</u>. the two remaining unhybridised p orbitals are <u>perpendicular</u> to the sp plane, and to each other.
	sp ³ sp ³ sp ³	sp^{2} sp^{2} p sp^{2}	sp ^{180°} p



Think about this...

The C-H bonds in ethane, ethene and ethyne are of different strengths (and thus length). Why is this so?

compound	H_3C-CH_2-H	$H_2C = CH - H$	HC≡C−H	
C-H bond length / nm	0.109	0.1076	0.106	
C-H bond strength / kJ mol ⁻¹	420	444	552	

Each type of hybrid orbital has different characteristics depending on its original atomic orbitals.

hybrid orbital	s character	p character
sp³		
sp ²		
sp		

The greater the ______ of the carbon hybrid orbitals, the _____ the bond and the ______ is the bond. This is because the electrons are held closer to the nucleus.

Example 5A

Covalent bonds are formed by orbital overlap. The shape of molecules can be explained in terms of hybridisation of orbitals.

Which bond is **not** present in $H = C^3 = C^2 = C^1$?

	present?	which bond in molecule?
a π bond formed by 2p–2p overlap		
a σ bond formed by 1s–2sp overlap		
a σ bond formed by 1s–2sp³ overlap		
a σ bond formed by $2\text{sp}^22\text{sp}^3$ overlap		
	a π bond formed by 2p–2p overlap a σ bond formed by 1s–2sp overlap a σ bond formed by 1s–2sp ³ overlap a σ bond formed by 2sp ² –2sp ³ overlap	a π bond formed by 2p–2p overlapa σ bond formed by 1s–2sp overlapa σ bond formed by 1s–2sp ³ overlapa σ bond formed by 2sp ² –2sp ³ overlap

Hybridisation in benzene

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LO (c) interpret, and use the following terminology associated with organic reactivities:
(i) delocalisation
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One of the major problems of elementary organic chemistry is the detailed structure of **benzene**, C_6H_6 . Although it is clearly unsaturated, it is much more stable than typical alkenes (see box below for details) and does not undergo the usual alkene reactions. Hence, the structure of benzene should be quite different from that of an alkene.



The **carbon–carbon bond lengths** in benzene are found to be **exactly the same**, 0.140 nm. This means that benzene is a regular hexagon with bond lengths somewhere in between the normal values of a single (0.154 nm) and a double (0.133 nm) bond. In addition, an electrostatic potential map shows that the **electron density** in all six carbon-carbon bonds is **identical**.



FYI: Electrostatic Potential Map

- Illustrates charge distributions of molecules three dimensionally • Low potential *i.e.* abundance of electrons: red • High potential *i.e.* absence of electrons: blue
- Allows us to visualise variably charged regions of a molecule, which can help us determine how
- Allows us to visualise variably charged reg molecules interact with one another

Hence, we know that benzene is a **planar** molecule with the shape of a regular hexagon, which in turn implies that all six carbon atoms in the ring are **sp**² **hybridised**, with a (singly occupied) 2p atomic orbital each perpendicular to the plane of the ring. Each carbon atom uses its sp² hybrid orbitals to form σ bonds with two other carbons and one hydrogen atom, and the unhybridised 2p orbital to form π bonds.

Overlapping of the 2p orbitals can take place either between (i) C_1 and C_2 , C_3 and C_4 , C_5 and C_6 ; or between (ii) C_1 and C_6 , C_2 and C_3 , C_4 and C_5 , leading to the two Kekulé structures for benzene that involve alternating double and single bonds.



However, such a structure does not support the differences benzene displays compared to alkenes. Rather, a more probable structure of benzene is one in which **all** six adjacent 2p orbitals could overlap, resulting in the formation of an annular π electron cloud, above and below the plane of the ring:



As the 2p electrons are no longer held between just two carbon atoms but are spread over the entire ring, the electrons are said to be **delocalised**. To represent the unique structure of benzene, we use the following symbol:



Making Thinking Visible

- **Q:** When we say that benzene is a planar molecule, so, it means that ALL the atoms of the molecule lie on a flat plane?
- A: Yes. Ethene (C_2H_4) and ethyne (C_2H_2) are two other planar molecule but ethane is not.
- **Q:** Hmm...so can I say that as long as a molecule contains at least one sp³ hybridised carbon atom, the molecule will not be planar?
- A: Absolutely spots on, Eunoian!
- **Q:** If the six π electrons are moving round the six-membered carbon ring, can we say that on average, the π bond between two carbon atoms is only formed by one electron?
- A: Yes, you may say that. And this is why the carbon-carbon bond length in benzene is intermediate between a C=C and a C-C bonds. The **bond order is 1.5**.

