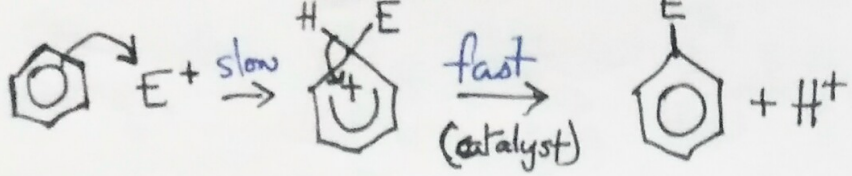
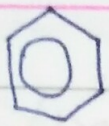
Mechanism: 

Benzene Overview 

* Electrophilic Substitution ~~only~~.

(1) Halogenation. (Cl_2 or Br_2)

Reagent: Cl_2 (or Br_2) in CCl_4

Conditions: • halogen carrier (Fe / $FeCl_3$ / $FeBr_3$ / $AlCl_3$) → all anhydrous (Catalyst) • room temperature

Observation: steamy white fumes (HCl / HBr)

$E = Cl^+$ or Br^+

(2) Nitration

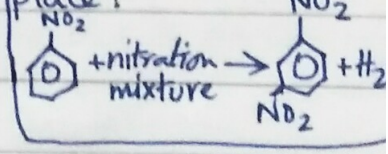
Reagent: conc. HNO_3 + conc. H_2SO_4 (catalyst) (nitration mixture)

condition: reflux at 50-60°C

observation: Yellow oil is formed (nitrobenzene)

$E = NO_2^+$

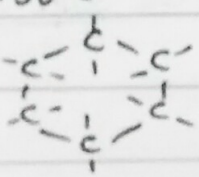
at temp >60°C → further substitution take place:



(3) Hydrogenation.

reagent: H_2 gas

conditions: • finely divided nickel (catalyst)
• 150°C • 20-200 atm

product: 

$C_6H_6 + 3H_2 \rightarrow C_6H_{12}$

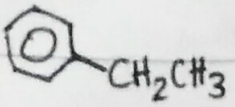
(4) Alkylation.

reagents: halogenoalkane (RX) and $AlCl_3$ anhydrous (HCl sometimes)

Catalyst: $RCl + AlCl_3 \rightleftharpoons AlCl_4^- + R^+$

$E = R^+$ (eg: $CH_3CH_2^+$)

equation: $C_6H_6 + C_2H_5Cl \rightarrow C_6H_5C_2H_5 + HCl$



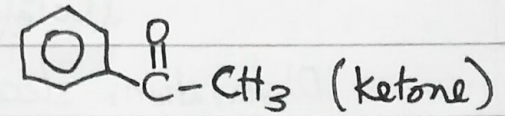
⑤ Acylation

reagents: acylchloride ($RCOCl$) and anhydrous $AlCl_3$

conditions: • reflux at 50°c
• dry inert solvent (ether)

$E = R\overset{+}{C}=O$ (eg: $CH_3\overset{+}{C}=O$)

equation: $C_6H_6 + CH_3COCl \rightarrow C_6H_5COCH_3 + HCl$



(ketone)

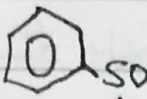
⑥ Sulfonation.

a) heat benzene under reflux with conc. H_2SO_4 for several hours

b) warm benzene under reflux with fuming sulphuric acid ($H_2S_2O_7$) for 20-30 mins

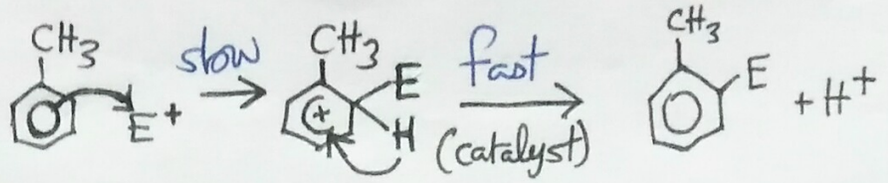
sulfur trioxide + conc. $H_2SO_4 \Rightarrow H_2S_2O_7$

$E = SO_3H^+$

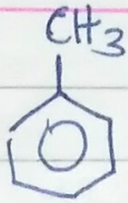
equation: $C_6H_6 + H_2SO_4 \rightarrow$ 

$+ H_2O$

benzene sulfonic acid.

Mechanism: 

Methylbenzene



→ alkyl side chain - undergoes free radical substitution.

→ aromatic ring - undergoes electrophilic substitution.

