REACTIONS OF ARENES & ALKYLARENES

1. HALOGENATION
2. NITRATION
3. FRIEDEL-CRAFT'S ALKYLATION
4. FRIEDEL-CRAFT'S ACYLATION

} ELECTROPHILIC SUBSTITUTION

5. COMPLETE OXIDATION
6. HYDROGENATION
7. COMBUSTION (COMPLETE & INCOMPLETE)

ELECTROPHILIC SUBSTITUTION

→ Arenes are very stable: delocalisation of π electrons in benzene ring; -ve charges spread out over entire molecule.

- During substitution reactions, delocalised ring maintained. (addition reactions disrupt aromatic stabilisation)

∴ Arenes undergo electrophilic substitution.

1 Generating Electrophile

- electrophile produced in situ by adding appropriate reagents to reaction mixture.

electrophile

electron-deficient species that acts as an electron pair acceptor; can be +ve ion / +ve end of polar molecule.

2 Electrophilic Attack on Benzene Ring

- 1 pair of e^- from benzene ring donated to electrophile to form covalent bond.
- Aromaticity of ring disrupted as only 4π electrons in ring, and +ve charge spread over 5 C atoms.

3 Regenerating Aromaticity of Benzene Ring

- Heterolytic cleavage of C-H bond: e^- from C-H bond → π-bond system.

DIRECTING EFFECTS OF SUBSTITUENTS ON ARENES

	Substituents	Activated positions
Electron-withdrawing	$-NO_2$ $-COOH$ $-COR$	3 and/or 5
Electron-donating	$-R$ $-OH$ $-NH_2$	2, 4 and/or 6

Electron-withdrawing	Electron-donating
- remove electron density from π system in benzene ring & make it less reactive.	- donate electron density into π system in benzene ring & make it more reactive.
- deactivate attack by electrophiles & direct incoming electrophile to attack 3 and/or 5 positions.	- activate attack by electrophiles & direct incoming electrophile to attack 2,4 and/or 6 positions.
eg. bromination of nitrobenzene: 3-bromonitrobenzene + 5-bromonitrobenzene	eg. bromination of methylbenzene: 2-bromomethylbenzene + 4-bromomethylbenzene

① HALOGENATION (electrophilic substitution)

of arenes & alkylarenes (free-radical OR substitution)

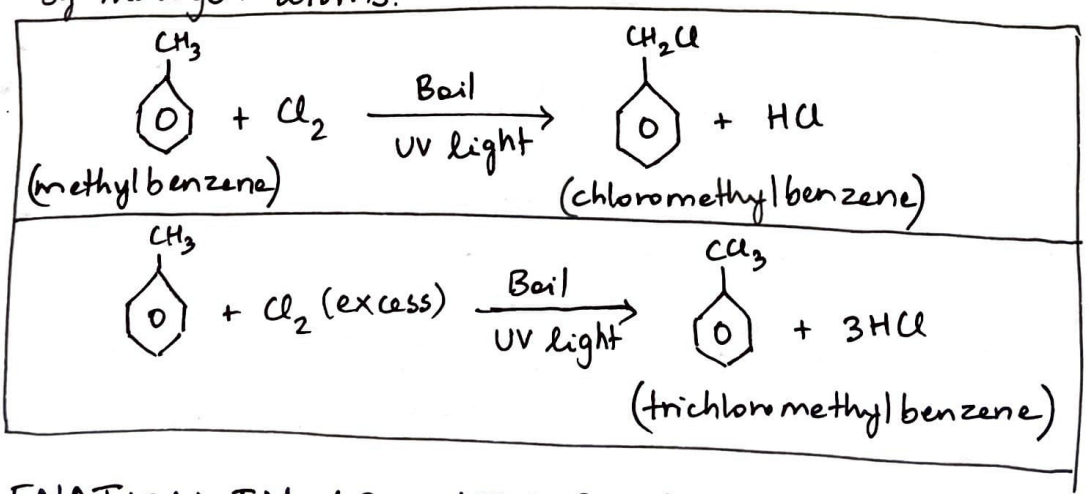
(i) Halogenation in Aromatic Ring (electrophilic sub.)

↳ occurs when halogen & anhydrous halogen carrier catalyst used.

(ii) Halogenation in Side Chain (free-radical sub.)

↳ occurs when halogen is passed into boiling alkylarene in presence of UV light.

→ if excess halogen, all H atoms in side chain substituted by halogen atoms.



HALOGENATION IN AROMATIC RING

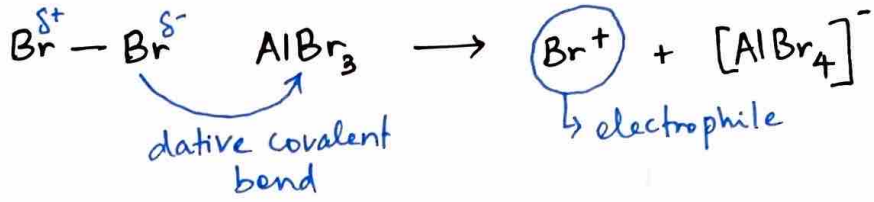
- electrophile: X^+ (Cl^+ or Br^+)
- catalyst: anhydrous halogen carrier (anhydrous $AlCl_3$ / $AlBr_3$)
- conditions: Cl_2 or Br_2 gas bubbled into arene / alkylarene at room temp.

→ H atom on benzene ring substituted for Cl or Br atom.

- products: halogenoarenes / aryl halides + HCl / HBr

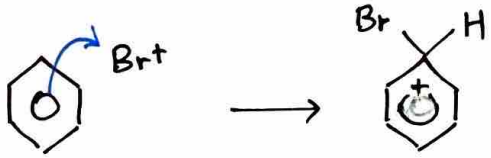
1 Generating X^+ electrophile

- halogen + halogen carrier.
- halogen molecule forms dative bond with halogen carrier: lone pair of e^- from one of the halogen atoms donated into empty 3p orbital of halogen carrier.



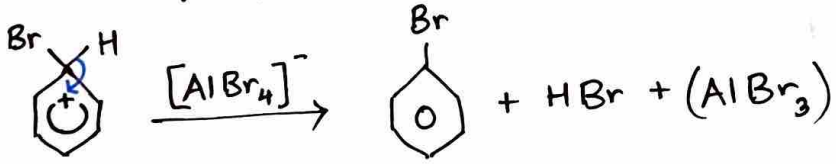
2 Electrophilic attack

- A pair of e^- from benzene ring donated to X^+ electrophile to form covalent bond.
- loss in aromaticity.



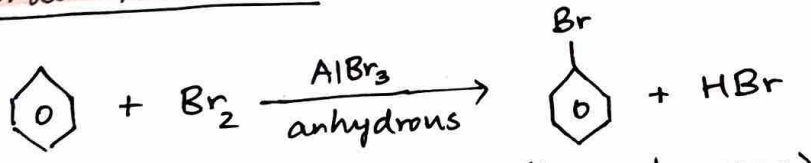
3 Regenerating aromaticity

- cleavage of C-H bond.



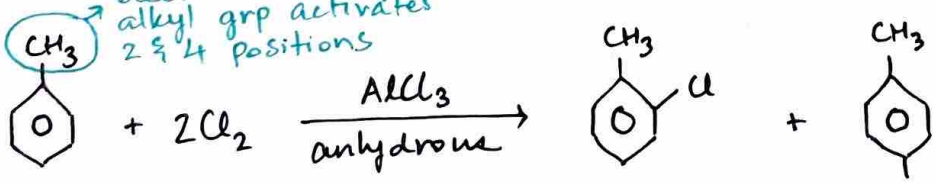
Overall Reactions:

(i)



(bromobenzene)

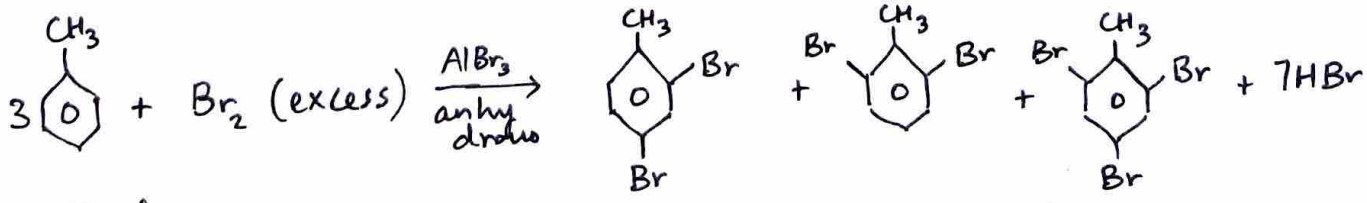
(ii)



(1-chloro-2-methylbenzene) (1-chloro-4-methylbenzene)

(2-chlorotoluene) (4-chlorotoluene)

(iii)



↳ multiple substitutions

(2,4-dichlorotoluene + 2,6-dichlorotoluene + 2,4,6-trichlorotoluene)

(2) NITRATION (electrophilic substitution)

- electrophile : NO_2^+ (nitronium ion) ↳ of arenes & alkylarenes
- catalyst : conc. H_2SO_4
- conditions : arene/alkylarene reacted with mixture of conc. HNO_3 & conc. H_2SO_4 at 25 - 60°C.

→ H atom on benzene ring substituted for nitro ($-NO_2$) group.

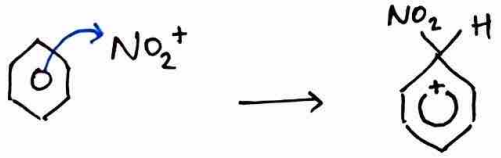
- products : nitroarenes + H_2O

[1] Generating NO_2^+ electrophile

$$HNO_3 + 2H_2SO_4 \longrightarrow \underset{\text{↳ electrophile}}{NO_2^+} + 2HSO_4^- + H_3O^+$$

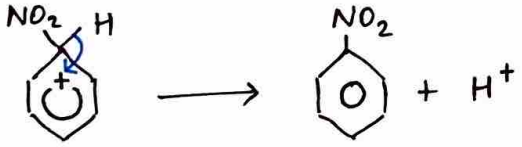
[2] Electrophilic attack

- pair of e^- from benzene ring donated to NO_2^+ electrophile to form covalent bond.
- loss in aromaticity.



