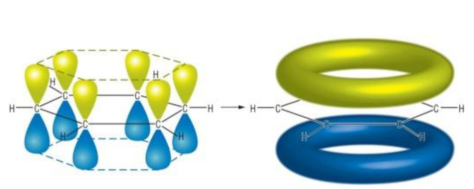
STANDARD ANSWERS AND DEFINITIONS

Evidence for Kekule's model to be wrong:

- All C-C bond lengths are the same length, between C-C and C=C.
- Only reacts with Br2 with a halogen carrier
- Benzene is lower in energy than Kekule's structure suggests its should be.

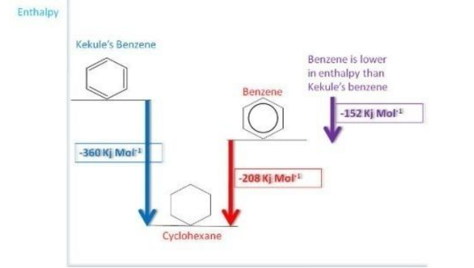
Discuss the structure and bonding in benzene / (comparing to kekule - structure):

<table>
<tr><td></td><td>

- **Label p orbitals and state that they overlap**
- **Label 'delocalised π orbitals'**
- **State the bond lengths are the same**
- **That it is a planar molecule**

</td></tr>
</table>

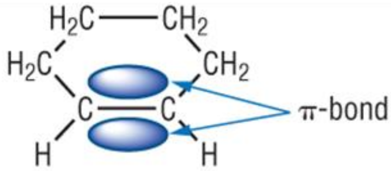
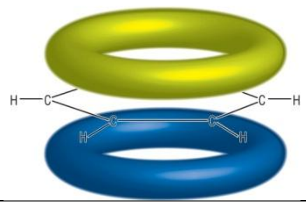
Discuss the relative low reactivity of benzene / (problems with Kekule – reactivity):

<table>
<tr><td>
</td><td>

- **Draw the enthalpy diagram**
- **This shows that benzene is not 3 c=c as it is lower in energy**
- **This means it is more stable**
- **Therefore is less reactive**

</td></tr>
</table>

Discuss the reactivity of benzene compared to alkenes

<table>
<tr><td>
</td><td></td></tr>
<tr><td>

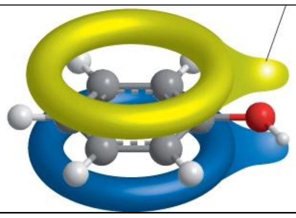
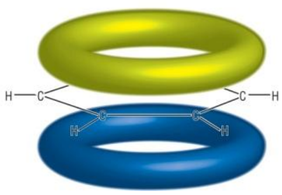
- Between the C-C: **2e** from a σ bond and **2e** from the **localised** π bond = **4e**
- Higher electron density
- Polarises electrophiles more.
- Alkenes do not need halogen carrier.
- Electrophilic addition reactions

</td><td>

- Between the C-C: **2e** from σ bond and **1e pre C-C** from delocalised π bond = **3e**
- Lower electron density
- Polarises electrophiles less.
- Benzene needs a halogen carrier.
- Electrophilic substitution reactions

</td></tr>
</table>

Discuss the reactivity of phenol compared to benzene

<table>
<tr><td></td><td></td></tr>
</table>

• Lone pair electrons on the O • Delocalise with the π electrons in the benzene ring • Makes it more electron rich • Ring becomes activated • Polarises electrophiles more. • Phenols do not need halogen carrier. • Are multiply substituted.	• Between the C-C: **2e** from σ bond and **1e** from **C-C** from delocalised π bond = **3e** • Lower electron density • Polarises electrophiles less. • Benzene needs a halogen carrier. • Only monosubstituted

Summary:

Benzene VS. Cyclohexene

Cyclohexene

- Electrophillic Addition
- Electrons are localised
- Between C-C 2e from σ bond and 2e from localised π bond = 4e
- Higher electron density, polarises electrophiles more
- Don't need a halogen carrier

