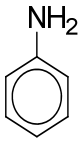
Victoria Junior College
Organic Chemistry Tutorial: Nitrogen Compounds [H2 Only]

SELF-CHECK EXERCISE

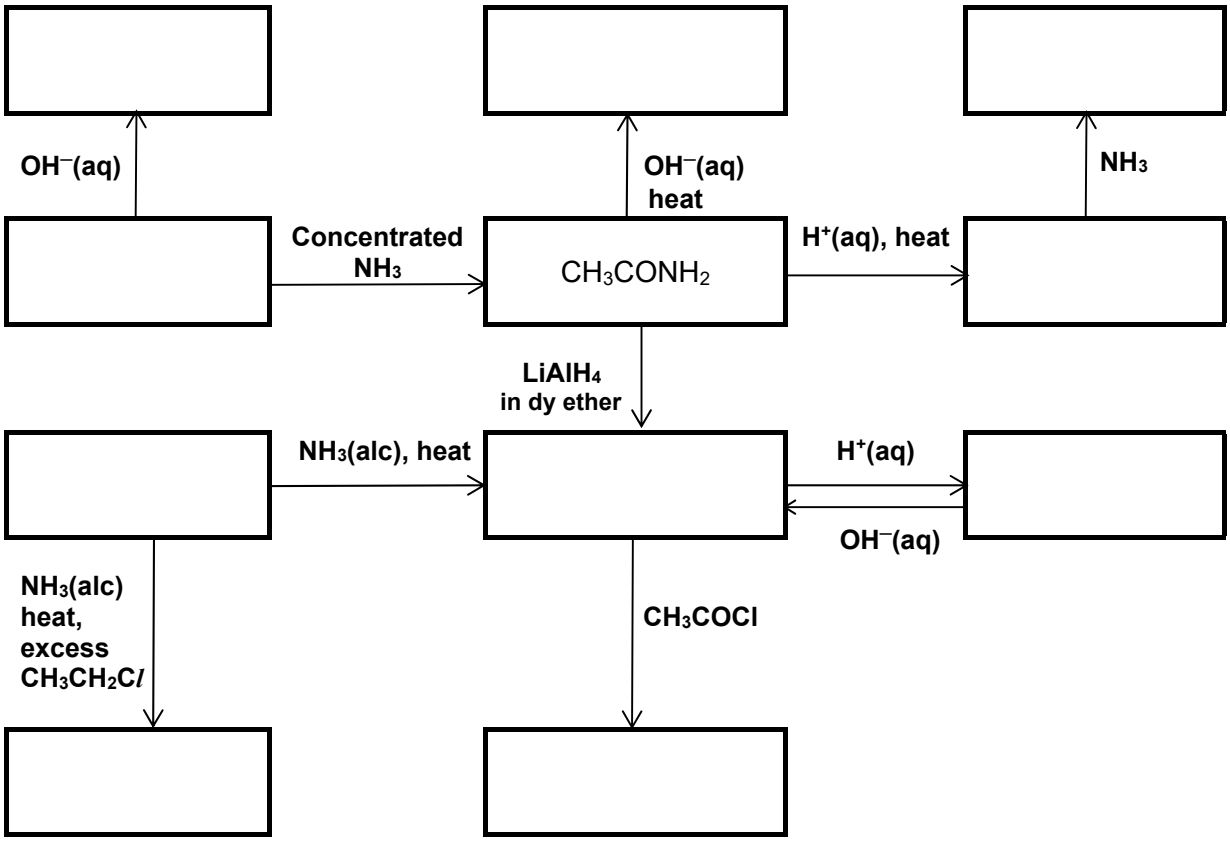
a) Complete the following tables.