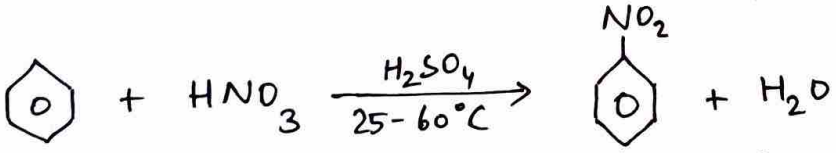
[3] Regenerating aromaticity

- Heterolytic cleavage of C-H bond.



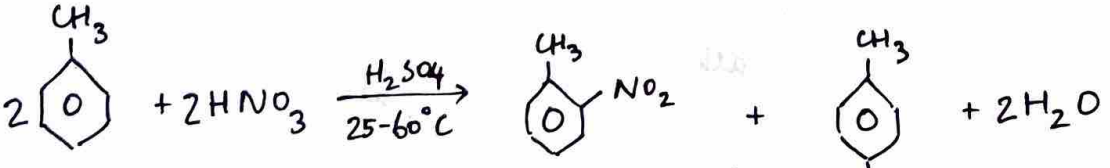
Overall Reactions:

(i)



(nitrobenzene)

(ii)



(2-nitrotoluene) (4-nitrotoluene)

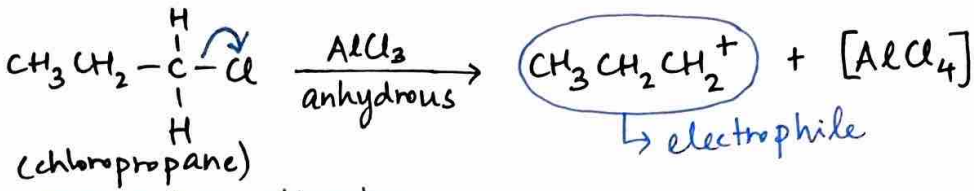
(3) FRIEDEL-CRAFT'S ALKYLATION (electrophilic substitution)
↳ of arenes

- ∘ electrophile: R^+
- ∘ catalyst: anhydrous $AlCl_3$
- ∘ conditions: react with chloroalkane and heat.

→ H atom on benzene ring substituted for alkyl (R) group.

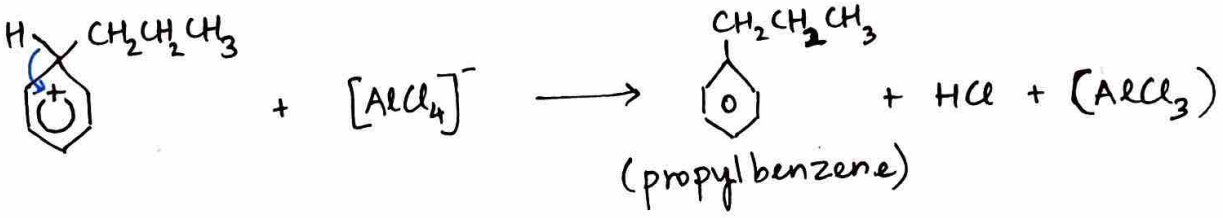
- ∘ products: alkylbenzene + HCl

[1] Generating R^+ electrophile

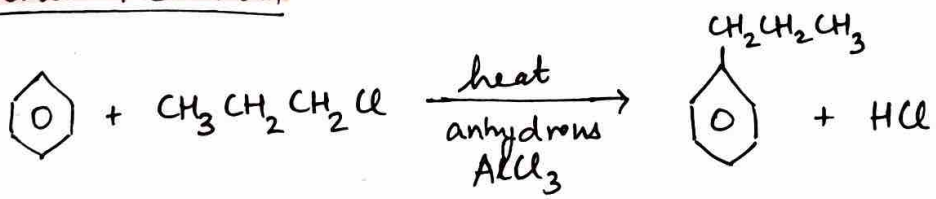


[2] Electrophilic attack

[3] Regenerating aromaticity



Overall Reaction:



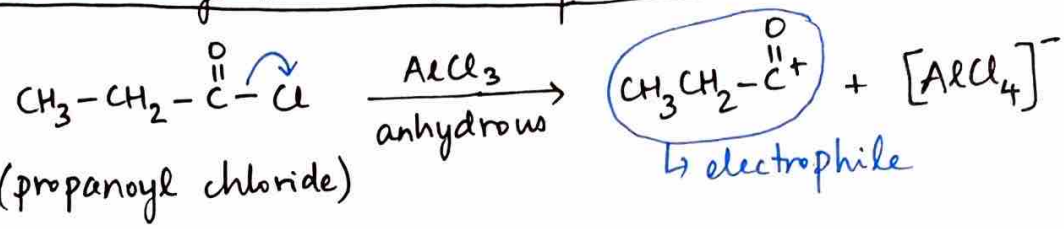
(4) FRIEDEL CRAFT'S ACYLATION (electrophilic substitution)
↳ of arenes & alkylarenes

- ∘ electrophile: $R-C=O^+$
- ∘ catalyst: anhydrous $AlCl_3$
- ∘ conditions: react with acyl chloride and heat.

→ H atom on benzene ring substituted for acyl (RCO) group.
acyl = alkyl + carbonyl (C=O)

- ∘ products: acylbenzene + HCl

1 Generating $R-C{=}O^+$ electrophile

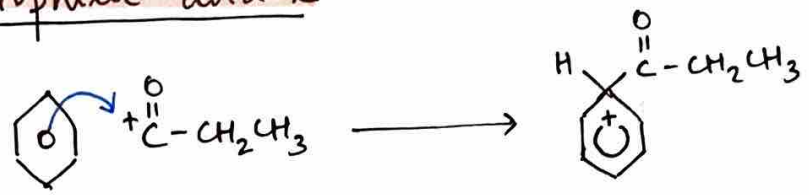


(propanoyl chloride)

↳ electrophile

2 Electrophilic attack

(i)



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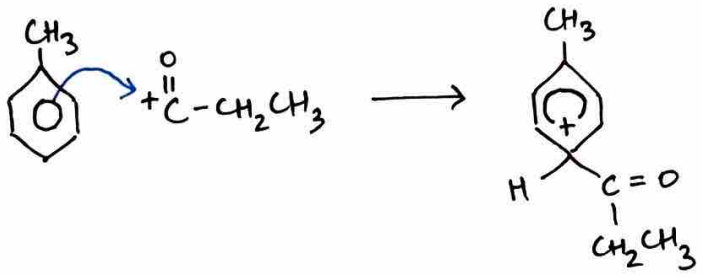
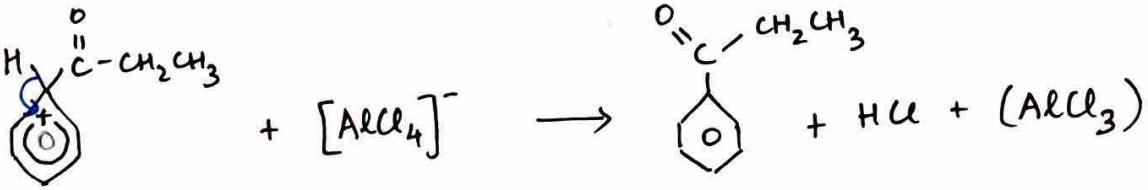
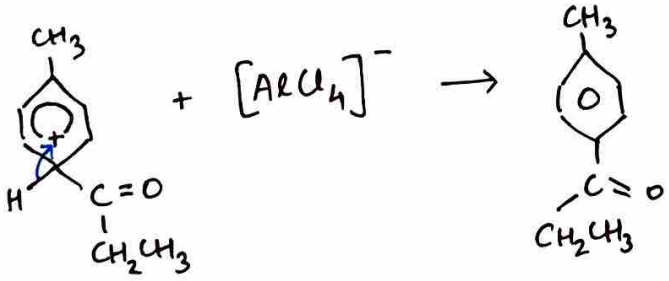


3 Regenerating aromaticity

(i)



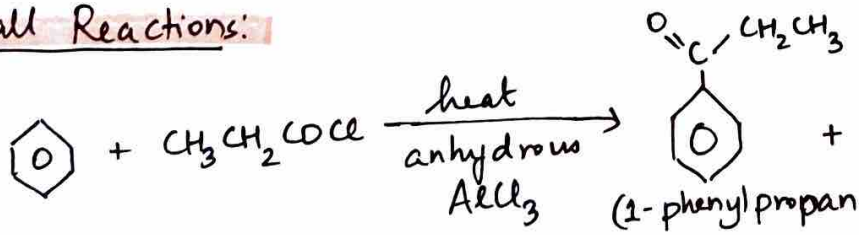
(ii)



* (substitution on position 4 due to electron-donating alkyl group)

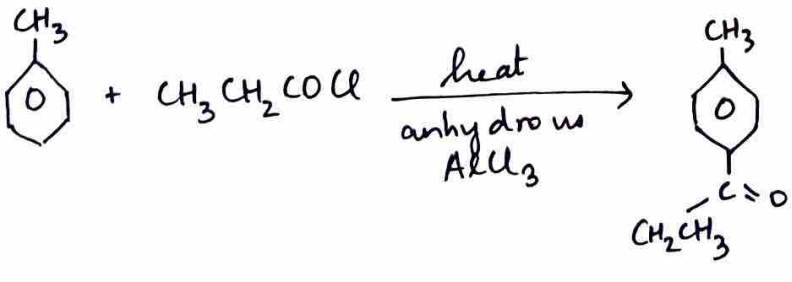
Overall Reactions:

(i)



(1-phenylpropan-1-one)

(ii)



(1-(4-methylphenyl)propan-1-one)

Friedel-Crafts Reactions

need to change structure of unreactive arene molecules to make them more reactive for use as starting materials for synthesis of other organic compounds.

⑤ COMPLETE OXIDATION

↳ of alkylarenes

→ alkanes not oxidised by ox. agents (eg. $KMnO_4$).
→ presence of benzene ring in alkylarenes affects properties of alkyl side chain → oxidised to carboxylic acid.

[1] Reflux with hot alkaline $KMnO_4$ – Oxidation

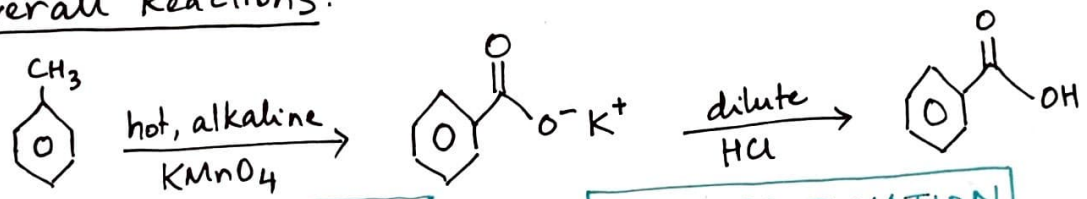
- Purple (Mn^{7+}) → colourless (Mn^{4+}).
- Brown ppt of MnO_2 formed.