Benzene

- Electrophillic Substitution
- Electrons are delocalised
- Between C-C 2e from σ bond and 1 e from the C-C from delocalised π bond = 3e
- Lower electron density, polarises electrons less
- Need a halogen carrier

Benzene VS. Phenol

Phenol- Multiple Substitution

- Lone pair of electrons on O
- Delocalise with the π electrons in the Benzene ring
- Makes more electron rich
- Ring becomes activated, polarises electrophiles more
- Phenols do not need a halogen carrier

Benzene- Mono-substitution

- Electrophillic Substitution
- Electrons are delocalised
- Between C-C 2e from σ bond and 1 e from pre C-C from delocalised π bond = 3e
- Lower electron density, polarises electrons less
- Need a halogen carrier

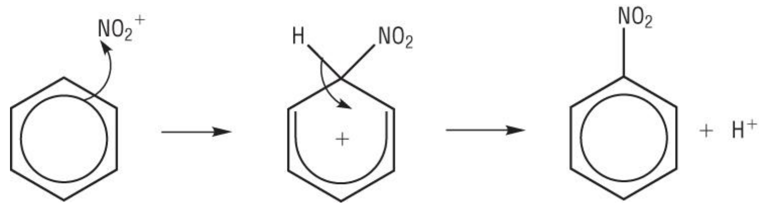
Nitration of benzene:

$$C_6H_6 + HNO_3 \xrightarrow[\text{Reflux } 50^{o}C]{\text{Conc } H_2SO_4} C_6H_5NO_2 + H_2O$$

Generation of the electrophile:

Conc HNO_3 + conc H_2SO_4 → NO_2^+ + HSO_4^- + H_2O

Nitryl ion is electrophile



Regeneration of the catalyst:

H^+ + HSO_4^- → H_2SO_4

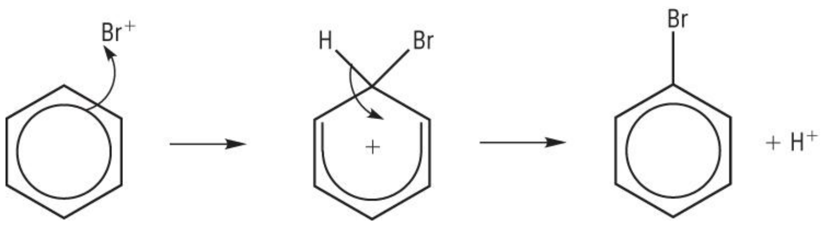
Halogenation of benzene:

$$C_6H_6 + Br_2 \xrightarrow{FeBr_3} C_6H_5Br + HBr$$

Generation of the electrophile:

$FeBr_3$ + Br_2 → Br^+ + $FeBr_4^-$

Bromonium ion is electrophile



Regeneration of the catalyst:

