

## ORGANIC REACTIONS AND SYNTHESIS OF DRUG MOLECULE

### 1 Mark

#### Easy

1. Write the name of one reagent which is used to oxidise alcohols to acids.

Potassium permanganate ( $\text{KMnO}_4$ )

2. What is the reactivity order of alkyl halide in  $\text{S}_\text{N}2$  mechanism?

$\text{MeX} > 1^\circ > 2^\circ > 3^\circ$ .

3. In  $\text{S}_\text{N}1$  type reaction which type of solvent is used?

In  $\text{S}_\text{N}1$  reaction polar aprotic solvent is used.

#### Moderate

1. Hydrolysis of Isopropyl chloride follows which type of mechanism?

It follows both  $\text{S}_\text{N}1$  and  $\text{S}_\text{N}2$  mechanism.

2. What is the hybridization of carbon atom in carrying the negative charge?

$\text{Sp}^3$  hybridization.

#### Hard

1. What are the important characteristics of a nucleophile?

Nucleophile must have lone pair of electrons.

### 5 Mark

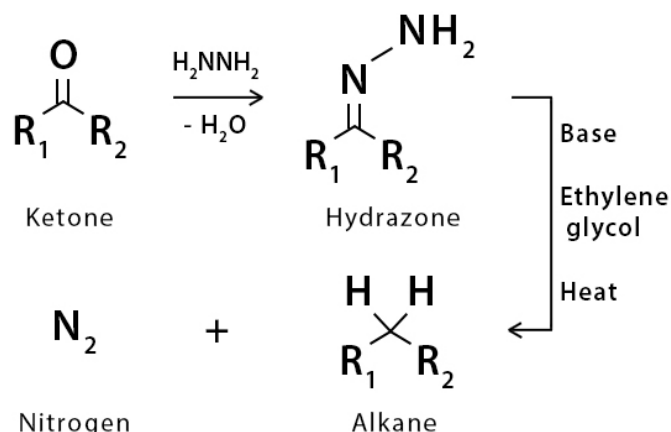
#### Easy

1. Explain the following reactions with a suitable example:

(a) Wolff – Kishner Reaction 3

(b) Cannizzaro Reaction 2

(a) Wolff – Kishner Reduction: In this reaction, ketone initially reacts with hydrazine to produce hydrazone which on heating in presence of  $\text{KOH}$  or  $\text{C}_2\text{H}_5\text{OH}$  in ethylene glycol solvent yields propane.