Important concepts to remember:

(i) I need to know how to predict the hybridisation state of an atom based on the following:

hybridisation	no. of bonds	shape	bond angle	
sp ³	4 σ bond (4 regions of electron densities)	tetrahedral	109.5º	
sp ²	3σ bond, 1 π bond (3 regions of electron densities)	trigonal planar	120º	
sp	2 σ bond, 2 π bond (2 regions of electron densities)	linear	180º	

(ii) I need to know that a σ carbon-carbon bond in an organic molecule can be formed through the following orbitals overlap:

*sp*³- *sp*³, *sp*³- *sp*², *sp*³-*sp*, *sp*²-*sp*², *sp*²-*sp*, *sp*-*sp*

The greater the percentage of s-character in the hybrid orbital, the stronger the bond formed.

(iii) I need to know how to draw the following:



(v) I need to know that carbon-carbon bond in benzene has a bond order of 1.5.

6 Organic Reactions

LO (b) interpret, and use the following terminology associated with organic reactions:

- (iii) homolytic and heterolytic fission
- (ví) electrophile (Lewis acid), nucleophile (Lewis base)
- (vii) addition, substitution, elimination, condensation, hydrolysis
- (viii) oxidation and reduction

In organic chemistry, we are interested in the type of reactions that occur and how they occur.

6.1 Types of Reactions

(a) Addition reactions

Addition reactions occur when two starting materials add together to form only one product, *i.e.* "1+1 = 1".

<u>Electrophilic addition</u> to alkenes

$$\begin{array}{cccc} H & H & H & H \\ C = C & + & H - Br & \longrightarrow & H - C - C - H \\ H & H & & H & Br \end{array}$$

• *Nucleophilic addition* to aldehydes and ketones

$$\begin{array}{|c|c|c|c|} O & & & & \\ I & I & + & H - C \equiv N & \xrightarrow{\text{trace } CN^{\ominus}} & OH & \\ R & & & R & & \\ R & & & R & \\ \hline & & & & R & \\ R & & & & C & \\ \hline & & & & & C & \\ R & & & & C & \\ \hline & & & & & C & \\ R & & & & C & \\ \hline & & & & & C & \\ R & & & & & C & \\ \hline & & & & & C & \\ R & & & & & C & \\ \hline & & & & & C & \\ R & & & & & C & \\ \hline & & & & & C & \\ R & & & & & C & \\ \hline & & & & & C & \\ R & & & & & C & \\ \hline & & & & & C & \\ R & & & & & C & \\ \hline & & & & & C & \\ R & & & & & C & \\ \hline & & & & & C & \\ R & & & & & C & \\ \hline & & & & & C & \\ R & & & & & C & \\ \hline & & & & & C & \\ R & & & & & C & \\ \hline & & & & & C & \\ R & & & & & C & \\ \hline & & & & & C & \\ R & & & & & C & \\ \hline & & & & & C & \\ R & & & & & C & \\ \hline & & & & & C & \\ R & & & & C & \\ \hline & & & & & C & \\ R & & & & & C & \\ \hline & & & & & C & \\ R & & & & C & \\ \hline & & & & & C & \\ R & & & & & C & \\ \hline & & & & & C & \\ R & & & & & C & \\ \hline & & & & & C & \\ R & & & & & C & \\ \hline & & & & & C & \\ R & & & & & C & \\ \hline & & & & & C & \\ R & & & & & C & \\ \hline & & & & & C & \\ R & & & & & C & \\ \hline & & & & & C & \\ R & & & & & C & \\ \hline & & & & & C & \\ R & & & & & C & \\ \hline & & & & & C & \\ R & & & & & C & \\ \hline & & & & & C & \\ R & & & & & C & \\ \hline & & & & & C & \\ R & & & & & C & \\ \hline & & & & & C & \\ R & & & & & C & \\ \hline & & & & & C & \\ R & & & & & C & \\ \hline & & & & & C & \\ R & & & & & C & \\ \hline & & & & & C & \\ R & & & & & C & \\ \hline & & & & & C & \\ R & & & & & C & \\ R & & & & & C & \\ R & & & & & C & \\ R & & & & & C & \\ R & & & & & C & \\ R & & & & & C & \\ R & & & & & C & \\ R & & & & & C & \\ R & & & & & C & \\ R & & & & & C & \\ R & & & & & C & \\ R & & & & C & \\ R & & & & \\$$

(b) Substitution reactions

Substitution reactions occur when two starting materials exchange groups to form two new products, *i.e.* "1+1 = 1+1".

 $A-B + C-D \longrightarrow A-C + B-D$

• Electrophilic substitution of benzene



<u>Nucleophilic substitution</u> of halogenoalkanes

$$H_3C-I + H-OH \longrightarrow H_3C-OH + H-X$$

(c) Elimination reactions

Elimination reactions are the opposite of addition reactions. One starting material is converted into two products, *i.e.* "**1** = **1**+**1**".