Reactant	Reaction Type, Reagents & Conditions	Intermediate	Reaction Type, Reagents & Conditions	Products
	Nucleophilic substitution excess NH_3, heat in a sealed tube	CH_3**CH_2NH_2** ethylamine	**Nucleophilic substitution** $CH_3CH_2C\mathit{l}$, heat	
			Condensation $CH_3COC\mathit{l}$	
	Reduction • $LiA\mathit{l}H_4$ in dry ether		**Neutralisation** $HC\mathit{l}$	
	Reduction • H_2, Ni catalyst, heat • H_2, Pt catalyst • $LiA\mathit{l}H_4$ in dry ether		**Neutralisation** RCO_2H	

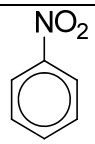
Reactant	Reaction Type, Reagents & Conditions	Intermediate	Reaction Type, Reagents & Conditions	Products
	Reduction Sn and concentrated $HC\mathit{l}$, heat then add alkali such as NaOH(aq)	 phenylamine	**Nucleophilic substitution** $CH_3CH_2C\mathit{l}$, heat	
			Condensation $CH_3COC\mathit{l}$	
			Neutralisation $HC\mathit{l}$	
			Electrophilic substitution Br_2(aq)	

Reactant	Reaction Type, Reagents & Conditions	Intermediate	Reaction Type, Reagents & Conditions	Products
	Nucleophilic substitution Concentrated NH_3	CH_3**CONH$_2$** ethanamide	**Acid hydrolysis** HC*l*(aq), heat	
			Base hydrolysis NaOH(aq), heat	
			Reduction LiA*l*H$_4$ in dry ether	

b) Write down the organic compounds in the following mind map.



c) Tick the functional groups that would be reduced.

Reducing agents	**Alkene**	**RCHO**	**RCOR**	**RCO_2H**	**$RCONH_2$**	**RCN**	 **Nitrobenzene**
$LiAlH_4$ in dry ether							
H_2, Pt							
$NaBH_4$ in methanol							
Sn in concentrated HCl, heat, followed by NaOH							

d) State the type of reactions that would occur.

Reagents & conditions	**Alkene**	**RX**	**1° or 2° ROH**	**RCHO**	**RCOR**	**RCO_2H**	**$RCONH_2$**	**RCN**	**RCOCl**
$KMnO_4$, H_2SO_4(aq), heat									
$K_2Cr_2O_7$, H_2SO_4(aq), heat									
OH^-(aq), heat									
H_2O									

Relative basicities of amines

*Recall: Based on **availability of lone pair of electrons** on N (as Lewis base)*

- *Basic strength **increases** when the **lone pair of electrons** on N is **more available** for donation to an acid.*
- *Factors that affect **availability of lone electron pair** on N:*
  - ***Inductive effect***
  - ***Delocalisation** (resonance effect)*
  - ***Steric hindrance** – block acid from approaching the N atom*

1 (a) Suggest and explain the relative basicities of methylamine and ethylamine in gaseous state in terms of Lewis bases.

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(b) Explain in terms of structures why ammonia is a stronger base than phenylamine but a weaker base than methylamine in aqueous state.

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(c) 4–methylphenylamine and benzylamine are isomers.

4-methylphenylamine benzylamine

(i) Suggest how the basicity of 4–methylphenylamine might compare to that of phenylamine, and how the basicity of benzylamine might compare to that of ethylamine. Give reasons for your answers.

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(ii) Suggest how bromine water could be used to distinguish between 4–methylphenylamine and benzylamine.

State any observations you would make with each compound, and write balanced equations for any reactions that might occur.

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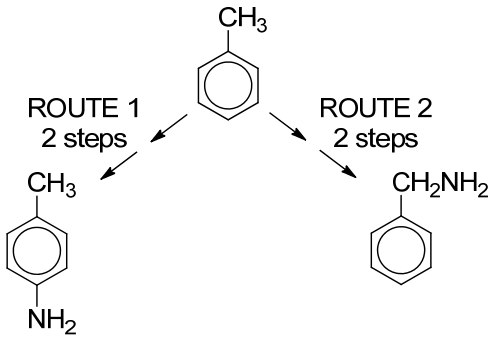
Each of these compounds can be made from methylbenzene in two steps.



(iii) State reagents and conditions for each of the two steps in these two routes, and give the structures of the intermediate compounds.

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(d) pK_b values of three amines in aqueous solution are shown below. Suggest and explain the relative basicity of these amines in **aqueous** solution.