Note: electrophilic substitution
- quicker with methylbenzene
- because the methyl group donates electrons into the benzene ring making it more susceptible

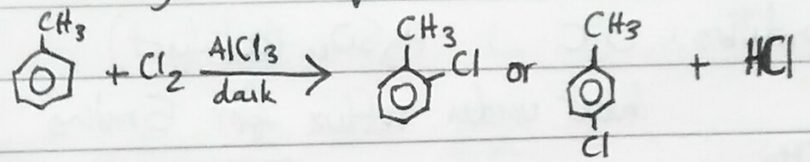
* Electrophilic Substitution & Free Radical

① Halogenation

reagent: Cl_2 in CCl_4

conditions: • halogen carrier as catalyst
• room temperature • dark

observation: steamy white fumes.

equation: 

② Nitration.

reagent: conc. HNO_3 + conc. H_2SO_4 (catalyst)

conditions: 30°C → lower temperature due to electron donating effect of methyl group making benzene more reactive.

observation: yellow oil (~~ii~~) formed.

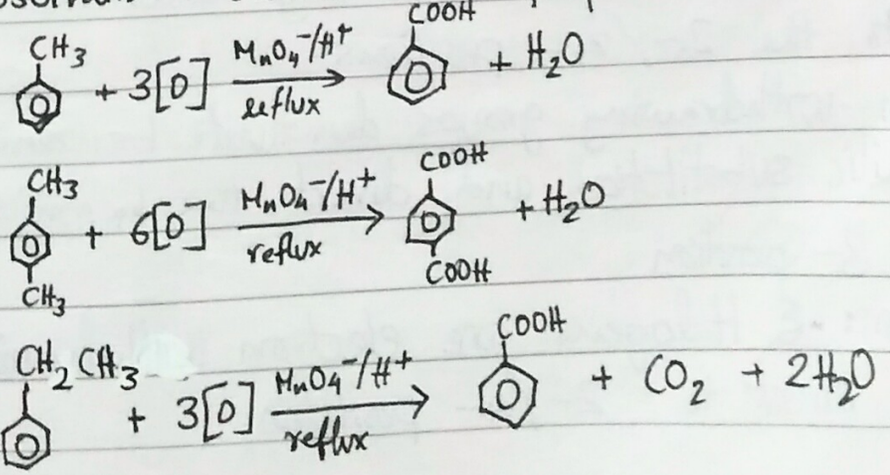
③ Hydrogenation → no change from benzene.

④ Oxidation.

reagent: $KMnO_4/H^+(aq)$

condition: reflux

observation: decolourisation: purple → colourless



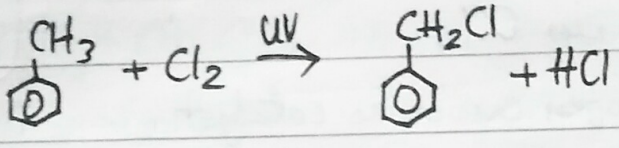
⑤ Halogenation of Alkanes

reagent: Cl_2 in CCl_4

condition: presence of UV light

product: mono-, di-, tri- substituted products.

observation: steamy white fumes.

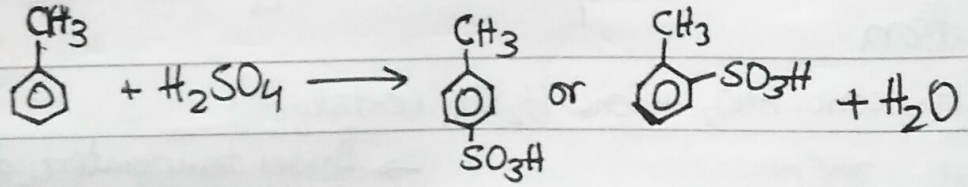
equation: 

⑥ Sulfonation.

reagent: fuming sulfuric acid ($H_2S_2O_7$)

condition: 0°C ; H_2SO_4 (catalyst)

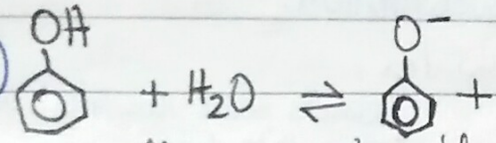
heat under reflux for 5mins



- Only about 5-10% are the 4-isomer. As the temperature increases proportions of the 4-isomer increases and the 2-isomer decreases.

* Electron-donating groups activate benzene for electrophilic substitution and usually direct the incoming group to the 2-/4- positions.
* Electron-withdrawing groups deactivate benzene for electriphilic substitution and direct the incoming group to the 3- position.
* Exception: Halogens are electron withdrawing but direct to 2-/4- positions.

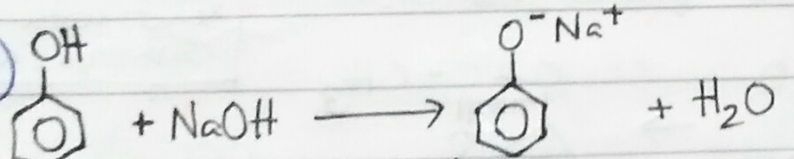
Phenols

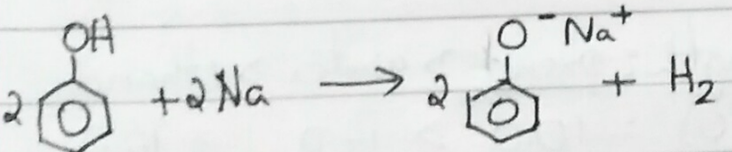
① 
(weak acid) phenoxide ion.