[2] Acidification with dilute acid – Protonation

- dil. HCl / dil. H_2SO_4 protonates organic product.
- carboxylic acid formed.

Overall Reactions:

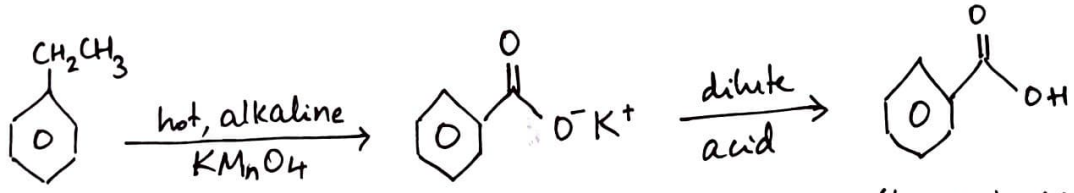
(i)



Step 1: OXIDATION | Step 2: PROTONATION

methylbenzene → benzoic acid

(ii)



(ethylbenzene) (benzoic acid)

⑥ HYDROGENATION (addition)

↳ of arenes & alkylarenes

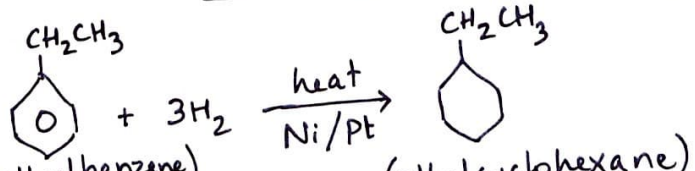
- catalyst: Pt / Ni
- conditions: heat with H_2 gas
- products: cyclohexane / alkylcyclohexane

aromatic stabilisation of arene completely lost. Cyclohexane formed is less energetically stable than benzene.

(i)

(benzene) (cyclohexane)

(ii)



(ethylbenzene) (ethylcyclohexane)

PRODUCTION OF HALOGENOARENES

① ELECTROPHILIC SUBSTITUTION / HALOGENATION OF ARENES/ ALKYLARENES

REACTIVITY OF HALOGENOARENES

↙

very unreactive compared to halogenoalkanes.

Halogenoalkanes

- undergo nucleophilic sub.
- nucleophile (eg. OH^-) attacks δ^+ C atom.
- covalent bond formed btwn C atom & nucleophile.
- C-X bond breaks & halogen atom substituted for nucleophile.

Halogenoarenes

- don't readily undergo nucleophilic sub.
- partial overlap of one of the lone pairs of e^- on halogen atom with π system in benzene ring; delocalisation.
- thus C-X bond has partial double bond character which strengthens bond & causes additional stabilisation.
- ∴ C-X bond cannot easily break → less reactivity.
- only in extreme harsh conditions (200°C & 200 atm), Cl atom in chlorobenzene is replaced by OH^- nucleophile.

PRODUCTION OF PHENOL

① DIAZOTISATION REACTION

(Phenylamine + Nitrous acid)

- **conditions**:
  - $NaNO_2$ w/ dil. acid (HCl) → step 1
  - ice to keep temp. <10°C → step 1 & 2
  - heat → step 3

- **catalyst**: HCl

1 Formation of nitrous acid

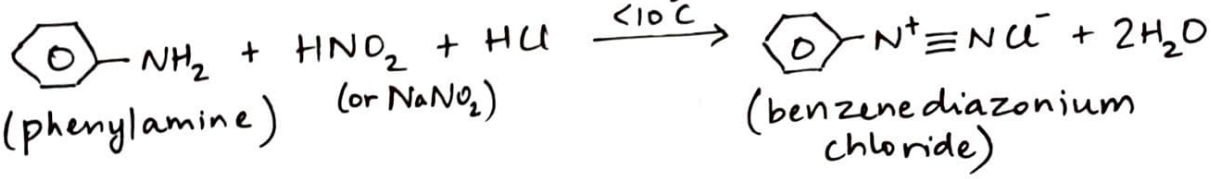
- HNO_2 very unstable ∴ prepared in test-tube by reacting $NaNO_2$ w/ HCl (dil.), keeping temp. <10°C using ice.

$$NaNO_2 + HCl \xrightarrow[<10°C]{ice} HNO_2 + NaCl$$

(sodium nitrite) (nitrous acid)

2 Diazotisation

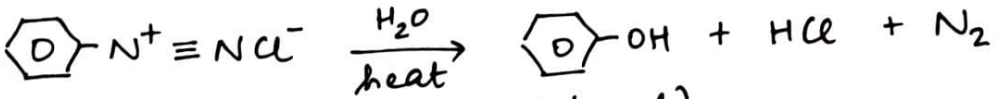
- HNO_2 reacts w/ phenylamine and dil. HCl to form diazonium ion / unstable diazonium salt.



(phenylamine) (or $NaNO_2$) (benzenediazonium chloride)

3 Thermal decomposition

- diazonium salt is very unstable, so thermally decomposes when heated to form phenol.



(phenol)

REACTIONS OF PHENOL

① ACID-BASE REACTION – PHENOL + BASE
② ACID - BASE REACTION – PHENOL + REACTIVE METAL
③ COUPLING REACTION - PHENOL + DIAZONIUM SALT
④ ESTERIFICATION

} REACTIONS OF –OH GROUP

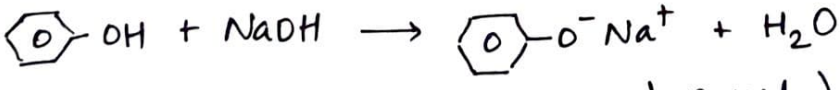
⑤ ELECTROPHILIC SUBSTITUTION – NITRATION
⑥ ELECTROPHILIC SUBSTITUTION – BROMINATION

} REACTIONS OF AROMATIC RING

* –OH group of phenol has slightly acidic character ∴ behaves as acid.
- phenols are only slightly soluble in water due to large non-polar benzene ring.

① PHENOL + BASE (acid-base)

Phenol + Base → Soluble salt + Water



(sodium phenoxide)

② PHENOL + REACTIVE METAL (acid-base)

Phenol + Reactive metal → Soluble salt + Hydrogen

(sodium phenoxide)

* molten phenols react vigorously w/ reactive metals.

(3) PHENOL + DIAZONIUM SALT – COUPLING (electrophilic substitution)

~~(i) Diazonium salt + alkaline solution of phenol → azo compound~~

~~(ii) Diazonium salt + neutral phenol → azo compound + HCl (eg.)~~

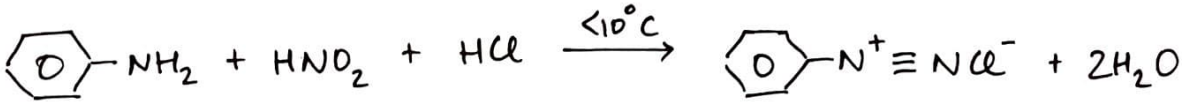
eg. Coupling of Benzenediazonium chloride with phenol in NaOH:

[1] Formation of nitrous acid

$$NaNO_2 + HCl \xrightarrow[<10°C]{ice} HNO_2 + NaCl$$

* steps [1] & [2] are used in production of phenol.

[2] Diazotisation



- Reaction mixture is kept <10°C to prevent thermal decomposition of benzenediazonium ion to benzene & nitrogen.

[3] Coupling reaction

- electrophile = diazonium ion
  ↳ substitutes into position 4 of benzene ring of phenol.
- alkaline conditions (NaOH) needed to deprotonate organic product & form azo compound.

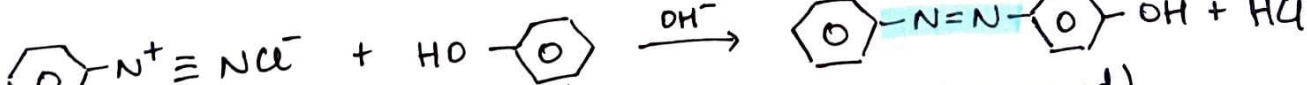
(i) 

(phenol) (sodium phenoxide)

(ii) 

(benzenediazonium ion) (phenoxide ion) (azo compound)

OR



(benzenediazonium chloride) (phenol) (azo compound)

Azo Compounds (Diazonium compounds)

- $R_1-N=N-R_2$ group
- used as dyes
- delocalised e^- in π-bonding system of the 2 benzene rings is extended through $-N=N-$ bridge.
- Due to delocalisation of e^- throughout the compound, azo compounds are very stable.

④ ESTERIFICATION (addition-elimination)

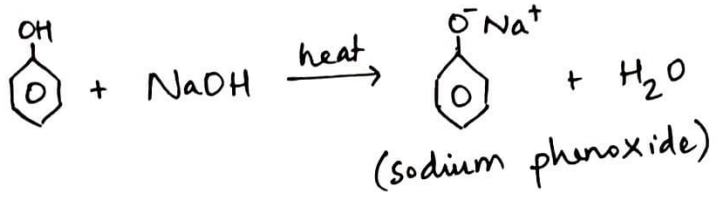
- Phenol + Acyl chloride → Ester + NaCl + H_2O

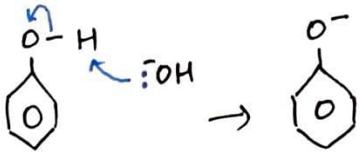
- **Conditions:**
  - heat
  - base (dil. NaOH)

→ phenol molecule added across C=O bond.
→ NaCl molecule eliminated

1 Generating nucleophile

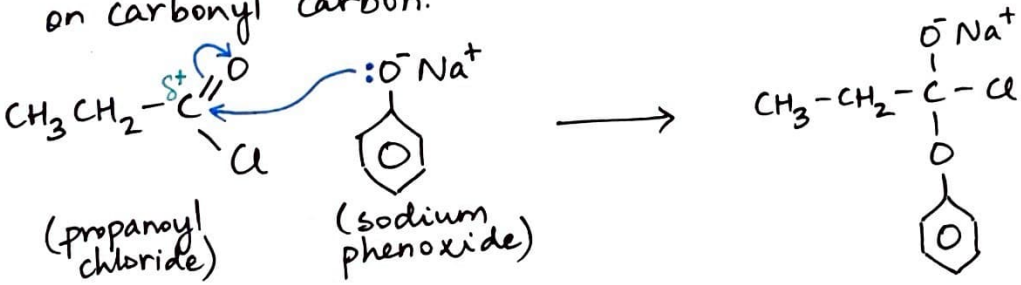
- Base (NaOH) deprotonates phenol → phenoxide ion.
- Phenoxide ion is a better nucleophile than phenol molecule.