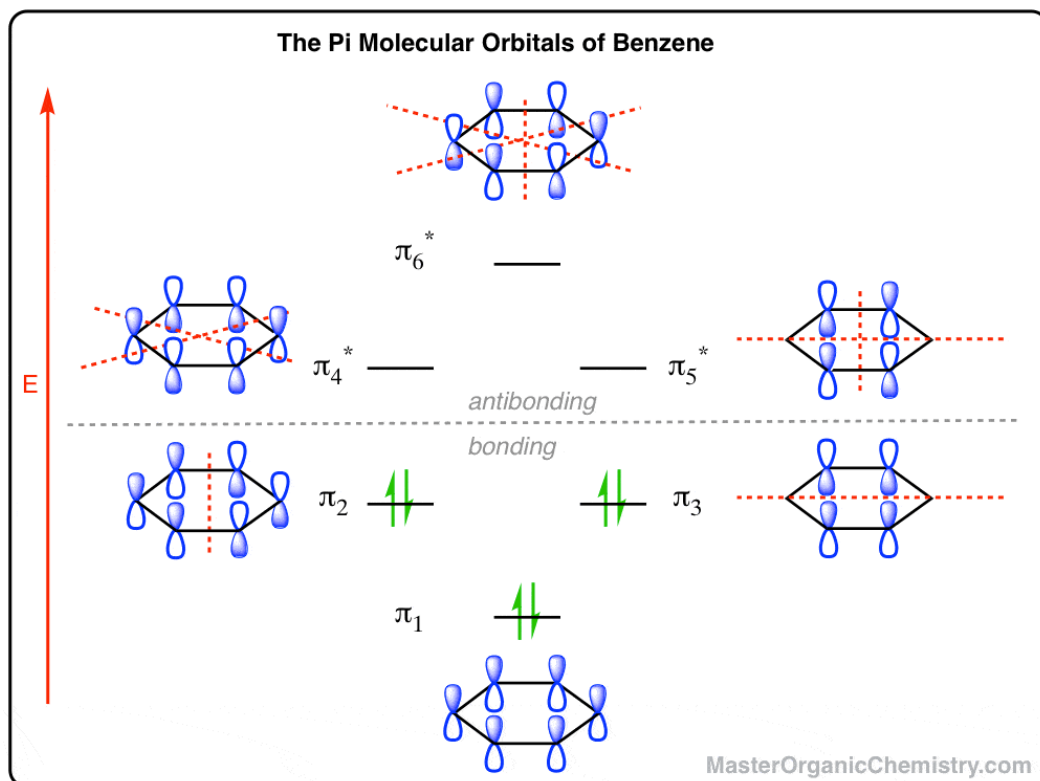


(b) Cannizzaro Reaction: Aldehydes having no  $\alpha$ -hydrogen undergo self-oxidation reduction reaction in presence of strong base like ethanoic  $\text{KOH}$  to produce corresponding acid and alcohol. This is called Cannizzaro reaction.

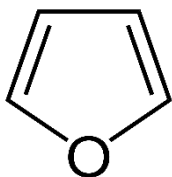
Example: Reaction between two formaldehyde molecules (having no  $\alpha$ -hydrogen) produce sodium or potassium formate and methyl alcohol in presence of 50% ethanoic  $\text{NaOH}$  or  $\text{KOH}$  solution.



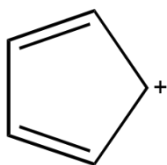
(a)  $\pi$  – molecular orbital diagram of Benzene



Furan: Furan is an aromatic heterocyclic compound with  $6\pi$  electrons. It is a planar cyclic system.



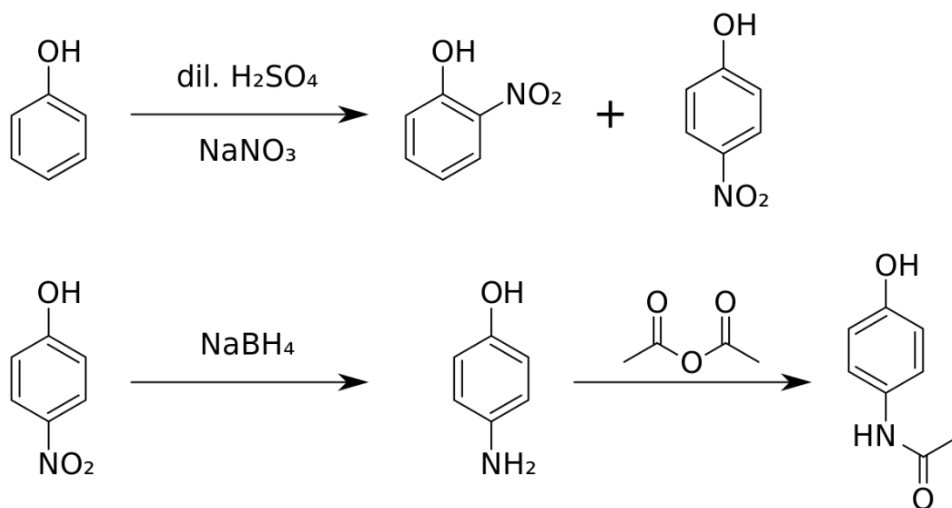
Cyclopentadienyl cation: Cyclopentadienyl cation is an aromatic heterocyclic system with positive charge. It is a  $2\pi$  – electron system.  $[(4n + 2)\pi$  electrons, where  $n = 0$ ]