The -ve charge of the phenoxide ion is spread over the whole ion as ~~the~~ one of the lone pairs on the oxygen overlaps with the delocalised π bonding system in the benzene ring.

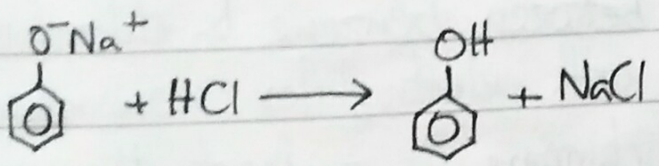
This reduces the charge density of -ve charge compared to OH^- or $C_2H_5O^-$ and so the H^+ ions are not very strongly attracted to the phenoxide ion.

Phenol ionises to form a more stable negative ion, so the ionisation of phenol is more likely. Position of equilibrium on right.

② 
sodium phenoxide



- Observation: gas evolved; more vigorous than with ethanol.

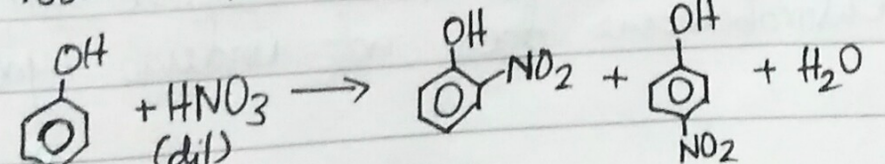


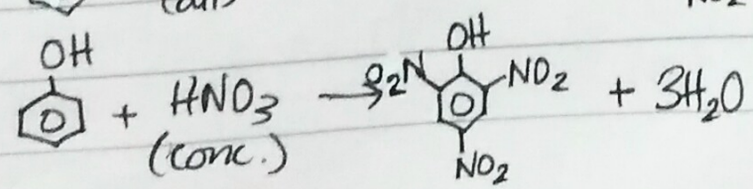
- Phenol is recovered from sodium phenoxide.

③ Nitration. - Electrophilic substitution.

Reagent: ~~dil~~ HNO_3 (H_2SO_4 is not required)

Condition: room temperature.

equation: 



④ Halogenation - Electrophilic substitution.

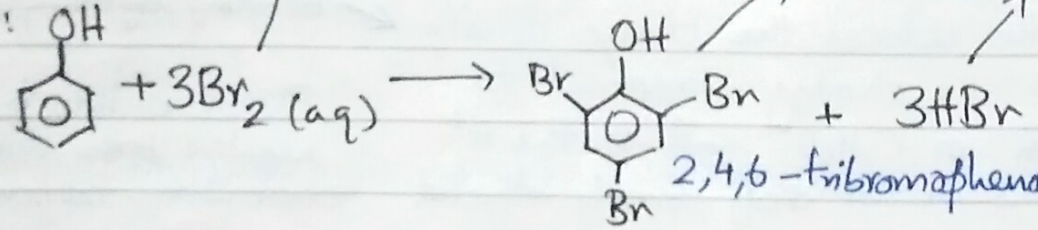
Reagent: Br_2 (aq) ← Bromine water.

Conditions: room temperature.

- reacts more readily with phenol than with benzene so no halogen carrier

Observation: reddish brown solution decolourises; white ppt; steamy fumes

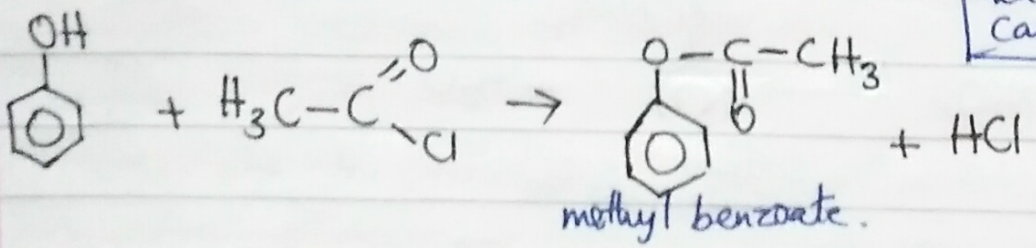
Equation:



2,4,6-tribromophenol.

⑤ Acid chloride and phenol reaction.

Note: phenol doesn't react with carboxylic acids



methyl benzoate.

* Order of acid strength: phenol > water > ethanol.

pKa (25°C) : 10.0 14.0 16.0

* Difference in reactivity between benzene & chlorobenzene:
  - Chlorobenzene reacts with electrophiles more slowly than benzene as chlorine is a deactivating group
  - Chlorine is more electronegative than carbon so it draws the electrons in the ring towards itself making the ring less attractive for electrophiles.
  - Chlorobenzene does not undergo hydrolysis

Acyl Chlorides (-yl) $R-C(=O^{\delta-})-Cl^{\delta-}$ (C: $\delta+$)

- relatively large +ve partial charge on carbon → highly attractive to nucleophile.