H^+ + $FeBr_4^-$ → $FeBr_3$ + HBr

Carbonyl Test

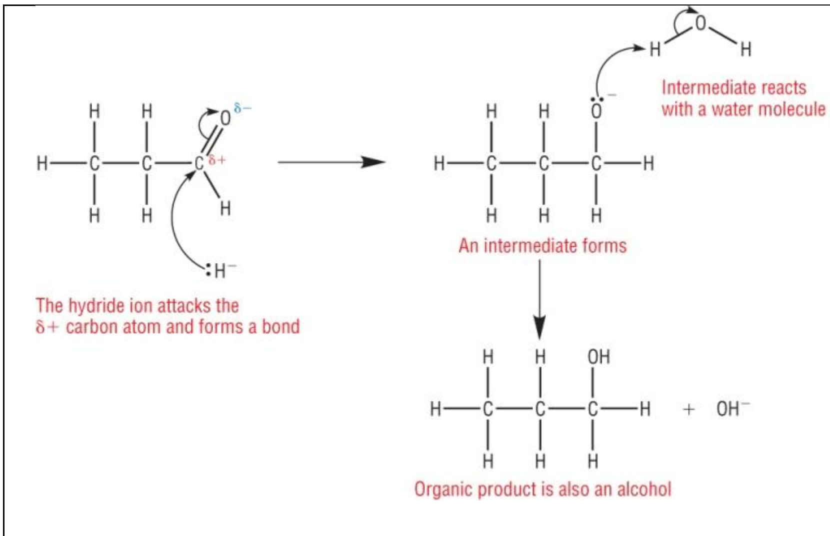
Test for Carbonyl Group

- 2,4,DNPH (Brady's Reagent)
- If present, orange precipitate formed
- FILTER, RECRYSTALISE, FILTER, MELTING POINT DETERMINATIO0N / COMPARE TO KNOW DATA

Test to distinguish between Aldehyde and Ketone

- Warm with Tollens Reagent (silver nitrate dissolved in ammonia)
- If aldehyde present, silver mirror forms as the aldehyde is oxidised
- If ketone present no change as ketone cannot be oxidised

Reduction of Aldehydes / ketonesMechanism of reducing an Aldehyde

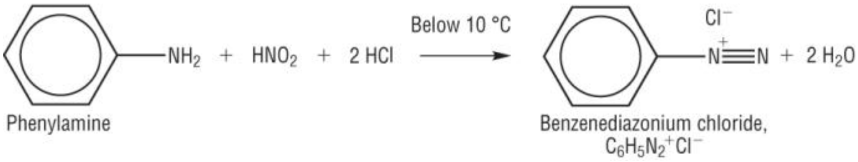


$NaBH_4$: Source of hydride ions, H^-

Azo Dyes

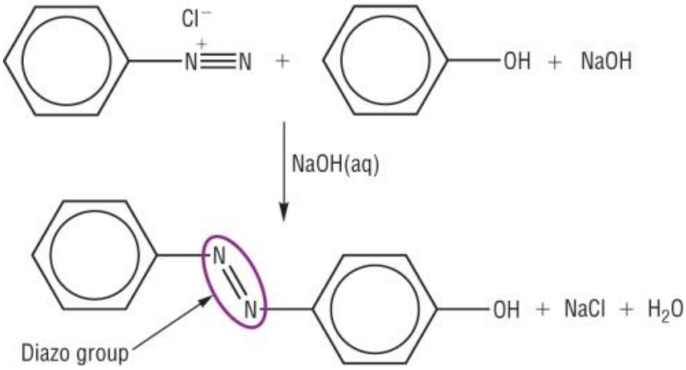
1) **Make Nitrous Acid**
   $NaNO_2 + HCl \rightarrow NaCl + HNO_2$ (below 10oC)

2) **Make Diazonium Salt**



- Below $10^{o}C$ because N_2 is unstable – decomposes releasing nitrogen gas
- Benzenediazonium salts are stabilized as the benzene ring allows the electrons from the diazonium functional group to be delocalised over the benzene ring

3) **Coupling**



- The Azo dye is now stable as there is extensive delocalisation over both arenas via the azo group, -N=N-
- This also gives rise to the colours

Amines

- A weak base because of lone pair of electrons on N accept protons
- proton acceptors
- lone pair electrons are donated forming a dative covalent bond

Inductive Effect

- **Alkyl groups**- positive inductive effect – stronger base
- The alkyl group gives a small push of electrons towards LP on the N
- This makes it form a dative covalent bond more readily
- **Ammonia -** no inductive effect as nothing attached to functional group
- **Benzene Ring** – Negative inductive effect
- Benzene ring has small pull of electrons away from Nitrogen atom
- The LP electrons are delocalised into the benzene ring
- Makes them less readily available to form a dative covalent bond
- Weaker base

Fatty acid - shorthand:

- Fatty acids can be written in shorthand:

Number of carbon atoms		Number of double bonds	Position of double bonds
18	:	1	(9)

Fatty Acid		Risk	Reason	Packing	State	Cause
Saturated		Heart disease	Raises blood cholesterol	Close	Solid	Blocks arteries
Unsaturated	Trans	Coronary heart disease	Raises blood cholesterol	Close	Solid	Blocks arteries
	Cis	No Health risk		Cannot pack close together	Liquid	No effect