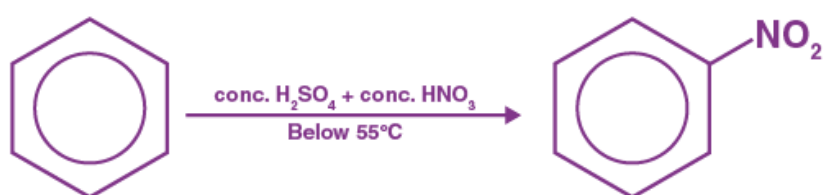
(b) Synthesis of paracetamol: Paracetamol is synthesized by nitration of phenol using sodium nitrate which yields a mixture of ortho and para nitro phenol, from which para nitrophenol (b. p.  $279^\circ\text{C}$ ) is separated out by steam distillation. Nitration in phenol is an electrophilic substitution and requires mild conditions as compared to nitration in benzene as phenol's oxygen is highly activating. The nitro group of para nitro phenol is then reduced to para amino phenol. At the final stage, the amino group is acetylated using acetic anhydride. For the reduction of the nitro group, sodium borohydride is used in the laboratory, but for industrial production, direct hydrogenation is used.

Medical Utility:

Paracetamol is used to give relief from fever caused by common cold, influenza, viral infection. It also helps to get relief from muscle pain, sinus pain etc.

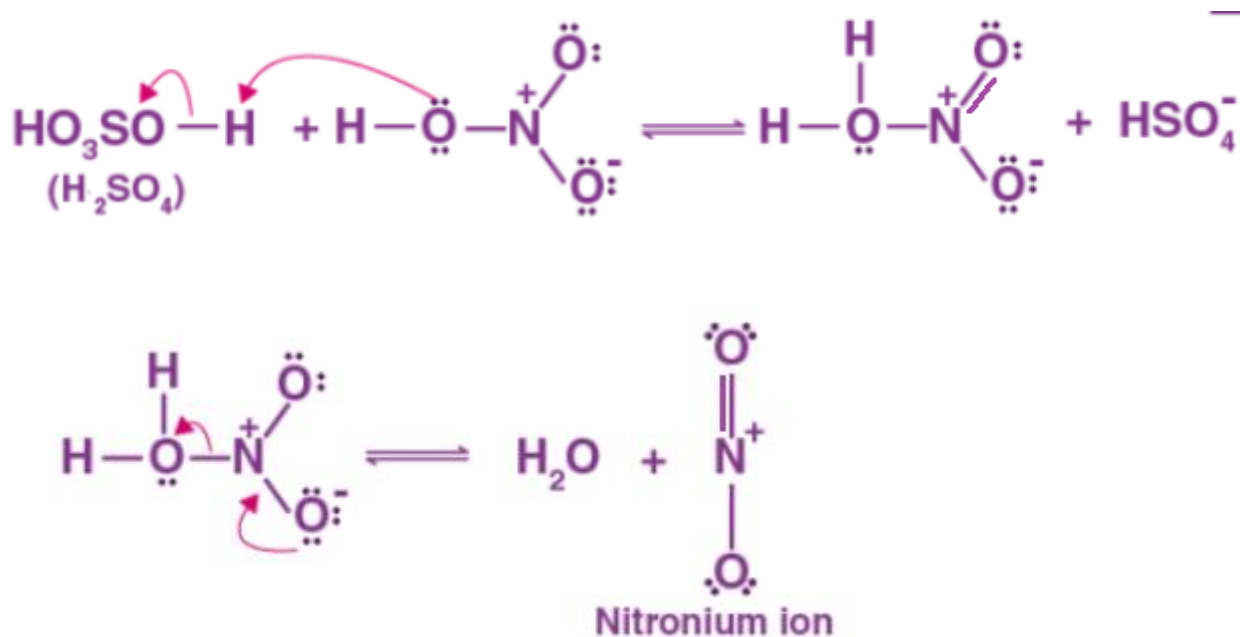


(c) Benzene reacts with concentrated nitric acid at 323-333K in the presence of concentrated [sulphuric acid](#) to form nitrobenzene. This reaction is known as nitration of benzene.