① Formation from carboxylic acids.

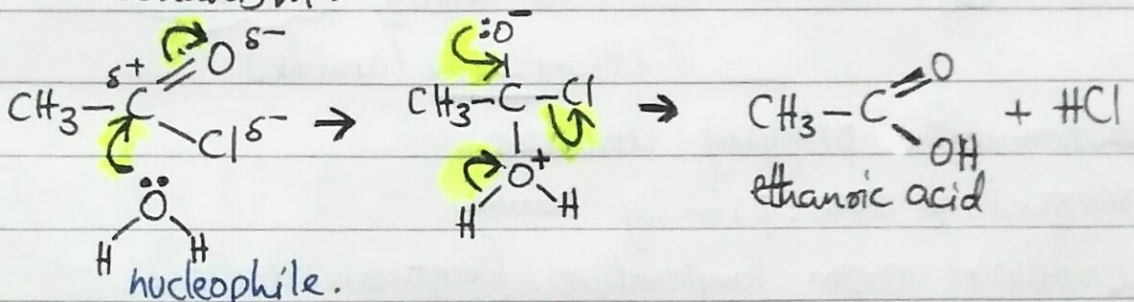
$$CH_3COOH + PCl_5 \rightarrow CH_3COCl + POCl_3 + HCl$$

$$CH_3COOH + SOCl_2 \rightarrow CH_3COCl + SO_2 + HCl$$

$$CH_3COOH + PCl_3 \xrightarrow{heat} CH_3COCl + H_3PO_4$$

② Hydrolysis (addition-elimination reaction) condensation.

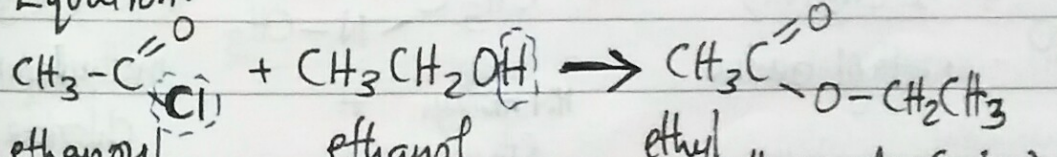
- very fast and vigorous
- mechanism:



③ Reaction with alcohol.

Condition: room temperature. (vigorous reaction)

Equation:

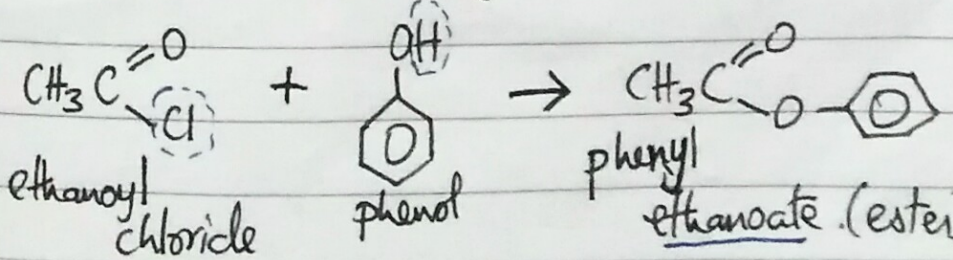


$+ HCl$

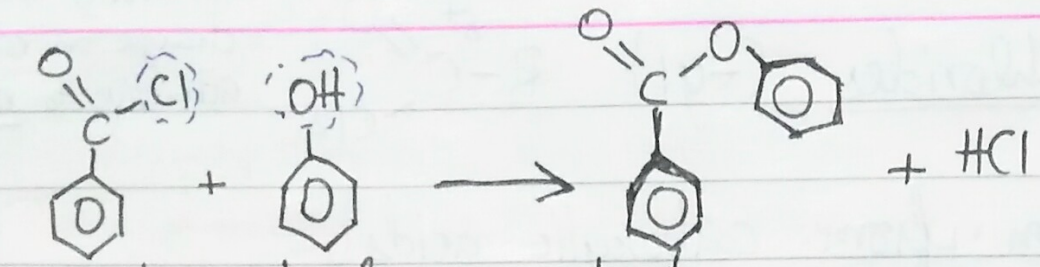
Note: no equilibrium though an ester forms

④ Reaction with phenol.

Condition: warming.