Trans fats cholesterol:

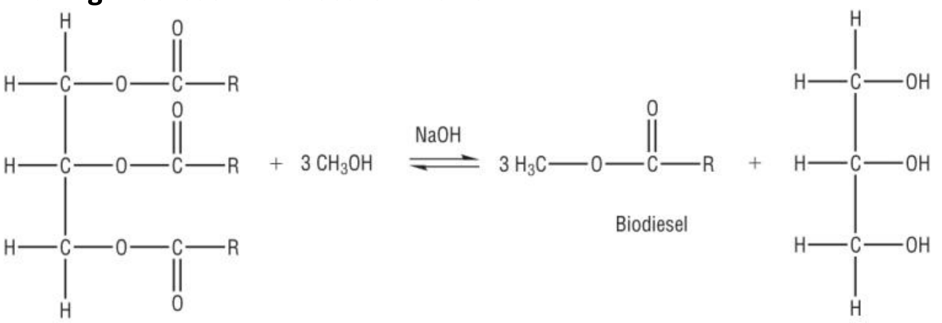
High Density Lipoproteins

- Carry cholesterol out of the blood and out of the body
- Good

Low Density Lipoproteins

- Carry about 65% of cholesterol around the body and deposit lipids onto artery walls
- This restricts blood flow
- Bad

Making Biodiesel - Transesterification:



- The waste oil is filtered then reacted with methanol and sodium hydroxide (catalyst) to form biodiesel.
- This also increases the atom economy of fats.

Preparation of Alphatic Amines

- Warm halogenoalkens with excess ammonia
- $CH_3CH_2Cl + NH_3 \rightarrow CH_3CH_2NH_2 + HCl$
- $NH_3 + HCl \rightarrow NH_4Cl$

Preparation of Primary/Secondary aliphatic amines

- $CH_3CH_2NH_2 + CH_3CH_2Cl \rightarrow (CH_3CH_2)_2NH$
- $(CH_3CH_2)_2NH + CH_3CH_2Cl \rightarrow (CH_3CH_2)_3N$

Isoelectric Point

- Usually PH6 as COOH is slightly more acidic that NH2 is basic
- Depends on side groups, hence the different points

Acid Hydrolysis

- Heat under reflux with 6mHCl for 24 hours
- Always gives COOH and NH_3^+

Alkali Hydrolysis

- Solution of NaOH, reflux
- Always gives COO^-Na^+ and NH_2

Hydrolysis of Polyesters/Polyamides

- Hot aq Acid/ aq Alkali
- As above for acid / alkali hydrolysis products

Photodegradable polymers

- Blended with light sensitive catalysts so become weak, brittle when exposed to light
- Can also have C=O which absorb UV light and break
- Photodegradable plastics break to form shorter waxy hydrocarbon molecules before bacteria breaks them further into CO_2 and H_2O

Chromatography

Stationary phase

- is in a fixed place (paper in paper chromatography)
- molecules interact with stationary phase slowing down their movement – **ADSORPTION**

Mobile phase

- moved in a definite direction (water rises up in paper chromatography)
- molecules interact with mobile phase speeding up their movement – **SOLUBILITY**

Thin Layer Chromatography – TLC

- Is used to check purity / separate amino acids/ monitor the extent of a reaction.
- Solid stationary phase- Silica Gel
- Liquid mobile phase- Solvent

Producing the chromatogram in TLC:

- Dissolve sample.
- Draw a pencil line and spot sample using a capillary tube, allow to dry.
- Place plate in a tank of solvent - solvent must be below line, seal the tank.
- Separation is by **adsorption** - allow solvent to almost reach the top, draw a line here - solvent front.