A−B → A + B

• *Elimination* of halogenoalkanes



(d) Condensation reactions

Condensation reactions occur when two reactants are added together to form a single product with the elimination of a small molecule, *e.g.* H_2O , HCl, NH_3 , etc.

 $A - H + B - OH \longrightarrow A - B + H_2O$

• Esterification (a type of condensation reaction)



(e) Hydrolysis reactions

Hydrolysis reactions occur when a single reactant is split into two by the action of water.

 $A - B + H_2O \longrightarrow A - H + B - OH$

<u>Hydrolysis</u> of esters



(Note: Hydro- means water, -lysis means break up.)

(f) Oxidation reactions

Oxidation reactions occur when there is an increase in oxygen and/or decrease in hydrogen.

• <u>Oxidation</u> of aldehydes



(Note: [O] symbol is used to balance the equation.)

Reduction reactions (g)

Reduction reactions occur when there is a decrease in oxygen and/or increase in hydrogen.

Reduction of aldehydes



(Note: [H] symbol is used to balance the equation.)

Radical reactions (h)

Free-radical substitution of alkanes

$$H_3C-H + Cl-Cl \xrightarrow{uv \text{ light}} H_3C-Cl + H-Cl$$

6.2 **Reaction Mechanisms**

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

Reaction mechanisms provides a description of how a reaction occurs. It details what takes place at each stage of a chemical transformation - which bonds are broken/formed and the order in which they do so, as well as the relative rates of the different steps within the reaction (recall what you have learnt in the topic of Reaction Kinetics).

6.2.1 The Breaking and Forming of Bonds

All chemical reactions involve the bond breaking and bond formation. A covalent bond between two atoms can be broken essentially in the following ways:



In homolytic fission, each atom separates with one electron, leading to the formation of highly reactive entities called (free) radicals, owing their reactivity to their unpaired electron; this is referred to as homolytic fission or cleavage of the bond.

To show the movement of a single, unpaired electron, a half-arrow or fish hook is used.

 $R \xrightarrow{f} X \longrightarrow R \cdot + \cdot X$ The two-electron bond is split radical radical radical one electron moves to each of the atoms

Alternatively, one atom may hold on to <u>both electrons</u>, leaving none for the other, resulting in the formation of an <u>ion pair</u>, consisting of a negative and a positive ion; this is referred to as heterolytic fission or cleavage of the bond.

When R and X are not identical, the fission can take place in either of two ways, depending on whether R or X retains the electron pair.

To show the movement of a pair of electrons, a **<u>full arrow</u>** is used.

 $\begin{array}{cccc} R & & & & & \\ & & & & \\ & & & & \\ R & & & \\ & & & \\ R & & & \\ & & &$

Both electrons in the two-electron bond move to only one atom; lons contain an even number of electrons

Formation of a covalent bond can take place by the reversal of any of the bond breaking processes:

Homolytic bond formation

 $R \cdot + X \longrightarrow R-X$ radical radical

The arrows point to the middle of the bond that is formed

Heterolytic bond formation

 $R: + X^{+} \longrightarrow R-X$ anion cation $R^{+} + X^{-} \longrightarrow R-X$ cation anion

The arrow points directly to the cation

and also, by the attack of first-formed radicals or ions on other species:

 $R \cdot + W Br Br Br \longrightarrow R - Br + Br \cdot$ $R \cdot + H - OH \longrightarrow R - OH + H^+$

In general, regardless of whether we are looking at bond breaking or bond formation, movement of electrons (and hence direction of arrows) always occurs from electron <u>rich</u> regions to electron <u>poor</u> regions.

Reactions that involve symmetrical homolytic bond cleavage or formation are known as <u>radical</u> <u>reactions</u>. These reactions tend to occur in the **gas phase** and in solution in **non-polar** solvents, and are usually catalysed by light and by the addition of other radicals.

Reactions that involve asymmetrical heterolytic bond cleavage or formation are known as **polar (or ionic)** reactions. These reactions take place more readily in solution in **polar** solvents, because the greater ease of separation of charge therein, and very often because of the stabilisation of the resultant ion pairs through solvation (ion–dipole interactions).

6.2.2 Types of Reagents

In Polar Reactions

All polar reactions take place between an electron-poor site and an electron-rich site. Such reactions involve the donation of an electron pair from a nucleophile to an electrophile.



Electrophiles ('electron-loving') are electron-poor species that can form a covalent bond by accepting an electron pair from an electron-rich site. They are often positively charged (cations) although they can also be sites on neutral species carrying a **partial positive charge** (δ +).

For example, electron-rich (and hence nucleophilic) phenol can be attacked by electrophiles such as the positively charged nitronium cation, NO⁺₂, and the electron-deficient nitrogen atom of nitric acid (HNO₃) or dinitrogen pentoxide (N₂O₅):



The relative electrophilic strength (or electrophilicity) of a cation, or electrophilic site within a neutral molecule depends on the level of electron deficiency.