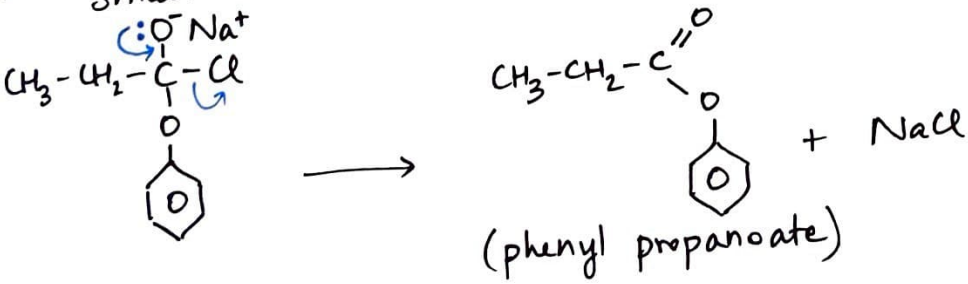
2 Nucleophilic addition

- Phenoxide ion acts as ~~electrophile~~ nucleophile & carries out initial attack on carbonyl carbon.

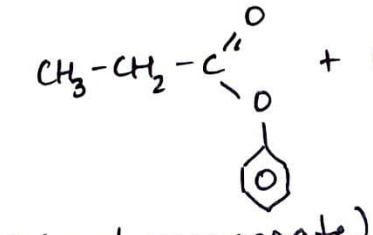


3 Elimination

- Small NaCl molecule eliminated.

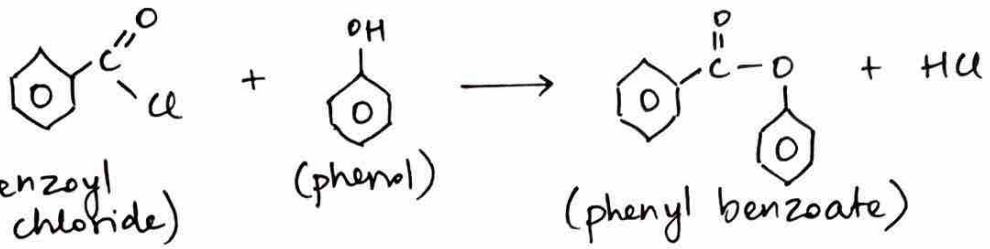


Overall Reactions:

(i) $CH_3-CH_2-C(=O)-Cl$ +  $\xrightarrow[\text{heat}]{NaOH}$  + NaCl + H_2O

(propanoyl chloride)

(phenyl propanoate)

(ii) 

(benzoyl chloride) (phenol) (phenyl benzoate)

Reactions of aromatic ring of phenol:

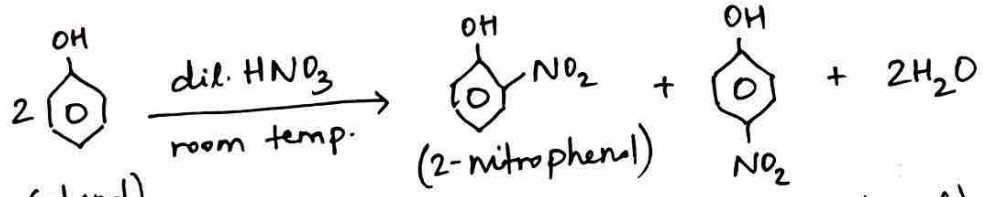
- phenols react more readily with electrophiles than benzene.
- lone pairs of e^- on O atom in -OH overlaps w/ π-bonding system.
- this increases e^- density of benzene ring and activates attack by electrophiles, directing incoming electrophile to 2,4,6 positions

-OH = electron-donating grp.

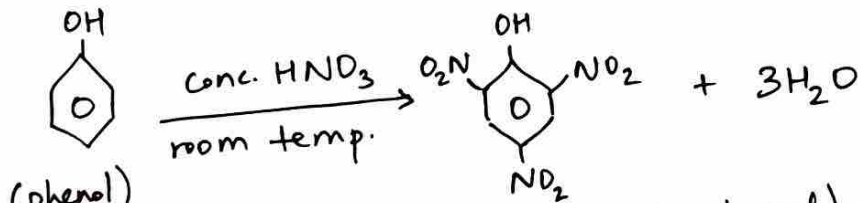
---

(5) NITRATION (electrophilic substitution)

- conditions: react with dil. (or conc.) HNO_3 at room temp.

(i) 

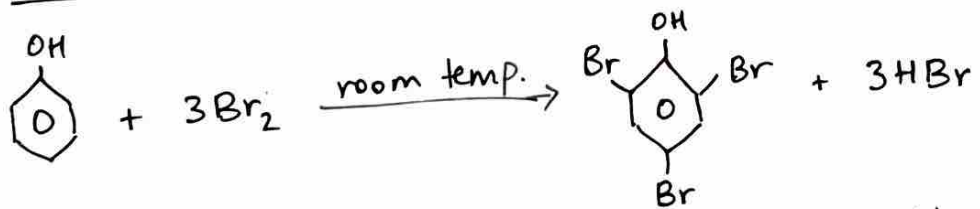
(phenol) (2-nitrophenol) (4-nitrophenol)

(ii) 

(phenol) (2,4,6-trinitrophenol)

(6) BROMINATION (electrophilic substitution)

- conditions: react with bromine water at room temp.



(2,4,6-tribromophenol)

* orange bromine water solution → white ppt of 2,4,6-tribromophenol.

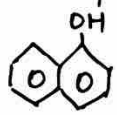
Reactivity of phenols > benzene

Reaction	Benzene	Phenol
Nitration	- conc. HNO_3 & conc. H_2SO_4 - reflux btwn 25 - 60°C	- dil. HNO_3 - room temp.
Bromination	- pure bromine - $AlBr_3$ catalyst	- bromine water - room temp.

Reactions of other phenolic compounds

phenolic compounds ⇒ have phenol grp.

eg. 1-naphthol



- OH group is electron-donating & activates benzene ring to electrophilic attack.
- electrophile directed to 2 & 4 positions. (6 not possible as there is no H atom on this carbon - bonded to C atom of 2nd benzene ring).

PRODUCTION OF BENZOIC ACID

① COMPLETE OXIDATION OF ALKYLARENES

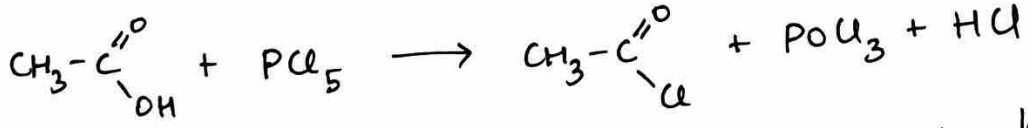
REACTIONS OF CARBOXYLIC ACIDS

① CHLORINATION (NUCLEOPHILIC SUBSTITUTION)

② FURTHER OXIDATION

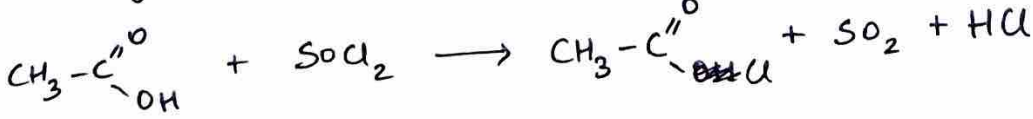
① CHLORINATION (nucleophilic Substitution)

(i) carboxylic acid + solid phosphorus (V) chloride → acyl chloride + $POCl_3$ + HCl



(ii) carboxylic acid + liquid phosphorus (III) chloride $\xrightarrow{heat}$ acyl chloride + H_3PO_3

(iii) carboxylic acid + liquid sulfur dichloride oxide → acyl chloride + SO_2 + HCl



(2) FURTHER OXIDATION

Primary alcohol $\xrightarrow{\text{oxidation}}$ aldehyde $\xrightarrow{\text{oxidation}}$ carboxylic acid.

(i) Methanoic acid

- strong R.A. ; further oxidised to CO_2.

[1] Mild oxidising agent
- warm w/ Fehling's solution OR Tollen's reagent
  - Fehling's : $Cu^{2+} \rightarrow Cu^{+}$; red ppt of Cu_2O.
  - Tollen's : $Ag^{+} \rightarrow Ag$; Silver mirror.

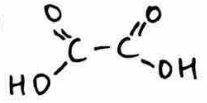
[2] Strong oxidising agent
- acidified $KMnO_4$ / acidified $K_2Cr_2O_7$
  - $KMnO_4$: Mn^{7+} (purple) $\rightarrow$ Mn^{2+} (colourless)
  - $K_2Cr_2O_7$: Cr^{6+} (orange) $\rightarrow$ Cr^{3+} (green)

(ii) Ethanedioic acid

- strong R.A ; further oxidised to CO_2.

[1] Strong oxidising agent
- warm acidified $KMnO_4$

(i) $HCOOH + [O] \rightarrow CO_2 + H_2O$

(ii)  $+ 2[O] \rightarrow 2CO_2 + 2H_2O$

RELATIVE ACIDITIES : CARBOXYLIC ACID, PHENOL, ALCOHOL

* smaller pKa = stronger acid

Comparison	Carb. Acid	Phenol	Alcohol
pKa @ 25°C	4 - 5	10	15 - 20
Strength of O-H bond	- e^- in O-H bond drawn towards C=O bond. - e^- in C-O bond drawn towards C=O bond. - O-H bond weakened due to electron-withdrawing C=O grp. - easier to lose proton and act as acid.	- no electron-withdrawing C=O group, so O-H bond not weakened. - harder to lose proton and act as acid.	- no electron-withdrawing C=O group, so O-H bond not weakened. - harder to lose proton and act as acid.
Conjugate base	carboxylate ion ($RCOO^-$)	phenoxide ion 	alkoxide ion (RO^-)

Comparison	Carb. Acid	Phenol	Alcohol
Stability of conjugate base	- carbonyl grp is electron-withdrawing & withdraws e^- density from O atom - charge density on O atom spread over entire ion; delocalised. - e^- on O atom less available for bond formation w/ H^+ to reform undissociated acid molecule w/ -COOH grp. - conjugate base is more stable than carb. acid. - carboxylate ions more stable than phenoxide & alkoxide ions.	- charge density on O atom spread over entire ion; delocalised. - ∵ one of the lone pairs of e^- on O atom overlaps w/ π system of benzene ring. - e^- on O atom less available for bond formation w/ H^+ to reform undissociated phenol molecule w/ -OH grp. - Conjugate base is more stable than phenol. - Phenoxide ions less stable than carboxylate, more stable than alkoxide ions	- alkyl grp is electron-donating and donates e^- density to O atom. - charge density on O atom not spread out over entire ion; localised. - e^- on O atom more readily available for bond formation w/ H^+ to reform undissociated alcohol molecule w/ -OH grp. - Conjugate base less stable than alcohol. - alkoxide ions less stable than carboxylate & phenoxide ions.
Position of dissociation eq.	- lies more to RHS than alcohols & phenols. - favours dissociated carboxylate ions.	- lies more to RHS than alcohols, less to RHS than carb. acids. - favours dissociated phenoxide ions.	- lies more to LHS than carb. acids & phenols - favours undissociated alcohol molecule.
Acidic character	Stronger acid than phenols & alcohols	Weaker acid than carb. acids; stronger acid than alcohols	Weaker acid than carb. acids & phenols.