$+ HCl$

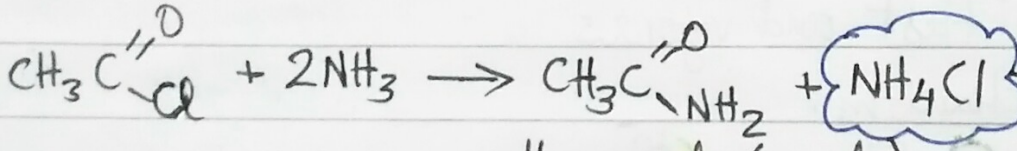


benzoyl chloride + phenol → phenyl benzoate (ester) + HCl

⑤ Reaction with ammonia.

reagent: conc. ammonia.

condition: room temperature (violent reaction; produces lots of white smoke)



$CH_3COCl + 2NH_3 \rightarrow CH_3CONH_2 + NH_4Cl$

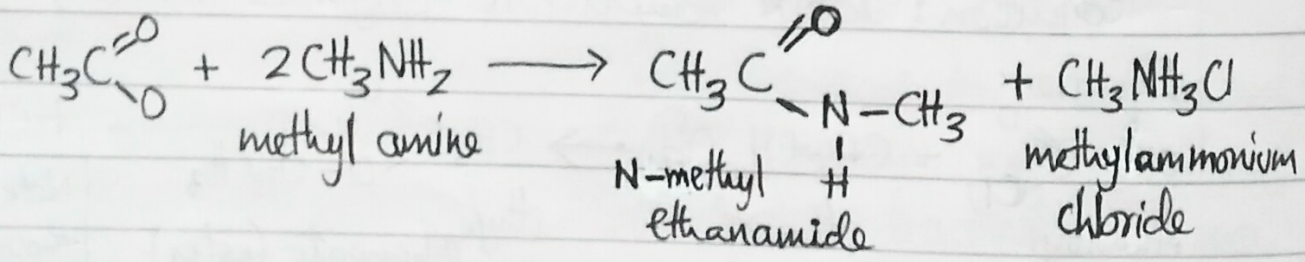
ethanamide (amide)

⑥ Reaction with primary amines

reagent: conc. primary amine

condition: room temperature. (vigorous reaction)

product: N-substituted amide



$CH_3COOH + 2CH_3NH_2 \rightarrow CH_3CONHCH_3 + CH_3NH_3Cl$

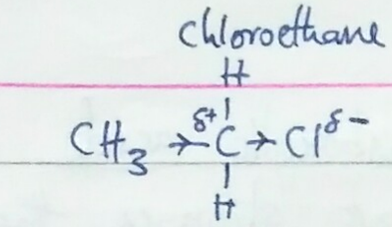
methyl amine

N-methyl ethanamide

methylammonium chloride

Alkyl Chlorides

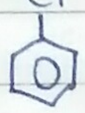
chloroethane



- δ^+ on C is smaller than δ^+ of C in COCl.
- less susceptible to nucleophilic attacks than acyl chlorids.

Hydrolysis with water alone is very slow unless under ~~#~~ added $NaOH_{(aq)}$ and heat.

Aryl Chloride



chlorobenzene. Does not undergo hydrolysis

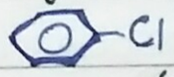
Relative ease of hydrolysis

* acyl chloride > alkyl chloride > aryl chloride.

reacts vigorously

R-Cl

reacts very slowly



no reaction.

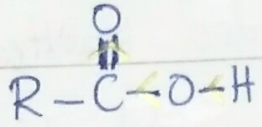
* This can be found by warming each chloride with NaOH then with excess $HNO_{3(aq)}$ and $AgNO_3$. Formation of a white ppt is a +ve observation.

→ Ethanoyl chloride gives immediate ppt – more vigorous reation than with water

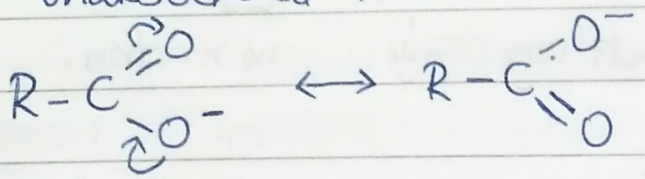
→ Chloroethane gives ppt after some time

Acidity of carboxylic acids

* Weak acids but stronger than alcohol & phenol.
* The OH bond in the acid is weakened by the C=O group



* Carboxylate ion is stabilised by the delocalisation of electrons around the $-COO^-$ group. This spreads out the negative charge making the COO^- less likely to bond with an H^+ ion. to reform the undissociated molecule.



* The strength of a carboxylic acid is affected by the nature of the substituent group which can be either electron-donating or electron-withdrawing.