 An electrophile with a positive charge is always a more powerful electrophile than its conjugate base (which is neutral).

Electrophilic strength



 Carbon atoms are electrophilic when attached to electronegative atoms. The more electronegative the atom(s) bonded to carbon, the more electrophilic the carbon atom.

Electrophilic strength

 $\begin{array}{c} O^{\delta^{-}} \\ II \\ R \\ C^{\delta^{++}} \\ R \\ C^{\delta^{+}} \end{array} > \begin{array}{c} O^{\delta^{-}} \\ II \\ C^{\delta^{+}} \\ R \\ R \\ R \\ R \\ R \end{array} \qquad \begin{array}{c} \text{The (carbonyl) carbon atom of} \\ \text{the acyl (acid) chloride is more} \\ \text{electrophilic because both O and} \end{array}$ acyl chloride ketone Cl atoms are electronegative

Nucleophiles ('nucleus-loving') are <u>electron-rich</u> species that can form a covalent bond by <u>donating</u> an electron pair to an <u>electron-deficient</u> site. They are usually **negatively charged** (anions) or neutral molecules that contain a **lone pair of electrons**.

For example, anions such as OH^- and CN^- and the electron-rich nitrogen atom in ammonia or amines, H_3N : or R_3N : can act as nucleophiles to attack the electron-deficient (and hence electrophilic) carbon atom in chloromethane.

$$H_3 \overset{\delta^+}{\overset{}{\leftarrow} \overset{-}{\overset{}{\leftarrow} \overset{-}{\overset{}{\leftarrow} \overset{-}{\overset{}{\leftarrow} \overset{-}{\overset{}{\leftarrow} \overset{-}{\overset{}{\leftarrow} \overset{-}{\overset{}{\leftarrow} \overset{-}{\overset{}{\leftarrow} \overset{-}{\overset{-} \overset{-}{\overset{}{\leftarrow} \overset{-}{\overset{}{\leftarrow} \overset{-}{\overset{-}}{\overset{-} \overset{-}{\overset{}{\leftarrow} \overset{-}{\overset{-}}{\overset{-} \overset{-}{\overset{-}}{\overset{-} \overset{-}{\overset{-}}{\overset{-} \overset{-}{\overset{-}}{\overset{-} \overset{-}{\overset{-}}{\overset{-}}{\overset{-} \overset{-}{\overset{-}}{\overset{-}}{\overset{-} \overset{-}{\overset{-}}{\overset{-}}{\overset{-}}{\overset{-} \overset{-}{\overset{-}}{\overset{$$

The relative nucleophilic strength (or nucleophilicity) of an anion, or nucleophilic site within a neutral molecule depends on the **availability of the pair of electrons**.

• A nucleophile with a negative charge is always a **more powerful** nucleophile than its conjugate acid (which is neutral).

Nucleophilic strength $HO^- > H_2O^-$

• The nucleophilic strength of anions, within the same period of the periodic table, follows the same order as basicity: the more electronegative the atom bearing the negative charge, the tighter the electrons are held to the nucleus, the weaker the nucleophile, and the weaker the base.

Nucleophilic strength (or basicity)	R ₃ C	>	R_2N^-	>	RO	>	F
Electronegativity	С	<	Ν	<	0	<	F
Nucleophilic strength (or basicity)		I	₹— Ň Η₂	>	ҡ −ӧн	>	R−Ë

• The nucleophilic strength of anions and neutral atoms increases on going down a group of the periodic table. The electrons are held less tightly to the nucleus as the atom size increases, and hence they are more available for forming bonds.

Nucleophilic strength	H₂Ŝ	>	H₂Ö			
	Ι_	>	Br [_]	>	C <i>l</i> [−] >	F^{-}

This electrophile/nucleophile dichotomy can be looked upon as a special case of the **Lewis acidbase concept**. Electrophiles and nucleophiles in organic reactions can be looked upon essentially as electron pair acceptors (<u>Lewis acids</u>) and donors (<u>Lewis bases</u>), respectively, from and to other atoms – most frequently **carbon**.

It is possible for a species to be either a nucleophile or an electrophile, depending on the circumstances. For example, water can act as a nucleophile in one reaction, and as an electrophile in another:

 $\frac{H_{3}\overset{\circ}{C}\overset{\leftarrow}{\smile}\overset{\circ}{B}\overset{\circ}{r}}{H}\overset{\circ}{\to}\overset{\circ}{H}\overset{\circ}{\to}\overset{\circ}{H}\overset{\circ}{\to}\overset{\circ}{H}\overset{\circ}{\to}^{\bullet}$ water as an electrophile water as a nucleophile

In Radical Reactions

Reactions involving **radicals** as the reactive entities are also known. These are much less susceptible to variations in electron density in the substrate than reactions involving polar intermediates.