Acidity of Water:

- pKa = 14
- no electron-donating alkyl grps, so less charge localisation than alc.
- no electron-withdrawing carbonyl grps & no overlap of lone pair of e^- w/ π system of benzene ring, so less charge delocalisation than carb. acids & phenols.
- conjugate base: hydroxide ion
- hydroxide ion more readily accepts H^+ than phenoxide & carboxylate, but less readily than ethoxide.
- eq. position lies more to RHS than alcohols, but less than phenols & carb. acids ∴ favours undissociated water molecules.

Acidity: carb. acid > phenol > water > alcohol

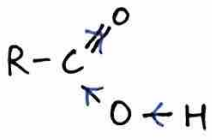
$CH_3CH_2-OH\,(aq) \rightleftharpoons CH_3CH_2O^-\,(aq) + H^+\,(aq)$ — weakest acid

$H_2O\,(l) \rightleftharpoons OH^-\,(aq) + H^+\,(aq)$

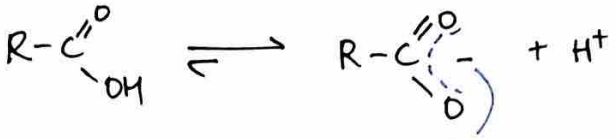
 $+ H^+\,(aq)$

$CH_3COOH\,(aq) \rightleftharpoons CH_3COO^- + H^+\,(aq)$ — strongest acid

(i)

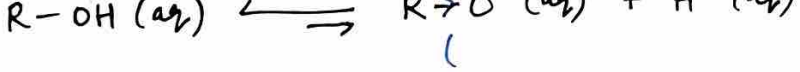


e^- are drawn towards C=O, causing O-H bond to become weaker.



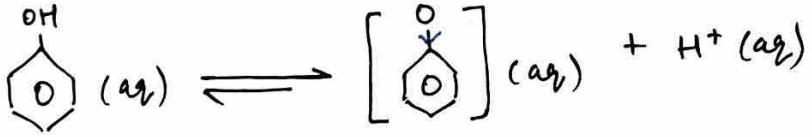
-ve charge spread over whole COO^- grp

(ii)



-ve charge conc. on O atom

(iii)

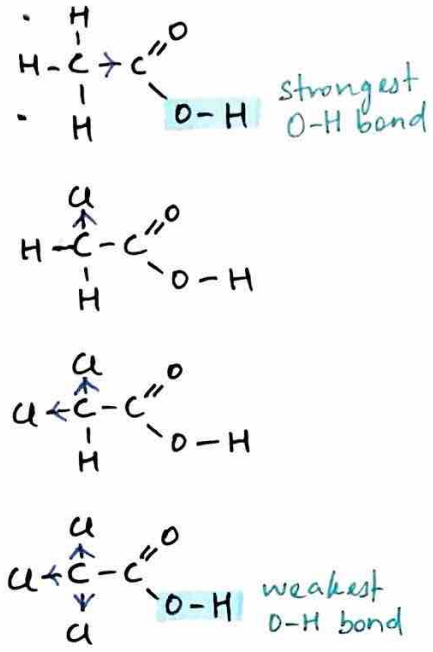


-ve charge spread over whole ion, but delocalised on the C.

Relative Acidities: Chlorine-substituted Carboxylic Acids

- chlorine-substituted carb. acids = ~~carb~~ carb. acids w/ electron-withdrawing groups.
- electron-withdrawing groups bonded to carbon attached to -COOH make carb. acids stronger acids.
- in undissociated carb. acid molecule, electron-withdrawing groups weaken O-H bond by drawing e^- from it.
- in dissociated carboxylate ion, electron-withdrawing groups increase delocalisation of -ve charge on O atom, making the ion more stable.
- more electron-withdrawing groups ⇒ stronger acid.

$$CH_3COOH < CH_2ClCOOH < CHCl_2COOH < CCl_3COOH$$

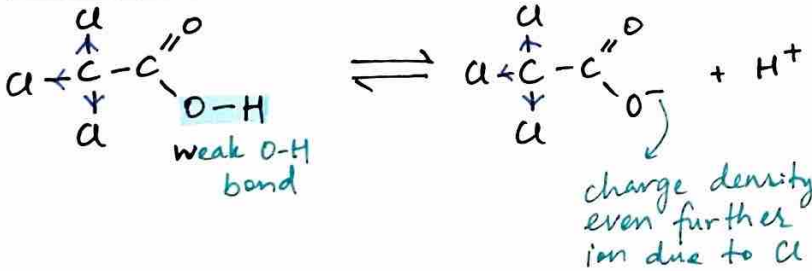


weakest acid (ethanoic acid)

strongest acid (trichloroethanoic acid)

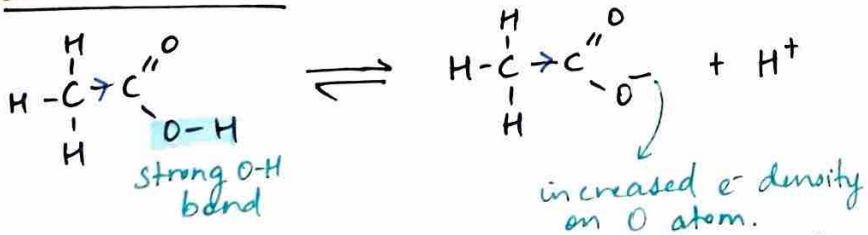
- weakest O-H bond
- most stable carboxylate ion
- carboxylate ion is least attracted to $H^+(aq)$ ions

Trichloroethanoic Acid



- O-H bond weakened by 3 electron-withdrawing groups — 3 Cl atoms.
- When O-H bond broken to form trichloroethanoate ion, -ve charge is further delocalised from COO^- grp due to 3 electron-withdrawing Cl atoms.
- trichloroethane ion is very stable ∴ less attracted to H^+ ions.

Ethanoic Acid



- O-H bond strengthened by electron-donating methyl group.
- when O-H bond broken to form ethanoate ion, -ve charge is donated to COO^- group by electron-donating alkyl group.
- ethanoate ion is less stable ∴ more attracted to H^+ ions.

PRODUCTION OF ACYL CHLORIDES

① CHLORINATION OF CARBOXYLIC ACIDS

REACTIONS OF ACYL CHLORIDES

↳ very reactive
↳ undergo addition-elimination reactions

Addition - Elimination

[1] Nucleophilic Addition
- addition of nucleophile across C=O bond.
- carbonyl carbon = electron deficient ∴ δ^+ charge.
- ∴ carbonyl carbon susceptible to nucleophilic attack.
- C-Cl bond breaks

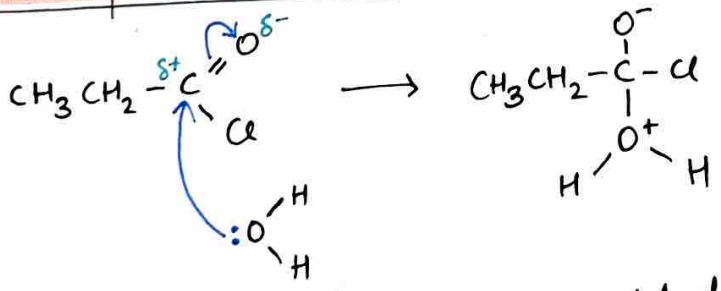
[2] Elimination
of small molecule – HCl (white fumes)

① HYDROLYSIS
② ESTERIFICATION
③ CONDENSATION WITH AMMONIA / AMINES

① HYDROLYSIS (addition-elimination)

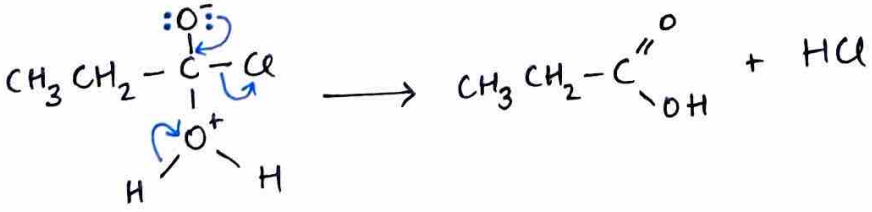
Acyl chloride + water → carboxylic acid + HCl

[1] Nucleophilic addition



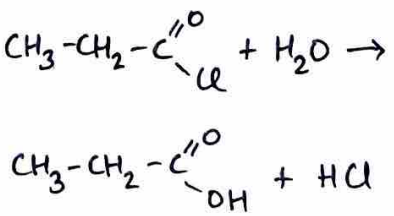
- nucleophile = H_2O molecule; added across C=O bond.
- lone pair of e^- on O atom of H_2O carries out initial attack on carbonyl carbon.

[2] Elimination



- HCl molecule is eliminated.

Overall Reaction:



(2) ESTERIFICATION (addition-elimination)

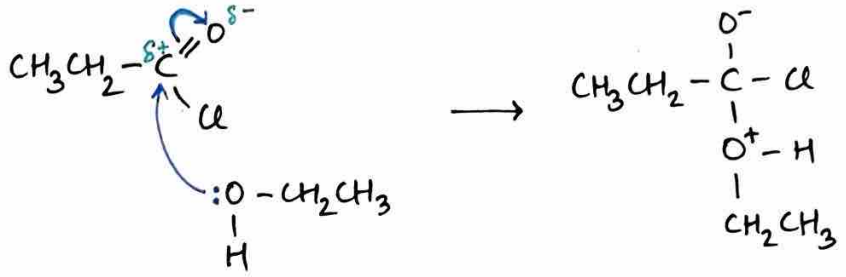
(i) Acyl chloride + alcohol ⟶ ester + HCl

→ alcohol molecule added across C=O bond.
→ HCl molecule eliminated.