Amines	pK_b
CH_3NH_2	3.34
$(CH_3)_2NH$	3.27
$(CH_3)_3N$	4.20

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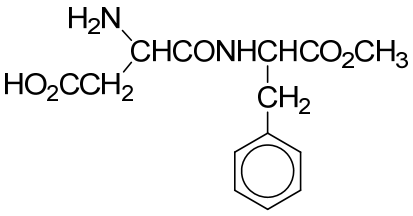
2 Why are amides, $RCONH_2$, less basic than amines, RNH_2?

A Amides form a zwitterion in which the nitrogen atom carries a positive charge.
B Amides have a resonance structure involving the movement of a pair of electrons from the nitrogen atom to the oxygen atom.
C Electrons on the nitrogen atom move on to the C–N bond giving it some double bond character so that it is more difficult to break.
D The amide carbonyl group withdraws electrons from the NH_2 group to make the hydrogen atoms acidic.

3 Which compounds liberate ammonia when boiled with aqueous sodium hydroxide?

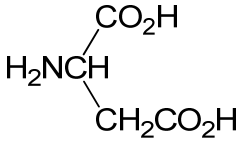
1 $CH_3CH_2NH_2$
2 $CH_3CH_2CONH_2$
3 $CH_3CH_2CO_2NH_4$

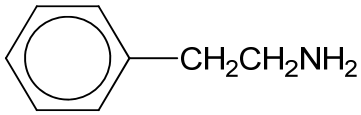
4 *Aspartame* is widely used as a sweetener in canned drinks.



Aspartame

Which compound would be a product of its hydrolysis?

A CH_3CO_2H
B $HO_2CCH_2CO_2H$
C


D


5(a) Describe the conditions needed to hydrolyse amides in the laboratory.

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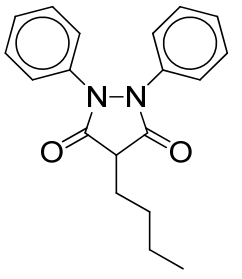
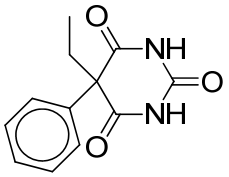
(b) Predict the products of the hydrolysis of the amide groups in the following two drugs.



phenylbutazone



phenobarbital

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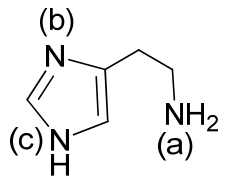
6(a) (i) Histamine is structurally similar to histidine in that it also contains the planar imidazole ring. Suggest the type of hybrid orbitals the lone pair of electrons occupy on N labelled (a) and (b). Hence, account for their relative basicity.

You may assume that the NH in the imidazole ring is inert.



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(ii) Hence, predict the structural formula of the organic product formed when 1 mol of histamine reacts with

(I) 1 mol of HC*l*(aq)

(II) 2 mol of HBr(aq)

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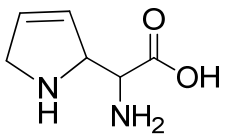
(b) Like histidine, compound **A** contains a 5–membered ring with more than one kind of atom.



Compound **A**

Draw the structural formula of the organic products formed when compound **A** is treated with the following reagents and state clearly the type of reaction that has taken place.

(i) hot $NaMnO_4$ / NaOH(aq)

(ii) ethanoyl chloride

7 The R group of aspartic acid is $–CH_2CO_2H$. The three pK_a values associated with aspartic acid are 1.88, 3.65 and 9.60. Which form would be predominant at pH 2.7?

A $H_2NCH(CH_2CO_2^-)CO_2^-$
B $H_3N^+CH(CH_2CO_2^-)CO_2^-$
C $H_3N^+CH(CH_2CO_2H)CO_2^-$
D $H_3N^+CH(CH_2CO_2H)CO_2H$

8 An amino acid residue of structure $H_2NCH(CH_2CO_2H)CO_2H$ was isolated after partial hydrolysis of an animal protein. Which form would be predominant at pH 12?