They are however greatly affected by the addition of small traces of substances that either produce or consume radicals.

Making Thinking Visible

Q: Hmm...can an electrophile react with any molecule that it encounters?

- A: No! Not necessary. The electrophile will attack a species that is electron rich enough for it to react. So, please do not have the idea that any electrophile can react with a given nucleophile, and vice versa!
- **Q:** So, can I say that if an electrophile reacts with a nucleophile, it is actually an acid-base reaction?
- A: Yes, from a Lewis acid-base perspective! BUT if you are asked to name the organic reaction, you still need to state it as an electrophilic addition, nucleophilic substitution, *etc*.
- **Q:** A nucleophile uses a pair of electrons, either a lone pair or a covalent bond, to react with an electrophile. Can we say that a dative covalent bond is formed after the reaction?
- A: No, you can't! This is because when you do an electron count after the bond has been formed between the electrophile and nucleophile, it doesn't have the dative covalent bond feature.

Important concepts to remember:

(i) I need to know how to identify and name a reaction as:

fre	e-radical	electrophilic	electrophilic	nucleophilic	nucleophilic
sul	bstitution	addition	substitution	substitution	addition
eli	mination	oxidation	reduction	hydrolysis	condensation

- (ii) I need to know that a free-radical has unpaired electron. And it can even attack an electronically neutral atom.
- (iii) I need to know that an electrophile is an electron poor species. It is also a Lewis acid (electron pair acceptor).
- (iv) I need to know that a nucleophile is an electron rich species. It is also a Lewis base (electron pair donor).
- (v) The higher the level of electron deficiency of an electrophile, the stronger the electrophile.
- (vi) The greater the availability of the lone pair of electrons of a nucleophile, the stronger the nucleophile.
- (vii) The reaction between a nucleophile and electrophile can be perceived as a Lewis acidbase reaction.

7 Isomerism

An **isomer** is one of several species (or molecular entities) that have the **same** atomic composition (**molecular formula**) but different line formulae or different stereochemical formulae (*i.e.* **different molecular structures**) and hence different physical and/or chemical properties.

Isomers are subdivided into two major types, namely, **constitutional (structural) isomers** and **stereoisomers**:



7.1 Constitutional (Structural) Isomerism

LO (a) describe constitutional (structural) isomerism(i) deduce the possible isomers for an organic molecule of known molecular formula

Constitutional isomers have the same molecular formula but different structural formula.

There are three types of constitutional isomers:

Functional groups.
 group isomers: *E.g.* butan-1-ol, CH₃(CH₂)₃OH, and diethyl ether, CH₃CH₂OCH₂CH₃

OH VS. O

Skeletal / Constitutional isomers that differ with respect to branching of the carbon chain isomers:
 skeleton, *i.e.* different chain length / skeleton (same functional group).
 E.g. octane and 2,5-dimethylhexane



Positional isomers that differ only with respect to the point of attachment of a substituent (on the same chain / skeleton).

E.g. 1-chloropropane (ClCH₂CH₂CH₃) and 2-chloropropane (CH₃CHClCH₃)

$$3 2 1 Cl$$
 vs. Cl
 $3 2 1$



Making Thinking Visible

- **Q:** When we are asked to draw the various constitutional isomers, must we really draw in the skeletal form?
- A: No! Not necessary. If the question did not request for skeletal formula, you can draw the full structural formula form. Importantly, show the bonding between the atoms correctly.

7.2 Stereoisomerism

Stereoisomers are isomers that have the **same molecular and structural formulae** but differ in their **spatial arrangement** (3-dimensional orientation) of the atoms.

7.2.1 cis-trans Isomerism

LO (b) describe *cis-trans* isomerism in alkenes, and explain its origin in terms of restricted rotation due to the presence of π bonds
 (i) deduce the possible isomers for an organic molecule of known molecular formula
 (j) identify chiral centres and/or *cis-trans* isomerism in a molecule of given structural formula

 Occurs when free rotation of certain parts of a molecule relative to the rest is restricted by the presence of <u>multiple bonds</u> or <u>a ring structure</u>.

In order to have *cis-trans* isomers:

- 1. There must be **restricted rotation about a bond**. (e.g. C=C double bond or ring) (**Note:** a double bond is rigid because of presence of the π bond which prevents rotation, as rotation can only take place if the π bond / p-p orbital overlap is broken)
- 2. At point of restricted rotation, the 2 groups attached to the same C are different.

In general, alkenes have two adjacent sp² hybridised carbons. These carbon atoms together with the four atoms to which they are attached are co-planar. Above and below the plane defined by these six atoms, there exists a region of electron density, the π bond, which arises from the sideway overlap of p orbitals on the adjacent alkene carbons.