- vigorous
- white fumes of HCl produced

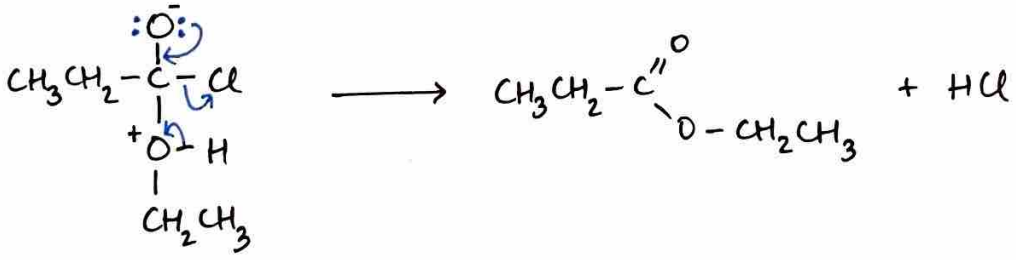
(1) Nucleophilic Addition

- alcohol molecule acts as nucleophile.
- lone pair of e^- on O atom of alcohol carries out initial attack on carbonyl carbon.

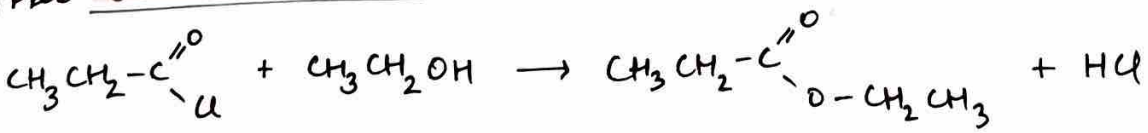


(2) Elimination

- HCl molecule eliminated.



Overall Reaction:



(ii) Acyl chloride + phenol — pg. 11

More effective to form esters from acyl chlorides than carb. acids:
① acyl chlorides are more reactive ⇒ faster production of ester.
② acyl chloride reactions go to completion ⇒ more ester produced.

③ CONDENSATION (addition - elimination)

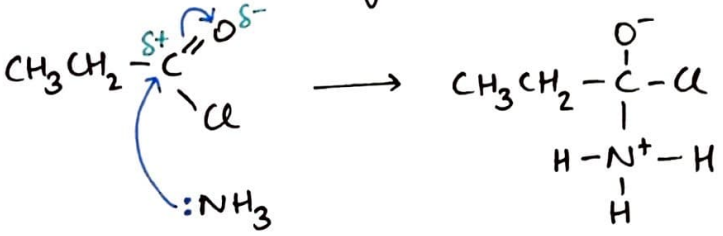
(i) **Acyl chloride + ammonia** → non-substituted amide + HCl

→ NH_3 molecule added across C=O bond.

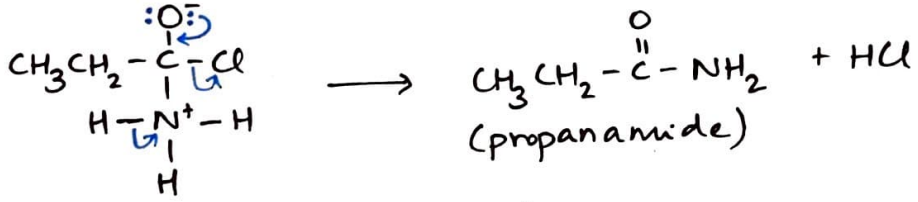
→ HCl molecule eliminated.

[1] Nucleophilic addition

- nucleophile = ammonia
- N atom in NH_3 has lone pair of e^- which carries out initial attack on carbonyl carbon.



[2] Elimination



- HCl molecule eliminated.

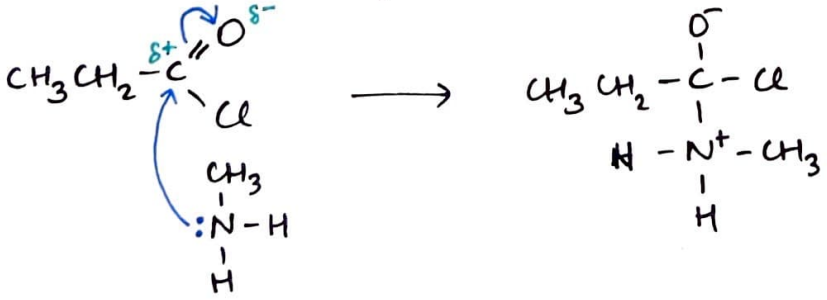
(ii) **Acyl chloride + primary/secondary amine** → substituted amide + HCl

→ amine molecule added across C=O bond.

→ HCl molecule eliminated.

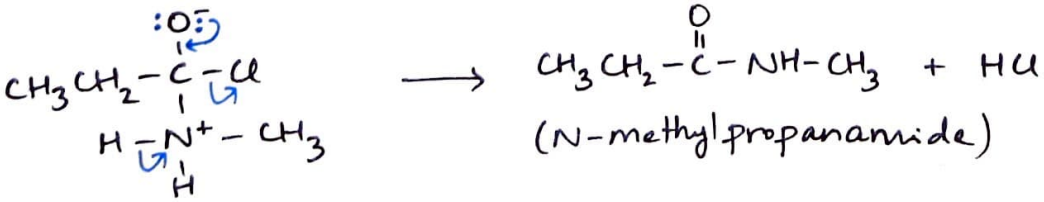
[1] Nucleophilic addition

- nucleophile = amine
- N atom in amine has lone pair of e^- which carries out initial attack on carbonyl carbon.



[2] Elimination

- HCl molecule eliminated.



3 Acid-base reaction

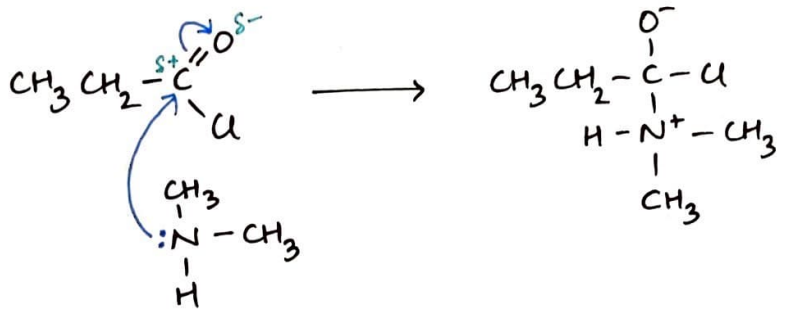
- -HCl formed reacts with unreacted amine to form organic ammonium salt.

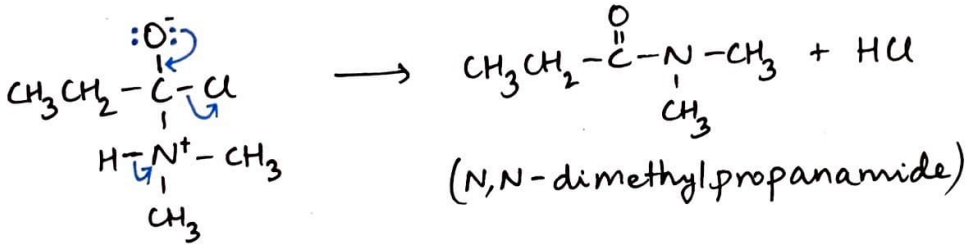
→ same nucleophile

$HCl + NH_2CH_3 \longrightarrow CH_3NH_3^+Cl^-$

(acid) (base) (ammonium salt)

(iii)

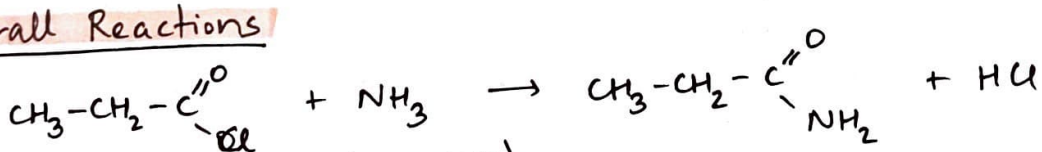
1 

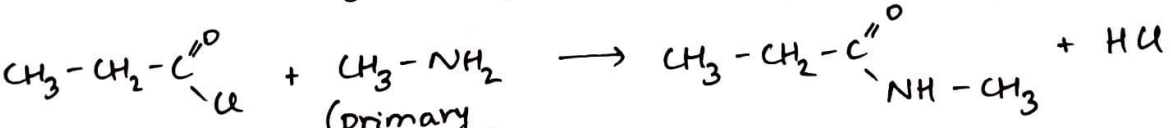
2 

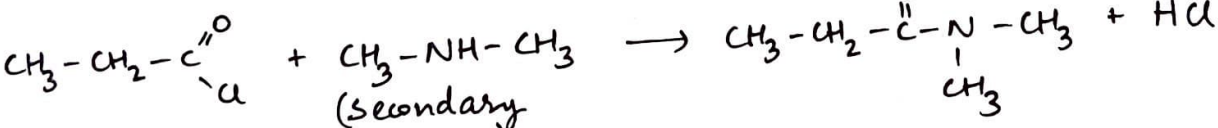
(N,N-dimethylpropanamide)

3 $HCl + NHC_2H_6 \longrightarrow C_2H_6NH_2^+Cl^-$

Overall Reactions

(i) 

(ii) 

(iii) 

with ammonia	with amine
vigorous reaction	vigorous reaction
non-substituted amide formed	substituted amide formed
white fumes of HCl formed.	HCl formed reacts w/ unreacted amine to form white organic ammonium salt.

RELATIVE EASE OF HYDROLYSIS: ACYL CHLORIDES, ALKYL CHLORIDES, ARYL HALIDES

Hydrolysis = breakdown of a compound using water!

Ease of Hydrolysis: acyl chloride > alkyl chloride > halogeno arene

↳ Determined by strength of C-Cl bond.