* **Electron-withdrawing group increases the acid strength of carboxylic acids**

- The electron withdrawing reduces the negative charge gathered on the O atom, thus stabilising the COO^- ion and weakening the $-OH$ bond.
- This improves the readiness of the acid to dissociate.
- Acidity:

$$Cl_3C-COOH > Cl_2CH-COOH > ClCH_2COOH$$

* **Electron-donating groups decrease the acid strength of carboxylic acids**
  - It intensifies the -ve charge on the O atom making the COO^- ion less stable.
  - COO^- ion prefers to associate back with the H^+ ion to form undissociated carboxylic acid molecules.
  - Acidity:

$$H-COOH > CH_3-COOH > CH_3CH_2COOH$$

* **Acidity increases with electronegativity of halogen.**
  - Electronegativity: F > Cl > Br > I
  - Acidity.

$$FCH_2-COOH > ClCH_2-COOH > BrCH_2-COOH > ICH_2-COOH$$

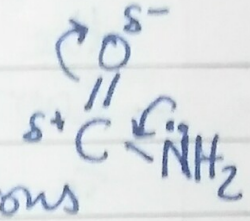
* The distance of the substituent group from the carboxyl group increases, acidity decreases
  - Acidity:

$$ClCH_2COOH > ClCH_2CH_2CH_2COOH$$

* The same applies to aromatic acids also. Electron-withdrawing groups ↑ increase the acidity of the aromatic acids.

Amides $-C(=O)-NH_2$

* Can form hydrogen bonds
  - high melting points
  - soluble in water.
- Solution of amide - neutral.
  - carbonyl group withdraws eletrons from N.



- Formation:
  acyl chloride + NH_3/amine
- Acid hydrolysis
  reagent: HCl (dil.)
  condition: heat
  product: carboxylic acid + ammonium salt.

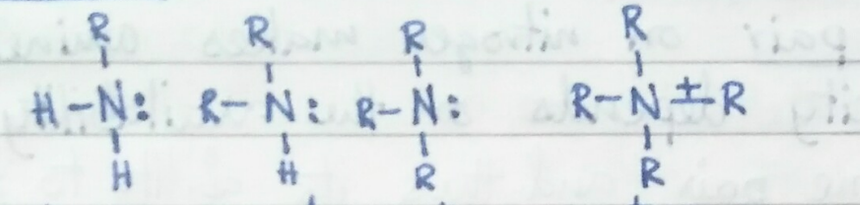
$$CH_3C(=O)NH_2 + H_2O + HCl \xrightarrow{heat} CH_3C(=O)OH + NH_4^+Cl^-$$

- Alkaline hydrolysis.
  reagent: NaOH(aq)
  conditions: heat
  product: sodium salt of carboxylic acid + ammonia.

$$CH_3C(=O)NH_2 + NaOH \xrightarrow{heat} CH_3C(=O)O^-Na^+ + NH_3$$

$$CH_3C(=O)O^-Na^+ + HCl \rightarrow CH_3C(=O)OH + NaCl$$

Amines



primary amines | secondary amines | tertiary amines | quaternary ammonium salts

* Ethylamine formation.

① Reduction of nitrile

Reagent: $LiAlH_4$ in dry ether

or pass H_2 over Ni at 140°C

or sodium + ethanol.

$$CH_3CN + 4[H] \longrightarrow CH_3CH_2NH_2$$

② Substitution of bromoethane with ammonia.

reagent: excess $NH_{3(aq)}$ + alcohol reflux with pressure

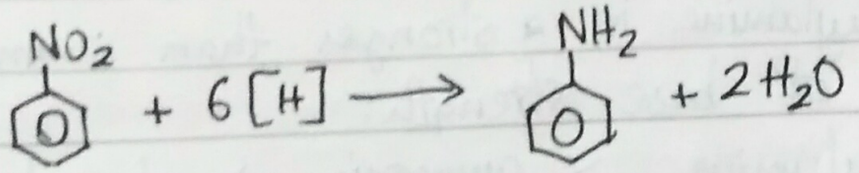
or conc. NH_3, heat and pressure.

$$CH_3CH_2Br + 2NH_3 \longrightarrow C_2H_5NH_3 + NH_4Br$$

NH_3 in excess so that the bromoethane molecule has more chance hitting an ammonia than hitting an amine. This will reduce the formation of secondary amines

* Phenylamine formation

reagent: tin + conc. HCl + reflux.

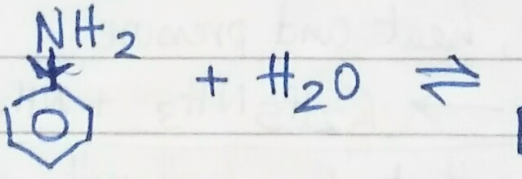


$LiAlH_4$ can also be used as reducing agent in laboratory.

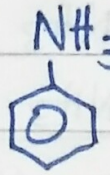
Basicity of Amines

* The lone pair on nitrogen makes amines basic
* Their basicity depends on the availability of their lone pair and thus its ability to pick up protons.
* The greater the electron density on N, the better it is as a base.
* Strength of amines depend on: availability of the lone pair on N and the stability of its conjugate acid.
* Electron withdrawing substituents lower the electron density on N and decrease the basicity of the amine.

$$NH_3 + H_2O \rightleftharpoons NH_4^+ + OH^-$$



$$+ H_2O \rightleftharpoons$$



$$+ OH^-$$

∴ Phenylamine is weaker than ammonia.