We have seen this in ethene in Section 5.1:



In but-2-ene, $CH_3CH=CHCH_3$, the two methyl groups can lie either on the same side or on opposite sides of the double bond.





Compound **1** with the two methyl groups on the <u>same</u> side is <u>cis</u>-but-2-ene, while compound **2** with the two methyl groups on <u>opposite</u> side is <u>trans</u>-but-2-ene. They are called **cis-trans** isomers (an obsolete name still seen in some textbooks refer to them as geometric isomers).

Compounds **1** and **2** can be regarded as <u>non-interconvertible</u> as changing from one form to the other will involve **breaking the** π **bond** (~240 kJ mol⁻¹), rotation about the σ bond, followed by reforming the π bond:



For *cis*-but-2-ene (**1**) and *trans*-but-2-ene (**2**), the enthalpy of hydrogenation is -119.6 kJ mol⁻¹ and -115.5 kJ mol⁻¹, respectively (both give butane upon hydrogenation).



Since the *cis*-isomer **1** releases about 4 kJ mol^{-1} more energy on hydrogenation than does **2**, it follows that *cis*-isomer **1** is more unstable because the methyl groups are closer together, resulting in greater **steric strain**.

With larger substituents, differences greater than 4 kJ mol⁻¹ are encountered, with the *trans*-alkene being more stable than the corresponding *cis*-alkene.

- ((intersection)) - ((intersect

- **Q:** For the term "non-convertible", does it mean that the *cis*-isomer cannot be converted to the *trans*-isomer and vice versa?
- A: No! The interconversion can still take place BUT just not easy under normal conditions.
- Q: Is the term "steric strain" some kind of inter-electronic repulsion?
- A: Absolutely right, Eunioan! If the two groups are too close to one another, their electron cloud would repel each other.

The *cis* and *trans* nomenclature is unambiguous for **disubstituted** alkenes; however, the situation is not clear-cut for tri- and tetrasubstituted alkenes. With these latter compounds, problems arise in the definition of which substituent is *cis* or *trans* to which.

Making Thinking Visible

- Q: Hmm...the two groups of atoms that are bonded to a carbon atom of the C=C bond, must it be the same two groups that are bonded to the other carbon atom of the C=C bond?
- **A:** Nope! The following are two different stereoisomers.



However, the *cis*- and *trans*- descriptors are not applicable in this case. There is another way to label such *cis*-*trans* isomers, which is not required at H2 level. BUT you will still need to know how to draw them!

- **Q:** What are some examples of *cis-trans* isomerism in ring systems where rotation around a single bond is prevented by linkage in a ring?
- A:



cis-1,3-dimethylcyclobutane



trans-1,3-dimethylcyclobutane

Important concepts to remember:

- (i) I need to know to differentiate constitutional isomerism from stereoisomerism, that's all!
- (ii) I need to know the two criteria for cis-trans isomerism:
 - restricted rotation about the C=C bond; and
 - two different groups of atoms bonded to each of the carbon atoms of the C=C bond.
- (iii) I need to know how to draw a pair of cis-trans isomers. When drawing the cis-trans isomers, the carbon atoms of the C=C bond must be shown with the trigonal planar structure.

7.2.2 Enantiomerism

- LO (c) explain what is meant by a chiral centre
 - (d) deduce whether a given molecule is chiral based on the presence or absence of chiral centres and/or a plane of symmetry
 (e) recognise that an optically active sample rotates plane-polarised light and contains chiral molecules
 (f) recognise that enantiomers have identical physical properties except in the direction in which they rotate plane-polarised light
 (g) recognise that enantiomers have identical chemical properties except in their interactions with another chiral molecule
 (i) deduce the possible isomers for an organic molecule of known molecular formula
 (j) identify chiral centres and/or *cis-trans* isomerism in a molecule of given structural formula

A sp³ hybridised tetrahedral carbon atom that is attached to **four different entities** (atoms or groups) is known as an asymmetric carbon atom.

A molecule with an asymmetric carbon atom (denoted by an **asterisk** (*) on the C), as in the diagram below, **cannot be superimposed on its mirror image**.



This is the same property that a right hand, say, placed in front of a plane mirror possess.



Molecules such as the one shown above and our hands are said to be **chiral** (or handed), from the Greek word 'cheir' for hand.

Chirality then is the property of handedness. It is the geometric property of a rigid object (or spatial arrangement of points or atoms) of being **non-superimposable on its mirror image**. The adjective 'chiral' refers to the molecule as a whole, rather than to a particular atom.

Molecules such as CCl_4 , CH_2Cl_2 and $CHFCl_2$ that can be superimposed on their mirror images are said to be '**achiral**'.