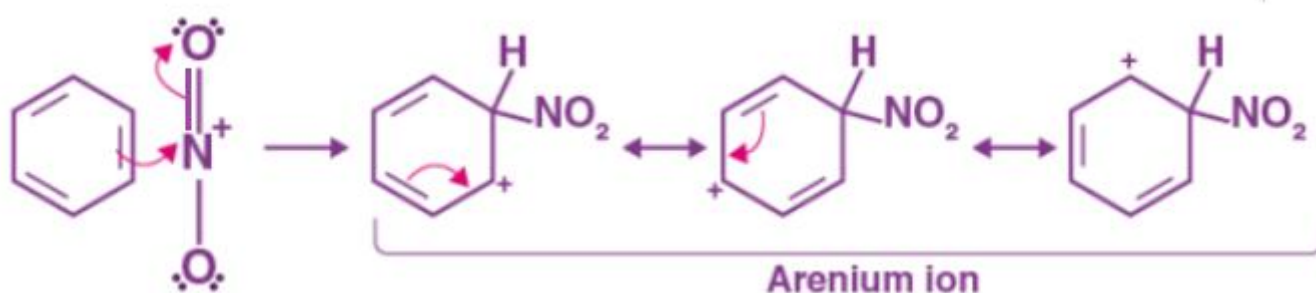


Mechanism of nitration of benzene:

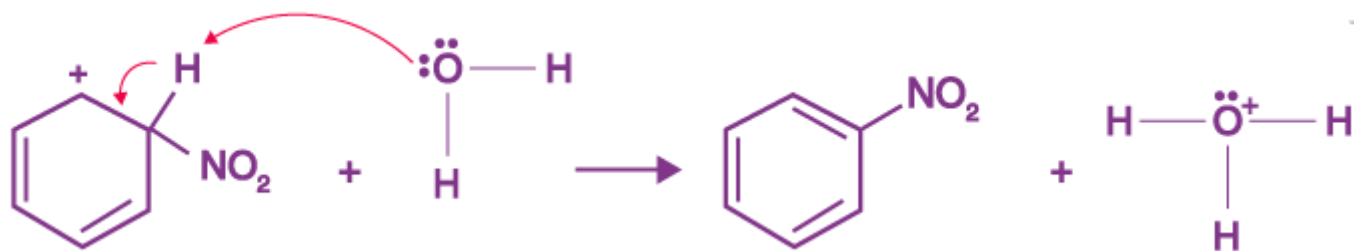
**Step 1:** Nitric acid accepts a proton from sulphuric acid and then dissociates to form nitronium ion.



**Step 2:** The nitronium ion acts as an electrophile in the process which further reacts with benzene to form an arenium ion.



**Step 3:** The arenium ion then loses its proton to Lewis base forming nitrobenzene.



**Moderate:**

1. (a) Write notes on synthesis of aspirin. What is its medical utility? 5

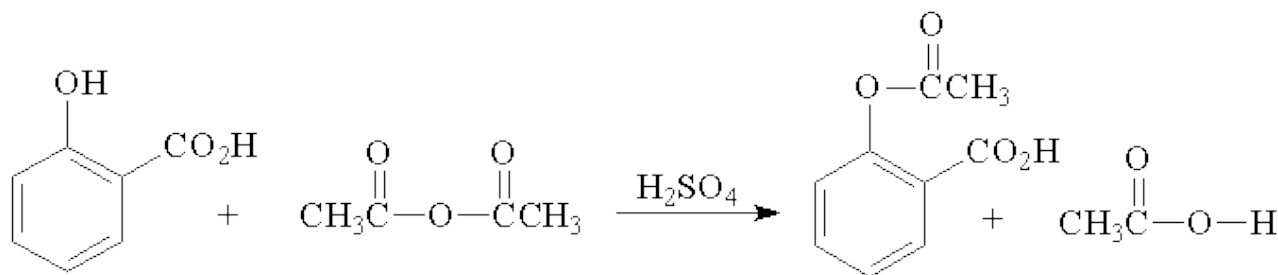
(b) Explain why – (i) p- nitrophenol has higher boiling point than o – nitrophenol.