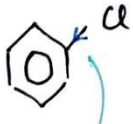
Acyl Chloride	Alkyl Chloride	Aryl Halide
- carbon bonded to chlorine atom is also attached to O atom ∴ 2 strong electronegative grps/atoms pulling e^- away from carbonyl carbon. - carbonyl carbon very δ^+.	- carbon is only attached to 1 electronegative Cl atom which pulls e^- away from it. - carbon atom not very δ^+.	- carbon atom bonded to Cl atom is part of delocalised π-bonding system of benzene ring. - one of the lone pairs of e^- on Cl atom overlaps w/ delocalised syste
C-Cl bond weakened.	C-Cl bond stronger than in acyl chlorides.	C-Cl bond very strong as it has partial double bond character.
readily hydrolysed at room temp.	need to be refluxed w/ strong alkali (NaOH) → OH^- hydrolyses alkyl chlorides ∴ stronger nucleophile than H_2O.	does not undergo hydrolysis.

(i) $R-C(=O)-Cl \xrightarrow[\text{room temp.}]{H_2O} R-C(=O)-OH + HCl$

2 electronegative atoms; very e^- deficient; weakened C-Cl bond

(ii) $R-C-Cl \xrightarrow[\text{heat}]{NaOH} R-C-OH + NaCl$

e^- deficient; 1 electronegative atom; relatively strong C-Cl bond

(iii)  $\xrightarrow{H_2O}$ no hydrolysis

C-Cl has partial double bond character ∴ very strong

PRODUCTION OF AMINES

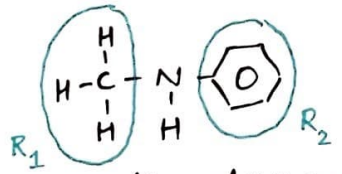
→ Primary amine = $-NH_2$ group attached to 1 alkyl / aryl group.

→ Secondary amine = $-NH$ group attached to 2 alkyl / aryl groups.

① AMINATION OF HALOGENOALKANES

② REDUCTION OF AMIDES

③ REDUCTION OF NITRILES



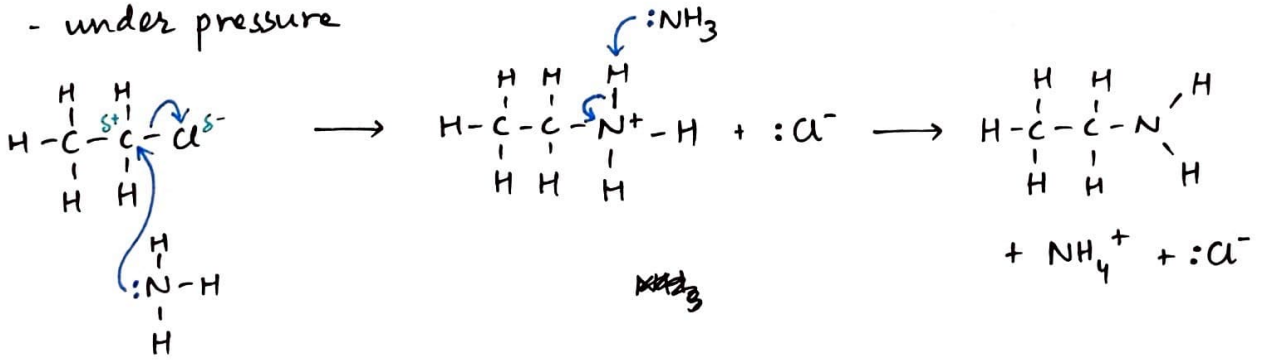
(secondary amine)

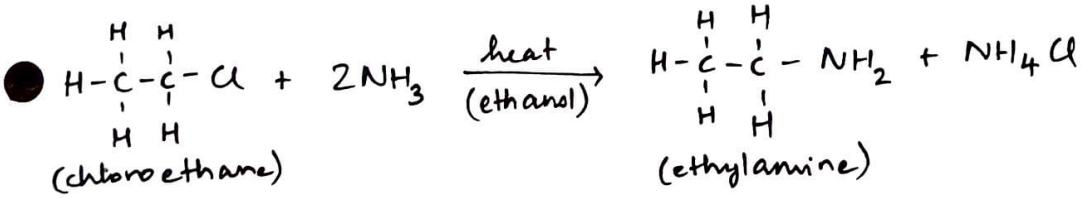
① AMMINATION OF HALOGENOALKANES (nucleophilic substitution)

(i) Halogenoalkane + Ammonia → Primary Amine + Ammonium Halide

- nucleophile: N atom
- conditions:
  - excess NH_3
  - ethanolic
  - heat
  - under pressure

→ $-NH_2$ group replaces halogen atom.



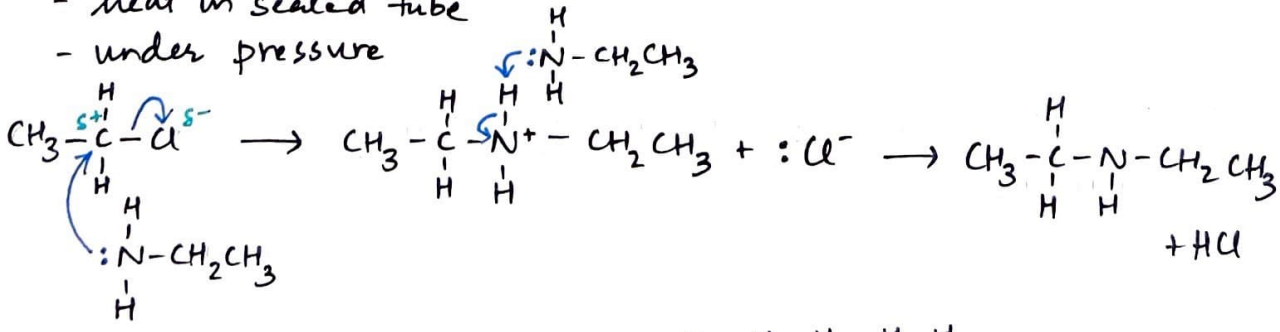


(chloroethane) (ethylamine)

(ii) Halogenoalkane + Primary Amine → Secondary Amine + HCl

- nucleophile: N atom
- conditions:
  - ethanolic
  - heat in sealed tube
  - under pressure

→ $-NH$ group replaces halogen atom.

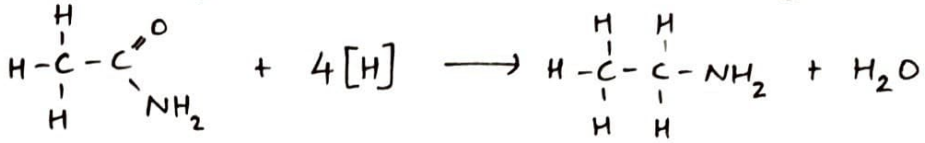


(2) REDUCTION OF AMIDES

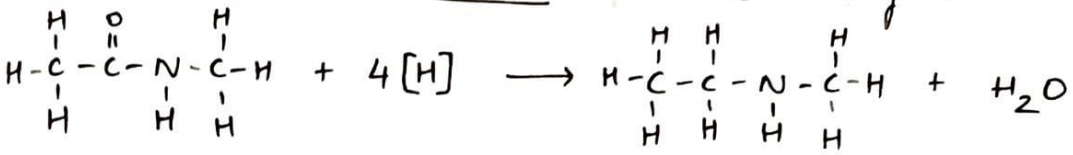
- reducing agent : $LiAlH_4$
- conditions: in dry ether

→ C=O group is reduced to amine.

(i) **Reduction of Primary amide** → Primary amine + H_2O



(ii) **Reduction of Secondary amide** → Secondary amine + H_2O



(3) REDUCTION OF NITRILES

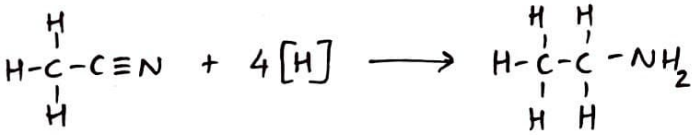
- reducing agent : $LiAlH_4$
- conditions: in dry ether

OR

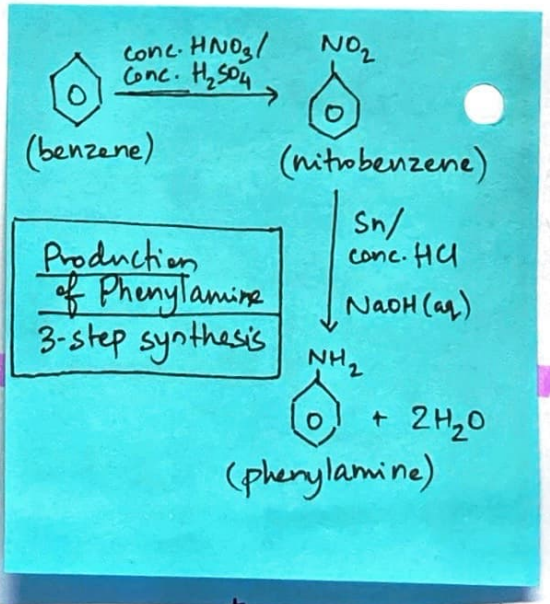
- conditions:
  - nitrile vapour
  - H_2 gas over Ni catalyst

Reduction of Nitrile → Primary amine

→ -CN group reduced to $-NH_2$ group.

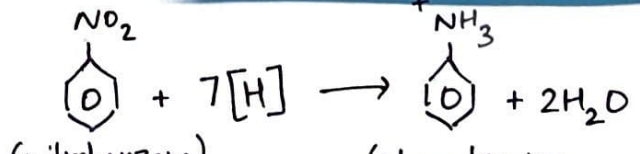


OR



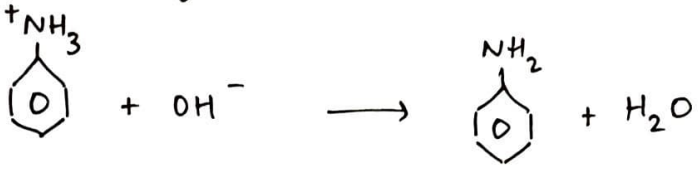
PRODUCTION OF PHENYLAMINE

1. Nitration of Benzene (pg. 4)
2. Reduction of Nitro Benzene
   - conditions:
     - hot tin + conc. HCl
     - under reflux
   - products:
     - acidic mixture containing phenyl amine ion.



3- **Deprotonation**

- NaOH is added to acidic mixture to deprotonate phenylamine ion to phenylamine.