A chair for example is also achiral as it can be superimposed on its mirror image.



An asymmetric carbon attached to four different substituents is said to be a chiral carbon or **chiral centre**, since the resulting molecule is chiral.

To represent three-dimensional molecules in two-dimension, the **wedge-and-dash notation** is used. In this notation, two bonds are drawn in the plane of the page (sticks: —), one bond is drawn coming toward you, out of the page (wedged: —), and one bond is drawn going away from you, behind the page (dashed: —). *E.g.* 2-bromobutane



A pair of molecules which are **mirror images** of each other and **non-superimposable**, such as molecules **1** and **2**, are **enantiomers**, from the Greek 'enantio' meaning opposite.

Enantiomers have **identical physical** (*e.g.* melting point, boiling point and solubility) **and chemical properties** under normal (achiral) conditions, with one exception – optical activity.

How to determine whether a molecule is chiral?

The ultimate way to test for molecular chirality is to construct models of the molecule and its mirror image and then determine whether they are superimposable. We can apply this test with actual models, or by attempting to superimpose them in our minds.

There are other aids, however, that will assist us in recognising chiral molecules.

We have seen one already: the presence of a *single chiral centre*.

However, when there are more than one chiral centre in a molecule, it may sometimes lead to an achiral molecule due to the presence of a plane of symmetry (see below). *E.g. meso*-tartaric acid



tartaric acid

Other aids are based on the absence of certain symmetry elements in the molecule.

A molecule will <u>not</u> be chiral if it possesses a **plane of symmetry**.

A plane of symmetry (also called a mirror plane) is defined as an imaginary plane that bisects a molecule in such a way that the two halves of the molecule are mirror image of each other.



However, the absence of a plane of symmetry does not necessarily guarantee that a molecule is chiral, although it is true in many cases.

Making Thinking Visible

- **Q:** Sir, what is the definition of a chiral carbon atom?
- A: A chiral carbon atom has four different groups of atoms bonded to it (Note: This is the definition of a chiral carbon atom).
- **Q:** So, in order to be a chiral atom, does it need to be sp³ hybridised?
- A: Yes! Because only a sp³ hybridised carbon atom can form four σ bonds. Hence, four groups of atoms bonded to it. Which means that if you have a sp² or sp hybridised atom, you can forget about looking for chirality.
- **Q:** So, the consequence of having a molecule with chiral atom is the molecule and its mirror image will be non-superimposable?
- A: Absolutely right!
- **Q:** But if a molecule has more than one chiral atom, the molecule MAY have a mirror image that is superimposable with it?
- A: Yes, you are right. A molecule with ONLY one chiral carbon guarantees a chiral molecule with non-superimposable mirror image. BUT if a molecule <u>has more than one chiral atom</u>, <u>resulting in an internal plane of symmetry within the molecule</u>, then this molecule and its mirror image are superimposable.
- **Q:** What is the definition of enantiomers?
- A: Enantiomers are <u>a pair of molecules that are mirror images of each other and and are</u> <u>non-superimposable</u>.



Optical Activity

Light may be regarded as a wave motion that contain oscillating perpendicular electric and magnetic fields, at right angles to the direction of propagation of the light wave:



In normal light, the electric and magnetic fields of light oscillate in all planes. Considering only the electric field components:



When a beam of normal light is passed through a device called a **polariser**, that in effect acts as a filter, only light waves that are oscillating in a single plane are allowed to pass through. The polariser thus serves to block the passage of light that is oscillating in all other planes. The light that emerges from the polariser is said to be **plane polarised**.

In 1815 the French physicist Biot made the important observation that when a beam of **plane polarised light** is passed through a solution of certain naturally occurring organic compounds, the plane of polarised light is rotated either to the left or to the right.

Molecules that are able to rotate the plane of polarisation of a beam of transmitted plane-polarised light is said to possess **optical activity** (or to be **optically active**).

An enantiomer causing rotation in a clockwise direction (when viewed in the direction facing the oncoming light beam) under specified conditions is called dextrorotatory and its chemical name or formula is designated by the prefix (+)-; one causing rotation in the opposite direction is laevorotatory and designated by the prefix (-)-.

An <u>equimolar</u> mixture of a pair of enantiomers, known as a <u>racemate or racemic mixture</u>, **does not** exhibit optical activity. The chemical name or formula of a racemate is distinguished from those of the enantiomers by the prefix (±).



Measurements of optical activity are carried out with a **polarimeter**, which is shown schematically in the figure below:



The direction and extent of the rotation, α , of the plane of polarised light is the basis of **specific rotation**, [α].

7.2.3 Biological Importance of Stereochemistry

LO (h) recognise that different stereoisomers exhibit different biological properties, for example in drug action

The origin of biological properties relating to chirality is often likened to the specificity of our hands for their respective gloves; the binding specificity for a chiral molecule (like a hand) at a chiral receptor site (a glove) is only favourable in one way.