- Each separated component is a spot, if colourless use ninhydrin and a UV lamp

Limitations of TLC

- Similar compounds often have too similar R_f values.
- Unknown compounds have no R_f value for comparison.
- It is hard to find a solvent that will have the correct amount of solubility - Goldilocks!!

$$R_f = \frac{\textbf{Distance moved by component}}{\textbf{Distance moved by solvent front}}$$

Gas Chromatography - GC

- Is used to separate volatile compounds (gases) in a mixture with low boiling points

The stationary phase:

- Depends what is separated whether you use a liquid or solid lining of the chromatography column
- e.g liquid long chain alkane (high boiling point)
- e.g solid silicone polymer

The mobile phase:

- Inert carrier gas e.g helium or nitrogen.

Separation

- Different components slowed by different amounts- separation – **retention times**
- Each component leaves the column at a different time and is detected as it leaves the column.
- Each peak represents a component
- Area under each peak is proportional to the abundance of each component

Limitations of gas chromatography:

- Similar retention times + peak shapes most compounds cannot be positively identified.
- Not all substances can be separated.
- Unknown compounds have no reference retention times.

Due to the limitations, gas chromatography is usually used in conjunction with spectroscopy.

Uses for GC-MS

1) Forensics - scenes of crime

2) Environmental analysis - air pollutants, waste water, pesticides in food.

3) Airport security - explosives in luggage / airport security

4) Space probes - planetary atmospheres

Chiral Compound

- Optical isomers are one type of Stereo isomers (cis / trans is the other).
- They are non-superimposable
- Chiral carbon has 4 different groups attached
- Always draw in 3D

Properties of optical isomers:

- They rotate plane polarised light.
- One isomer rotates it in one direction and the other in the opposite direction

Problems with Chiral drugs

- One optical isomer may have serious side effects
- Expensive/ difficult to separate isomers
- One optical isomer may have serious side effects
- Reduces the effectiveness
- Dose size

Overcoming Chiral drug synthesis problems

- Use and enzyme catalyst
- Chiral Synthesis
- Chiral Catalyst
- Chiral Pool Synthesis

1) Using enzymes as biological catalysts:

- Nature is steroespecific, if this can be used only one isomer will be produced.
- If a biocatalyst is used it will only catalyse the production of one isomer.

2) Chiral pool synthesis:

- This starts the synthesis pathway with a stereospecific enantiomer
- All of the following synthesis steps should lead to a pure optical isomeric drug

3) Use of transition metal complexes:

- Some act as catalysts that will produce only one optical isomer

Cause of Stereo Isomerism

a) Optical isomerism

- C with 4 different groups attatched
- Mirror images of each other

b) Cis trans isomerism

- C=C has restricted rotation
- Both C in C=C attached to two different groups

NMR:

Interpretation: always gives you 2 pieces of information

1) splitting pattern – number of adjacent H's

2) Chemical shift – adjacent functional groups

- If the numbers of H's are given above the peak, make sure you use these too

D_2O

- D replaces H in OH and NH protons
- Peak for OH / NH protons disappears
- This is due to D having 2 nucleons – no signal

TMS

- Reference Signal at 0

DEFINITIONS

Retention time- Is the time taken for a component to pass from inlet to detector.

Alpha Amino Acid-NH2 and COOH joined at the same C

Stereoisomers-Same structural formula different spatial arrangement of atoms

Amphoteric- Amino acids will react with both acids due to NH2 and alkalis due to COOH

Optical isomers- Mirror images **cannot** be superimposed upon each other

Achiral compounds- do not have 4 different groups around a carbon atom

Chiral compounds- have 4 different groups around a carbon atom

Enantiomers- the two different optical isomers

Racemic mixture - An equal mixture of the 2 isomers will not rotate plane polarised light as each isomer cancels the other out.

Stereospecific - Optical activity is important in biological systems as only one of the isomers will interact with enzymes.

Delocalised electrons – are shared between more than 2 atoms

Addition reaction – where a reactant is added to an unsaturated molecule

Substitution reaction – where an atom or group of atoms is replaced with a different atom/group of atoms

Electrophile – is an atom/group of atoms that is attracted to an electron rich centre where it accepts a pair of electrons to form a dative covalent bond

Substitution – is where one group is replaced by another group

Curly arrow – used in mechanisms to show the movement of an electron pair / forming, breaking bonds.