Steam Distillation - Separation / Purification

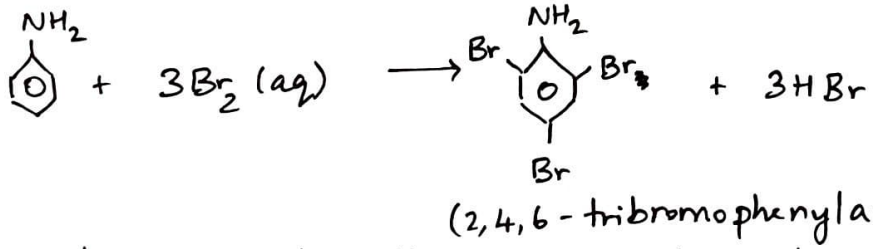
↳ to separate phenylamine from reaction mixture.

REACTIONS OF PHENYLAMINE

① BROMINATION

● FORMATION OF DIAZONIUM SALTS (pg 8 — 1 & 2)

① BROMINATION (electrophilic substitution)



(2,4,6 - tribromophenylamine)

- Conditions: react with bromine water at room temp.

PRODUCTION OF AMIDES

① CONDENSATION OF ACYL CHLORIDES WITH AMMONIA / AMINES

● (pg. 20) — Addition-elimination

Condensation = 2 org. molecules join together and eliminate a small molecule in the process.

* Condensation reactions btwn carb. acids and ammonia / amines can also form amides, but these reactions are slower and don't go to completion ∴ carb. acids are less reactive than acyl chlorides.

REACTIONS OF AMIDES

① HYDROLYSIS

② REDUCTION

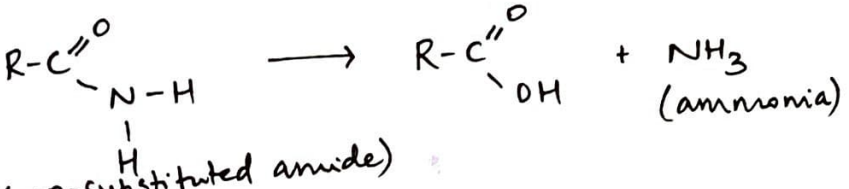
① HYDROLYSIS

↳ amide linkage broken

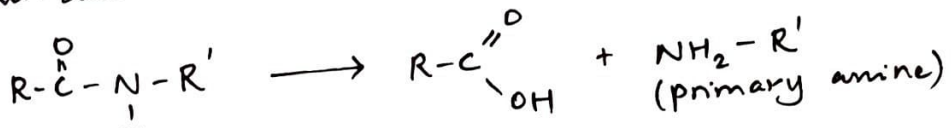
→ Hydrolysis of non-substituted amide → carboxylic acid + NH_3

→ Hydrolysis of substituted amide → carboxylic acid + primary amine

* Hydrolysis is done using aq. acid/alkali, and reflux.

(i) 

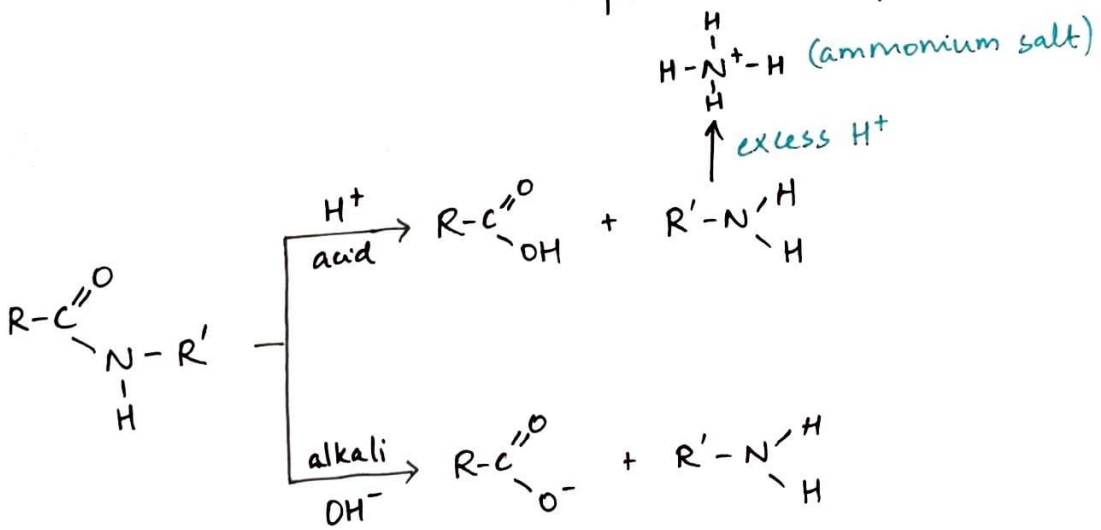
(non-substituted amide)

(ii) 

(Substituted amide)

When using excess acid/alkali:

- reflux w/ excess acid: NH_3 / primary amine will form ammonium salt.
- reflux w/ excess base: carboxylic acid produced will be deprotonated to form carboxylate ion.



② REDUCTION

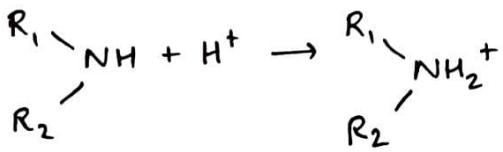
(pg. 24)

RELATIVE BASICITIES: AMMONIA, AMINES, AMIDES

- N atom of ammonia, amines & amides has lone pair of e^-.
- thus it can accept H^+ / proton.
- N atom donates lone pair of e^- to H^+ and forms dative bond w/ it.
- ∴ They act as bases in aq. solutions.

(i) $NH_3 + H^+ \longrightarrow NH_4^+$

(ii) $R\text{-}NH_2 + H^+ \longrightarrow R\text{-}NH_3^+$

(iii) 

- Strength of base depends on availability of lone pair of e^- on N atom for dative bond formation w/ H^+ ; more readily available ⇒ stronger base.

Amines

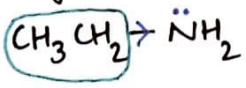
→ +I effect (electron-donating groups) : EDGs (eg. alkyl grps) donate electron density towards N atom, so lone pair of e^- more readily available for bond formation w/ H^+ ∴ Basicity↑.

→ Delocalisation (electron-withdrawing groups) : EWGs (eg. aromatic rings) cause delocalisation of electron density in π system of benzene ring, so lone pair of e^- less available for bond formation w/ H^+. ∴ Basicity↓.

Amides

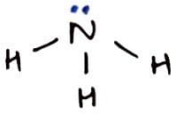
- electron-withdrawing O atom in amide group removes e^- density from N atom.
- lone pair of e^- on N atom less readily available for bond formation w/ H^+.
- ∴ much weaker bases than amines which don't have electron-withdrawing O atom.

Ethylamine



- +I effect of electron-donating alkyl group that donates e^- density to N atom
- lone pair of e^- on N more readily available for bond formation w/ H^+.

Ammonia



- no +I effect ∴ no electron-donating groups
- no delocalisation ∴ no aromatic ring.

Phenylamine

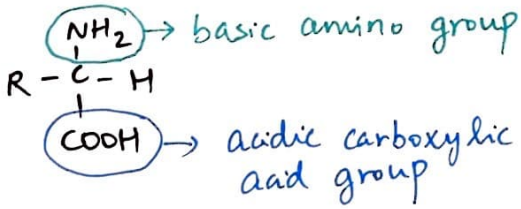
- delocalisation of lone pair of e^- on N into π system due to overlap.
- lone pair of e^- on N less available for bond formation w/ H^+.

Strongest base

↓

weakest base

ACIDIC / BASIC PROPERTIES OF AMINO ACIDS

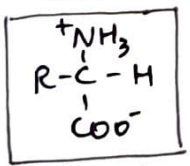


* R-group can be acidic / basic / neutral

Amino acids are <u>amphoteric</u>: have both acidic & basic groups ∴ can behave as both acids & bases.

Zwitterions

- amino acids interact intermolecularly to form <u>zwitterions</u>



ion which has both +ve & -ve charge (NH_3^+) (COO^-)

- due to charges in zwitterions, strong IMFs btwn amino acids ∴ they exist as soluble crystalline solids.

Isoelectric point

- aq. solution of amino acids = zwitterions w/ acidic & basic properties
  ↳ buffer solution ∴ it resists changes in pH when small amounts of acid/alkali added.

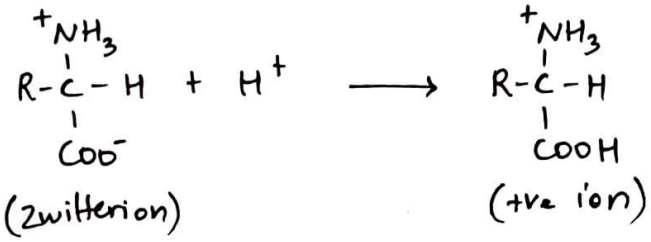
→ When acid added (pH lowered):

- COO^- part of zwitterion accepts H^+ to reform $-COOH$ group.
- Zwitterion → +ve charged ion.

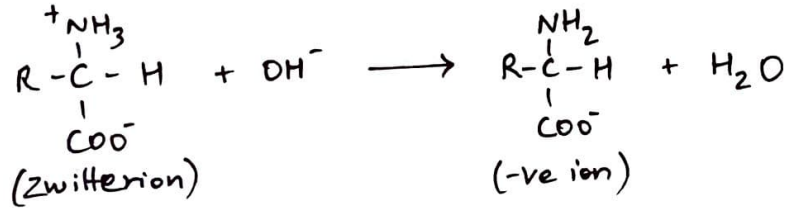
→ When alkali added (pH raised):

- NH_3^+ part of zwitterion donates H^+ to reform $-NH_2$ group.
- Zwitterion → -ve charged ion.

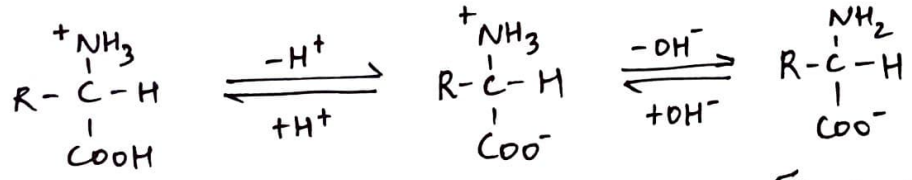
Isoelectric point = pH at which amino acid exists as neutral zwitterion (neither +ve or -ve charged ions dominate).



(Zwitterion) (+ve ion)



(Zwitterion) (-ve ion)



[low pH] [isoelectric point] [high pH]