If either the molecule or the biological receptor site had the wrong handedness, the natural physiological response (*e.g.* neural impulse, reaction catalysis) would not occur.

A diagram showing how only the (+)-isomer in a pair of enantiomers can interact in an optimal way with a hypothetical binding site (*e.g.* in an enzyme) is shown below.

Because of the chiral centre of the enantiomer, three-point binding can occur with proper alignment for only one of the two enantiomers.



binding site of the receptor



binding site of the receptor

Chiral molecules can show their handedness in many ways, including the way they affect human beings.

The (+)-enantiomeric form of a compound called limonene is primarily responsible for the odour of oranges and the other (–)-enantiomer for the odour of lemons.



The (+)-enantiomer of a compound called carvone is the essence of caraway, and the other is the essence of spearmint.

The activity of drugs containing chirality centres can similarly vary between enantiomers, sometimes with serious or even tragic consequences.

For several years before 1963 the drug thalidomide was used to alleviate the symptoms of morning sickness in pregnant women. In 1963 it was discovered that thalidomide was the cause of horrible birth defects in many children born subsequent to the use of the drug.



Even later, evidence began to appear indicating that whereas one of the thalidomide enantiomers (the right-handed molecule) has the intended effect of curing morning sickness, the other enantiomer, which was also present in the drug (in an equal amount), may be the cause of the birth defects.

The evidence regarding the effects of the two enantiomers is complicated by the fact that, under physiological conditions, the two enantiomers are interconverted.

Now, however, thalidomide is approved under highly strict regulations for treatment of some forms of cancer and a serious complication associated with leprosy. Its potential for use against other conditions including AIDS and rheumatoid arthritis is also under investigation.

7.2.4 Number of Stereoisomers

The maximum number of stereoisomers possible for a molecule with *n* chiral centres is given by 2ⁿ.

The actual number may be less since some of the isomers may possess internal symmetry elements.

E.g. consider tartaric acid, H = H = H, with two chiral centres. So there is a maximum of $HO_2C = CO_2H$

 $2^2 = 4$ stereoisomers.

There are two pairs of mirror images possible:



1 and 2 are a distinct pair of mirror images which are non-superimposable.

3 and **4**, although distinct from **1** and **2**, are however superimposable (due to the presence of an internal mirror plane). They are in fact the *same*!! This is the *meso* compound that we have seen earlier on page 41.

Hence there are only 3 distinct stereoisomers for tartaric acid.

The **maximum** number of stereoisomers possible for a molecule with *m* cis-trans double bond is also given by $2^{\underline{m}}$.

Again, the actual number may be less as some of the isomers are in fact the same compound due to the presence of internal symmetry elements.

In addition, it is not possible to have *cis-trans* isomerism for double bond in a small ring system.

E.g. for 1,2-dimethylcyclohexene, CH_3 , the two methyl groups can only assume a

cis-configuration, since it is geometrically not possible to bend the ring to be in a trans-configuration

For a molecule with *n* chiral centres and *m* cis-trans double bond, the maximum number of stereoisomers possible is given by 2^{n+m} .



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Important concepts to remember:

- (i) I need to know the definition of chirality:
 chiral carbon Four different groups bonded to the carbon atom.
 chiral molecule No internal plane of symmetry and rotate plane polarised light.
- (ii) I need to know how to identify whether a carbon atom is chiral or not.
- (iii) I need to know how to draw a pair of enantiomers using the wedge-and-dash notation.
- (iv) I need to know that a molecule containing only one chiral atom is non-superimposable with its mirror image. But if a molecule contains more than one chiral atom, the molecule may be achiral if there is a plane of symmetry within the molecule.
- (v) I need to know that a chiral molecule rotates plane polarised light. The mirror image of this molecule will rotate plane polarised light too, but in opposite direction with same magnitude of rotation.
- (vi) I need to know that chiral molecule and its mirror image have same physical properties except the rotation of plane polarised light.
- (vii) I need to know that chiral molecule and its mirror image have same chemical properties except when reacting with another chiral molecule.
- (viii)I need to know that a racemic mixture (or racemate) is optically inactive because it contains equimolar of the two enantiomers.
- (ix) I need to know how to count the number of stereoisomers that is possible with a given constitutional formula using the 2ⁿ rule, where n is the number of stereocenters (i.e. C=C double bond capable of cis-trans isomerism and number of chiral centers).

Answers to Self Check Questions:

1A: TFFTT FFTF

- 4A: (i) 4-bromo-3-methylbutanoic acid; (ii) 3-iodo-2,2-dimethylpropan-1-ol;
- (iii) 2-amino-2,3,3-trimethylbutanoic acid; (iv) 3-bromo-3-methylbutanal