A $H_2NCH(CH_2CO_2^-)CO_2^-$
B $H_3N^+CH(CH_2CO_2^-)CO_2^-$
C $H_3N^+CH(CH_2CO_2H)CO_2^-$
D $H_3N^+CH(CH_2CO_2H)CO_2H$

9 The sequence of amino acids (primary structure) of a polypeptide **A** can be determined by analysing the fragments obtained from different enzymatic hydrolysis.

The following fragments were obtained when **A** was hydrolysed using enzyme chymotrypsin which digests proteins at carboxylic acid end of phenylalanine, phe.
gly – lys – phe
val – lys – phe
tyr – asp

Another enzyme trpsin digests at carboxylic acid end of lysine, lys, gave the following fragments.
val – lys
phe – tyr – asp
phe – gly – lys

Deduce the sequence of amino acids (primary structure) of **A**.

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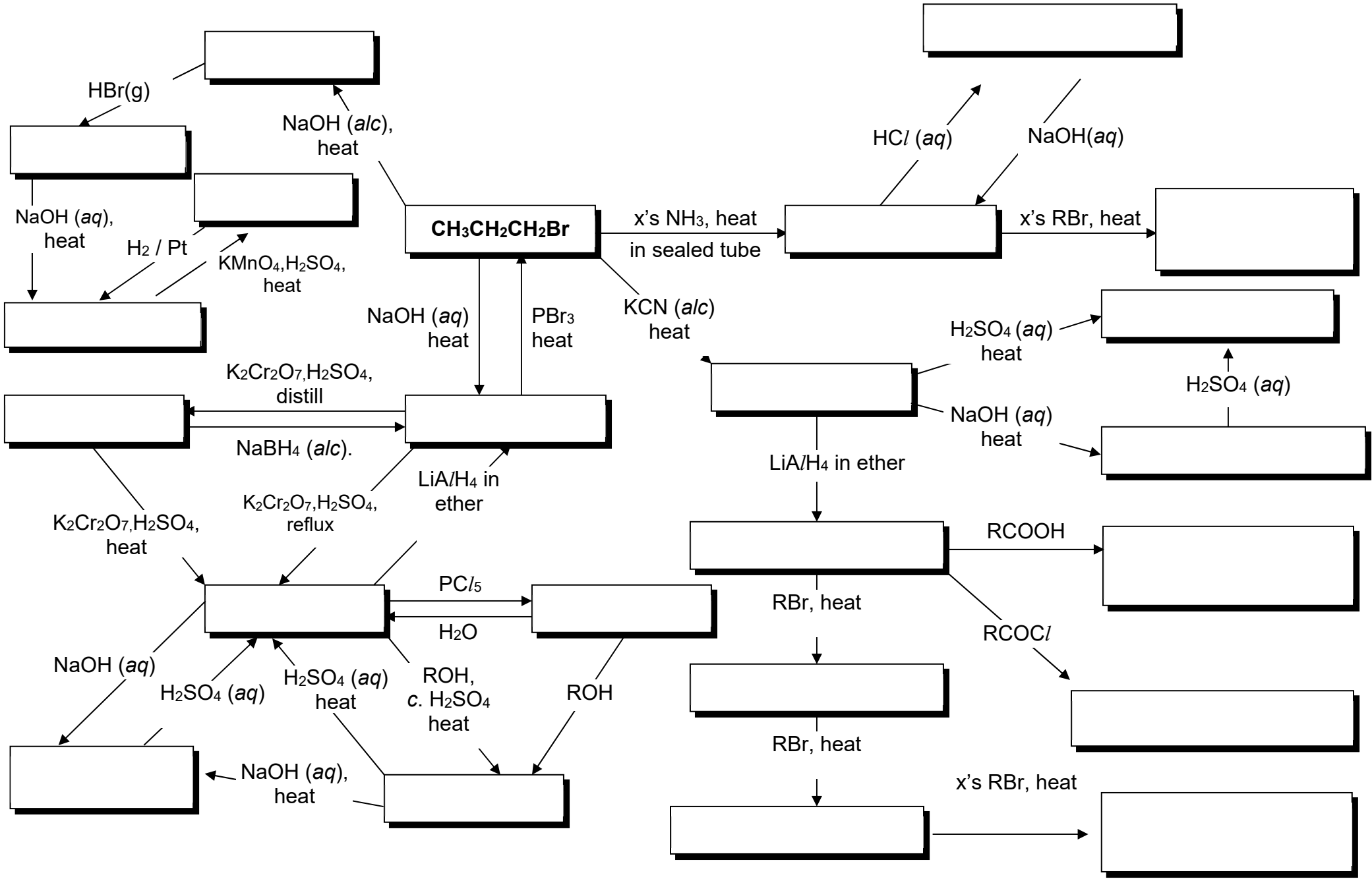
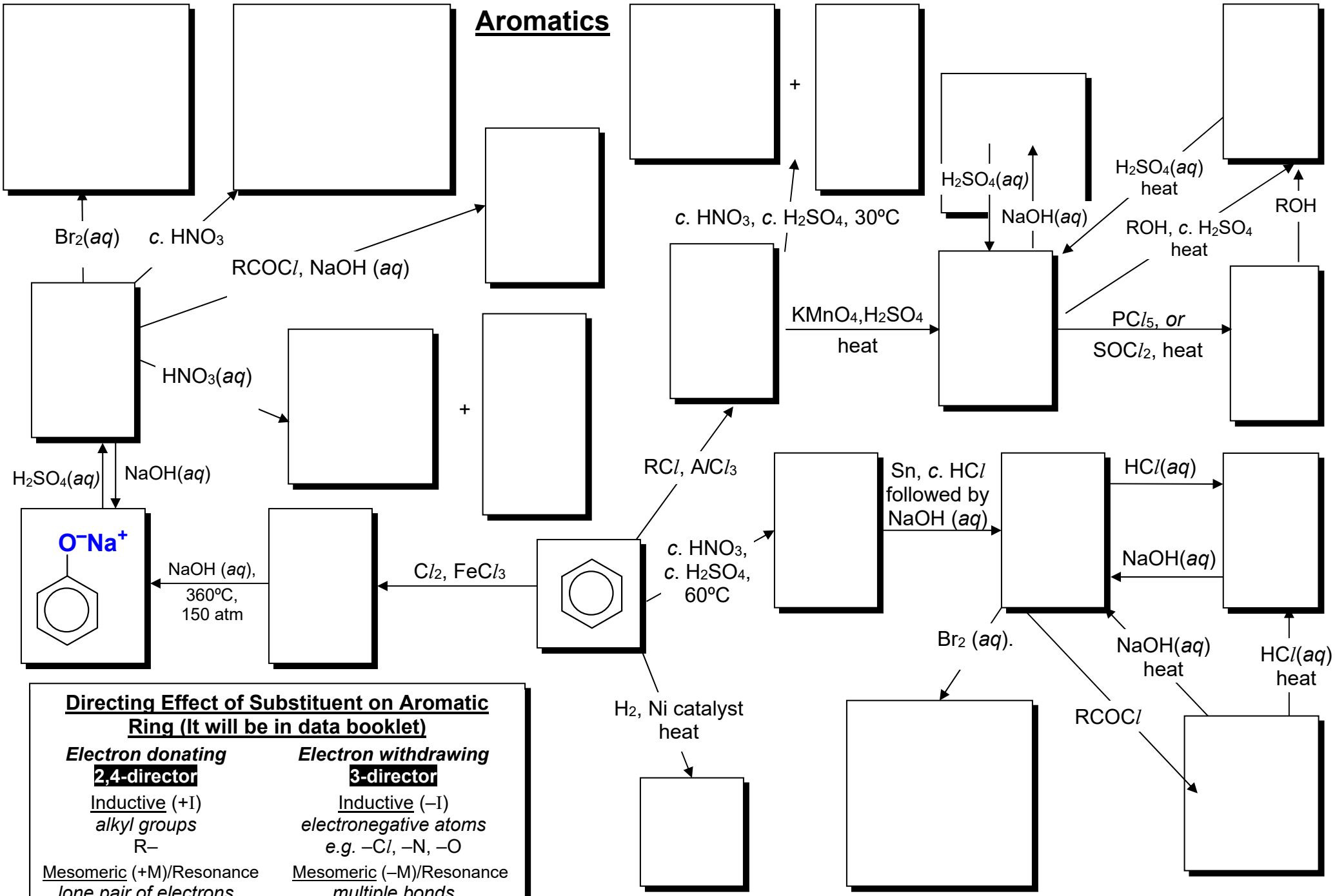
Reactions of Alkyl halides, Alcohols, Carboxylic acids and its derivatives, Amines