(ii) The amino group in aniline is o – and p – directing but the amine group is meta directing. 6

(c) What products are obtained when (i) Toluene is treated with alkaline  $\text{KMnO}_4$  (ii) Benzoic acid treated with lithium aluminium hydride. 4

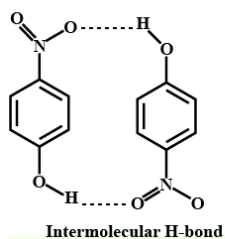
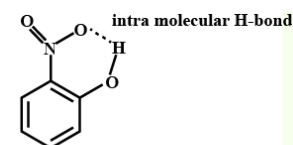
(a) Synthesis of Aspirin: The chemical name of Aspirin is 2 – acetoxybenzoic acid or acetylsalicylic acid. Aspirin is an analgesic and used to get relief from pain without causing any significant disturbance in our nervous system.

Synthesis: Aspirin is synthesised by treating salicylic acid with acetic anhydride in presence of a strong acid like  $\text{H}_3\text{PO}_4$  which acts as catalyst. The result of this reaction is acetylsalicylic acid or aspirin and acetic acid is released as by product of the reaction. Aspirin is sparingly soluble in water and therefore gets precipitated on addition of water. Under this process the hydroxyl group ( - OH ) of the salicylic acid turns into ester group ( - OCOCH<sub>3</sub> ).



Medical Utility: Aspirin is generally used to treat fever, headache and inflammatory diseases like rheumatoid arthritis. It is also as an analgesic for acute pain.

(b) (i)



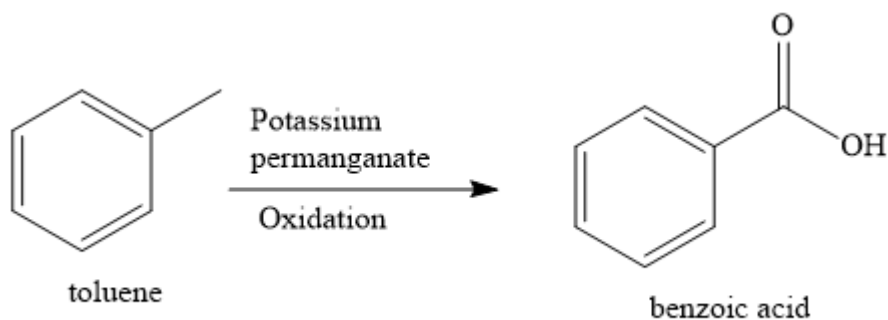
O-nitrophenol has intramolecular hydrogen bonding. P-nitrophenol has intermolecular hydrogen bonding. Intermolecular hydrogen bonding leads to a molecular association. This increases boiling point. Hence, O-nitrophenol has a lower boiling point than P-nitrophenol.

(ii) In aniline  $\text{NH}_2$  increases e density at o- and p- positions due to +R effect. But when it is nitrated by nitrating mixture, a substantial amount of m-nitro aniline is formed.

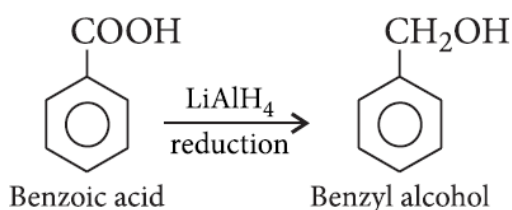
But in acidic medium (Nitrating mixture -  $\text{HNO}_3(\text{c}) + \text{H}_2\text{SO}_4(\text{c})$ ).

$\text{NH}_2 + \text{H}^+ \rightleftharpoons \text{NH}_3^+$  is  $e^-$  withdrawing group and so is m - directing. So gives larger amount of m- nitroaniline.