* Electron donating substituents increase the electron density on N and increase the basicity of the amine

$$CH_3CH_2 \rightarrow NH_2 + H_2O \rightleftharpoons CH_3CH_2NH_3^+ + OH^-$$

∴ Ethylamine is stronger than ammonia.

* Order of base strength:

ethylamine > ammonia > phenyl amine.

Amines Reactions

① **Amines in water.**

$CH_3CH_2NH_2 + H_2O \rightleftharpoons CH_3CH_2NH_3^+ + OH^-$

ethylamine — ethylammonium ion.

② **Amines dissolve in acids forming salts**

$CH_3CH_2NH_2 + HCl \longrightarrow CH_3CH_2NH_3^+Cl^-$

ethylammonium chloride

③ **To liberate amines, add alkali**

$CH_3CH_2NH_3^+ + OH^- \longrightarrow CH_3CH_2NH_2 + H_2O$

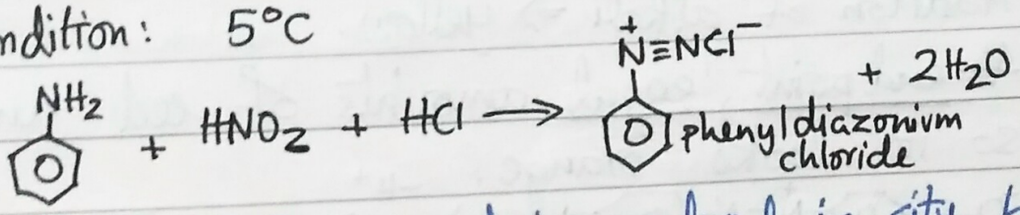
ethylammonium ion. — ethylamine

Phenylamine Reactions

① **Formation of Diazonium Salt (Diazotisation)**

reagent: HNO_2 in situ ($NaNO_2 + HCl$)

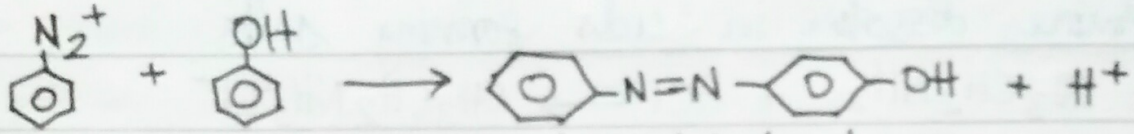
condition: 5°C



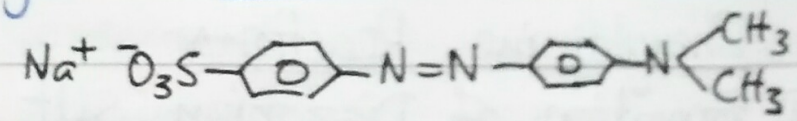
- HNO_2 is unstable and is produced in situ by reaction of $NaNO_2$ and dil. HCl
- the diazonium ~~ion~~ salt is unstable and will decompose readily at higher temperatures giving off N_2 gas. So the reaction mixture must be kept below 10°C
- At low temperatures, the delocalisation of the diazonium ion π bond electron over a benzene ring stabilises phenyldiazonium.

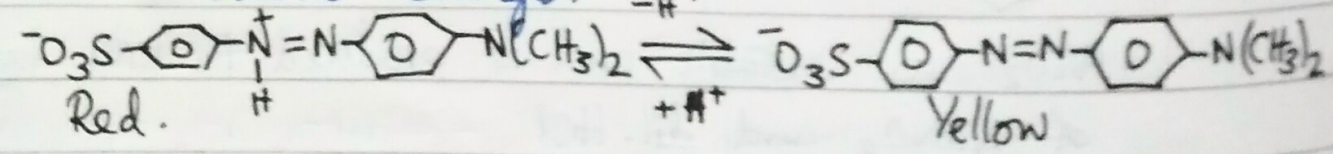
Coupling Reaction

* The phenyldiazonium ion behaves as an <u>electrophile</u> and will attack phenol or aromatic amines in alkaline conditions.

* 

4-hydroxyphenylazobenzene

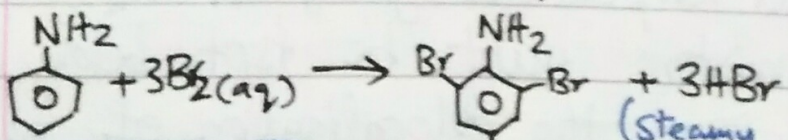
* $-N=N-$ azo group
* The extensive delocalisation of the electrons via the N=N double bonds makes the compound stable.
* The <u>orange</u> azodye is <u>stable</u> and <u>does not fade</u>
* <u>Methyl Orange</u> 

  - Addition of acid ⇒ red
    Addition of alkali ⇒ yellow.
    At <u>end point</u>, <u>equal</u> amounts of red and yellow so it looks orange.
  - 

Red. Yellow

(2) Phenylamine with $Br_{2(aq)}$

Condition : room temperature.



reddish brown bromine solution decolourises.