Aromatics



Directing Effect of Substituent on Aromatic Ring (It will be in data booklet)

Electron donating **2,4-director**	***Electron withdrawing*** **3-director**
Inductive (+I)	Inductive (–I)
alkyl groups	*electronegative atoms*
R–	*e.g.* –Cl, –N, –O
Mesomeric (+M)/Resonance	Mesomeric (–M)/Resonance
lone pair of electrons	*multiple bonds*
e.g. –Cl, –OH, –NH_2	*e.g.* –C≡N, –NO_2, –C(=O)–

SUPPLEMENTARY QUESTIONS

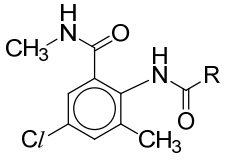
1 A manufacturer needs a stronger base than methylamine, CH_3NH_2 to add to a cleansing fluid.

Which of the following could be appropriate?

A $(CH_3)_2NH$ **B** $H_2NCH_2CO_2H$
C CH_3CONH_2 **D** $C_6H_5NH_2$

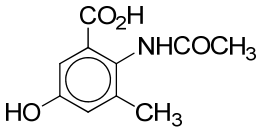
2 An insecticide, **J**, has been developed for killing pests that attack fruit such as grapes, apples and peaches. Its structure is shown below, where R is an inert group.

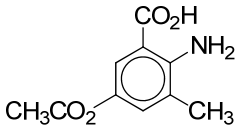
J is heated with aqueous NaOH under reflux, the solution neutralised and the product **K** isolated. **K** is then warmed with CH_3COCl in an inert solvent, to give **L**.

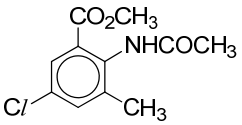


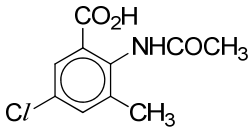
J

What is the final product **L**?

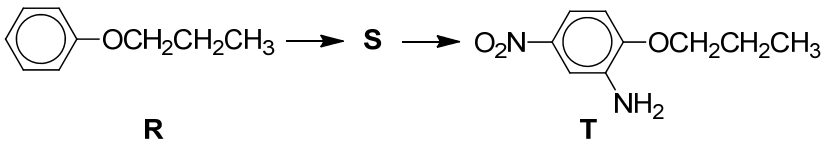
A


B


C


D


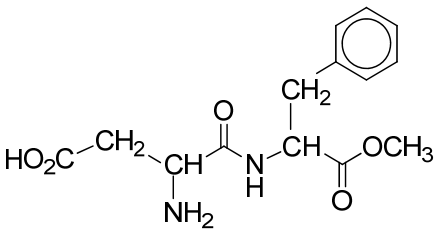
3(a) 5–nitro–2–propoxyphenylamine, **T**, is an artificial sweetening agent which is 4000 times as sweet as sucrose. It can be made from propoxybenzene, **R**.



R **T**

Suggest a two–stage synthesis of **T** starting from propoxybenzene, **R**, identifying the intermediate compound **S**. The reactivity of propoxybenzene is similar to that of phenol.

(b) Aspartame is another artificial sweetening agent, used in soft drinks and other foodstuffs.



aspartame

(i) Name the four functional groups in aspartame, other than the phenyl group.

(ii) When treated with hot NaOH(aq), aspartame is broken down into three other compounds. Draw their structural formulae.