(c) (i) When toluene (methyl benzene) is oxidized with alkaline potassium permanganate solution, benzoic acid product is obtained. The aliphatic methyl group is oxidized to the aromatic carboxylic functional group.



(ii) Benzoic acid can be reduced to benzyl alcohol by lithium aluminium hydride.



### **Hard:**

1. (a) Arrange  $\text{C}_6\text{H}_5\text{CHO}$ ,  $\text{C}_6\text{H}_5\text{COCH}_3$ ,  $\text{C}_6\text{H}_5\text{CO C}_6\text{H}_5$  in decreasing order of reactivity towards nucleophile addition reactions. Which of the species  $\text{NO}^+$ ,  $\text{CCl}_4$ ,  $\text{CH}_3$ ,  $\text{CN}^-$  is a nucleophile? 4 + 1

(b) Free radicals are paramagnetic, but carbonium ions and carbanions are diamagnetic. What is the main product of reaction of alkyl halide and potassium nitrite? 2 + 3

(c) The treatment of alkyl chloride with aqueous KOH leads to the formation of alcohols, whereas in the presence of alc. KOH, alkenes are formed as the major products. Explain. Name two acylating agents and their structure. 3 + 2

(a)  $\text{C}_6\text{H}_5\text{CHO} > \text{C}_6\text{H}_5\text{COCH}_3 > \text{C}_6\text{H}_5\text{CO C}_6\text{H}_5$

Reasons: (i) Benzene ring causes the electron – donating resonance effect (+ M effect); while the alkyl group causes the electron – donating inductive effect (+I). So both these group increases the electron density on the carbonyl carbon and, therefore, reduces the positive charge on the carbonyl carbon, thereby tendency of nucleophilic attack is reduced. Hence  $\text{C}_6\text{H}_5\text{CHO}$  is more reactive towards nucleophiles than  $\text{C}_6\text{H}_5\text{COCH}_3$  and  $\text{C}_6\text{H}_5\text{CO C}_6\text{H}_5$ .

(ii) The +I effect of alkyl group is weaker than +M effect of benzene ring. In other words, -  $\text{CH}_3$  group reduces the positive charge on the carbonyl caused by -  $\text{C}_6\text{H}_5$  group. Hence  $\text{C}_6\text{H}_5\text{COCH}_3$  is more reactive towards nucleophiles than  $\text{C}_6\text{H}_5\text{CO C}_6\text{H}_5$ .

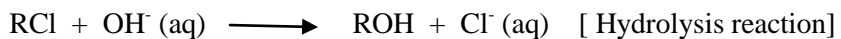
$\text{CN}^-$  is a nucleophile, since it has lone – pairs of electrons on both N atom and C atom.

(b) Free radicals possess odd electrons in them and are, therefore, paramagnetic in nature. While carbonium ion and carbanions have no unpaired electron in them and are diamagnetic.

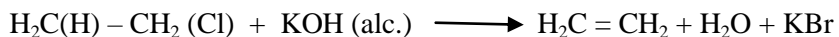
Alkyl nitrite, since  $\text{O}^- - \text{N} = \text{O}$  is an important ambident nucleophile.



(c) Aqueous KOH contains only  $\text{OH}^-$  ions, which act as nucleophile and these brings about hydrolysis of alkyl chloride to the corresponding alcohol.

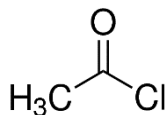


On the other hand, alcoholic KOH, contains ethoxy ions ( $\text{C}_2\text{H}_5\text{O}^-$ ), which are more than  $\text{OH}^-$  ions. Consequently, ethoxy ion preferentially bring about dehydrohalogenation to form alkenes.



On the other hand, in haloarenes ( $\text{Ar} - \text{X}$ ), the halogen atom releases electron to the benzene nucleus through resonance, thereby making ortho and para positions of benzene nucleus relatively electron – rich w.r.t. halogen atom. As a result, the electrophile attacks at ortho or para position. Hence, haloarenes undergo electrophilic substitution reaction.

Acylating agent : Acetyl Chloride



Acetic anhydride.