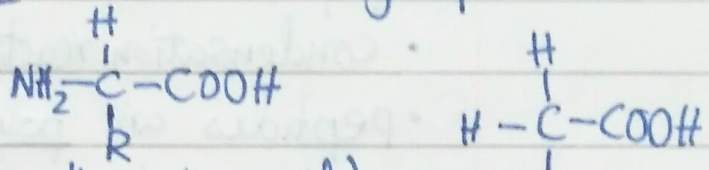
2,4,6-tribromo phenylamine (white ppt.)

+ 3HBr (steamy white fumes)

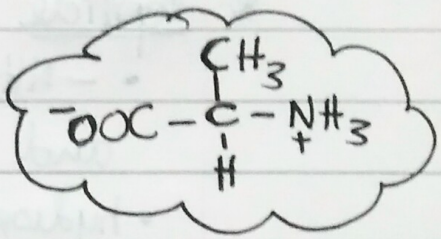
- NH_2 is ring activating group; 2,4-directing effect
- Nitrogen's lone pair gets drawn into ring of electrons
- Enhanced delocalisation makes benzene more attractive to electrophile attack.

Amino Acids

* Compounds containing $-NH_2$ and $-COOH$ groups
* 2-amino-carboxylic acids

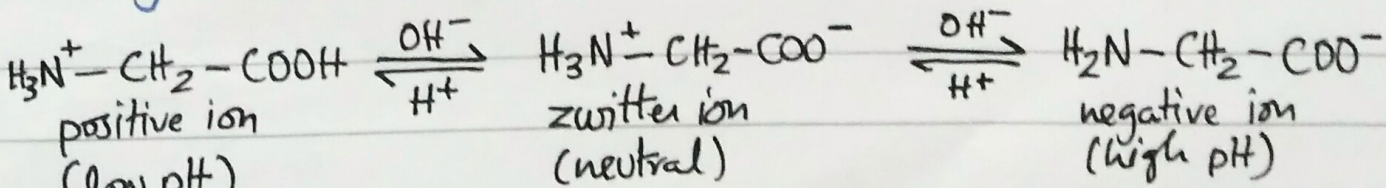


* All amino acids (except aminoethanoic acid) contain a chiral carbon.
* Zwitter ions
  - dipolar ion
  - proton from COOH moves to NH_2
  - amino acids exist as zwitterions at a certain pH called the isoelectric point



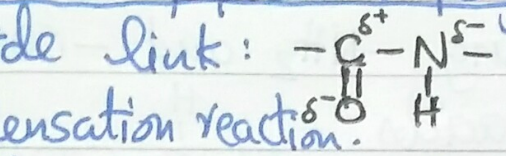
  - Produces increases inter-molecular forces (strong electrostatic forces of attraction between ions)
  - Melting and boiling points are higher.
  - Amino acids are soluble in water but insoluble in non-polar solvents.

* Acid/base Properties of amino acids
  - Amino acids behave as buffer solution, where pH remains almost unchanged when small amounts of H^+ or OH^- is added.
  - They can exist in 3 forms based on the pH of solution:



  - This principle is used to separate them during electrophoresis.

* Formation of peptides & polypeptides

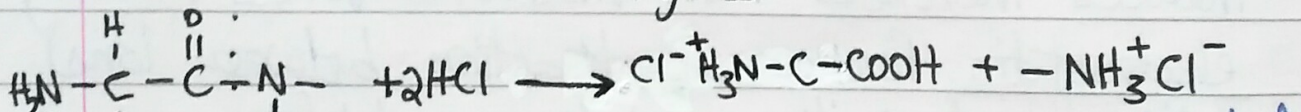
- peptide link: 
- condensation reaction.
- peptides are polyamides
- many amino acids joined together → polypeptide.

* Proteins

- $-NH_2$ group at left-hand end (N-terminal) and $-COOH$ group at right-hand end (C-terminal)
- hydrogen bonds exist between chains in the protein.
- Acid hydrolysis

  reagent: heat with dil. mineral acid

  condition: use enzymes.

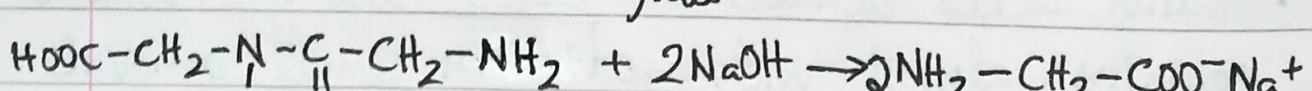


amine groups are protonated
acid groups remain.

- Alkaline hydrolysis

  reagent: heat with $NaOH_{(aq)}$

  condition: use enzymes.



The acid groups become sodium salts
and the amine groups remain.