(iii) Draw the structural formulae of the compounds formed when aspartame is treated with

- cold HC*l*(aq)
- CH_3COCl

4 This question is about compound **K**, C_6H_7ON, which is formed when phenylhydroxylamine, C_6H_5NHOH, is warmed with dilute sulfuric acid.

- Compound **K** is not very soluble in water, but dissolves in HC*l*(aq).
- It also dissolves in NaOH(aq), but not in Na_2CO_3(aq).
- On reaction with 1 mol of ethanoyl chloride, CH_3COCl, **K** forms compound **L**, $C_8H_9O_2N$.

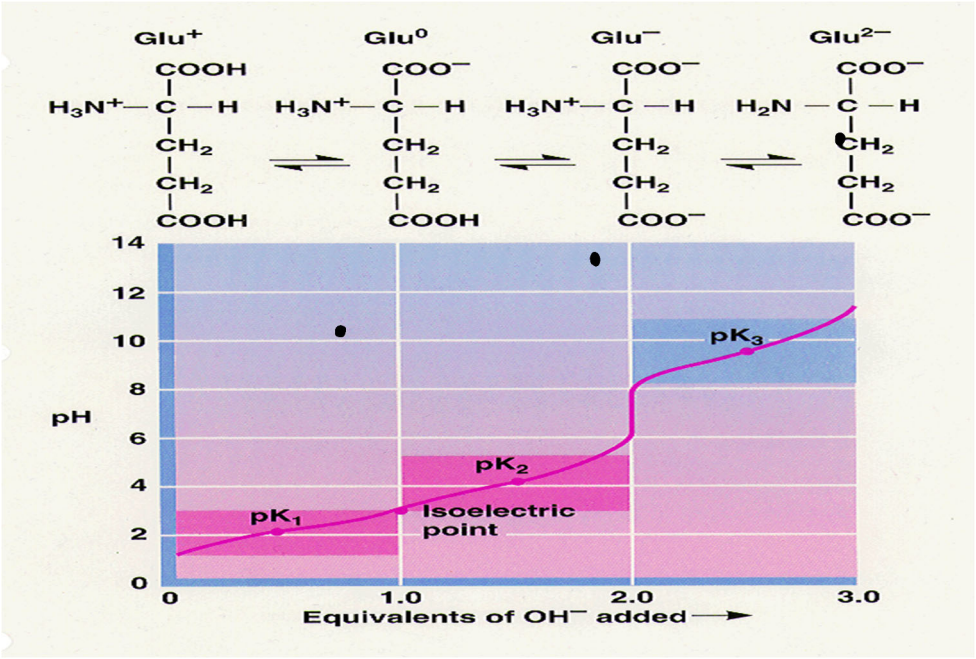
L is no longer soluble in HC*l*(aq), but is still soluble in NaOH(aq). On reaction with Br_2(aq), **L** produces compound **M**, $C_8H_7O_2NBr_2$. When **K** is reacted with 2 mol of ethanoyl chloride, it produces compound **N**, $C_{10}H_{11}O_3N$, which is not soluble in either HC*l*(aq) or NaOH(aq).

Compound **K** can be synthesised by treating phenol with dilute nitric acid, followed by reaction with zinc metal and hydrochloric acid.

Deduce the structures of compounds **K**, **L**, **M** and **N**. Explain the chemistry of the reactions described, writing equations where appropriate. [There is no need to comment on the chemistry of the formation of **K** from phenylhydroxylamine.]

[Refer to page 25 of the notes. You can approach this problem from the angle of a tribasic acid titration]

5 Below is the titration curve when 1 mol dm^{-3} NaOH is added to 1 mol dm^{-3} of fully protonated glutamic acid, **Glu**$^+$, $H_3N^+CH(CH_2CH_2CO_2H)CO_2H$ of the same molar concentration.



(a) Suggest the structure of the predominant species of glutamic acid at the following pH values.

- pH 1
- pH 3
- pH 7
- pH 12

(b) Give the structure of the species present when the following amount of NaOH is added to **one mole** of fully protonated glutamic acid. Suggest a value for the pH of the resulting solution and state the direction the amino acid will migrate during electrophoresis.

- 1 mol
- 2 mol
- 3 mol