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 ($KMnO_4$)

2. What is the reactivity order of alkyl halide in SN2 mechanism?

MeX > 1º > 2º > 3º.

3. In SN1 type reaction which type of solvent is used?

In SN1 reaction polar aprotic solvent is uned.

Moderate

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

It follows both SN1 and SN2 mechanism.

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

Sp^3 hybridization.

Hard

1. What is the important characteristics having a nucleophile?

Nucleophile must have lone pair of electrons.

5 Mark

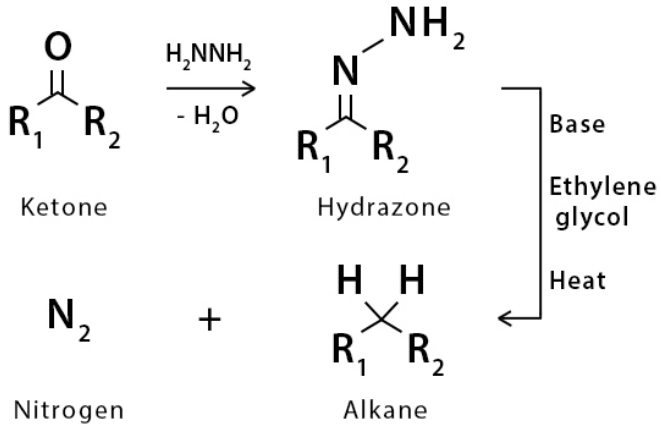
Easy

1. Explain the following reactions with a suitable example:

(a) Wolff – Kishner Reaction 3

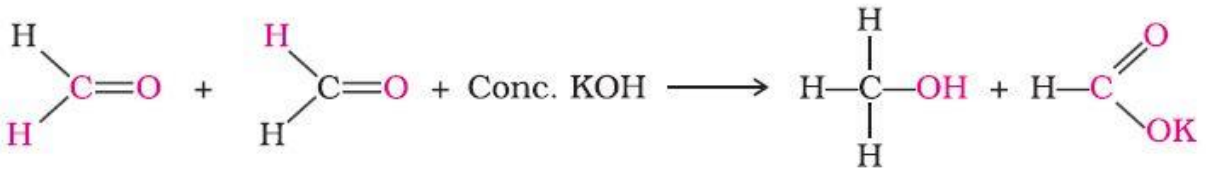
(b) Cannizzaro Reaction 2

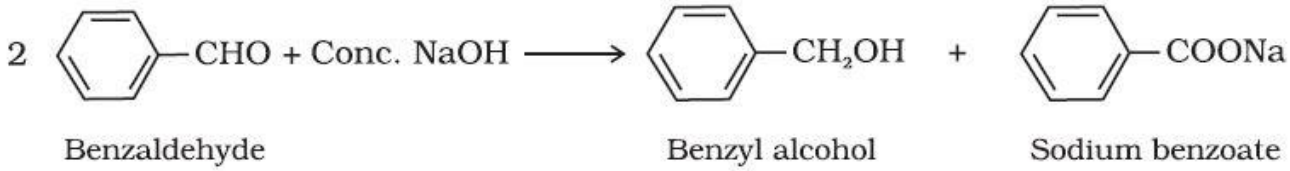
(a) Wolff – Kishner Reduction: In this reaction, ketone initially reacts with hydrazine to produce hydrazine which on heating in presence of KOH or C_2H_5OH in ethylene glycol solvent yields propane.



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

Example: Reaction between two formaldehyde molecules (having no α – hydrogen) produce sodium or potassium formate and methyl alcohol in presence of 50% ethanoic NaOH or KOH solution.





Moderate

1. What are the differences in between SN1 and SN2 reactions? Between $CH_3CH_2CH_2Cl$ and CH_3OCH_2Cl which would react faster in SN1 solvolysis?

Differences between SN1 and SN2 reactions:

SN1 Reaction	SN2 Reaction
It is a first order process and follows first order rate law.	It is a bimolecular process and follows second order rate law
Nucleophilic attack can take place from either side of the positively charged carbon atom.	Nucleophilic attack takes place from back side of the carbon atom bearing the leaving group.
Recimic mixture of the product is obtained but no inversion occurs.	Inversion of configuration takes place but no racemic mixture is obtained in the product.
It is favoured by the polar solvent.	It is favoured by the non polar solvent.
Low concentration of nucleophile favours the SN1 process.	High concentration of nucleophile favours the SN2 process.

Between $CH_3CH_2CH_2Cl$ and CH_3OCH_2Cl, the first compound would react faster in SN1 solvolysis. The reaction is, $CH_3CH_2CH_2Cl$ will produce stabler carbocation in step I compared to CH_3OCH_2Cl

$CH_3CH_2CH_2Cl \longrightarrow CH_3CH_2CH_2^+ + Cl^-$ (slow, rate determining step)

$CH_3CH_2CH_2^+ \longrightarrow CH_3CH^+CH_3$

The above compound can get internal rearrangement via 1 – 2 proton shift to produce stabler 2º carbocation.

$CH_3OCH_2Cl \longrightarrow CH_3OCH_2^+ + Cl$ (unstable 1º carbocation)

The second compound producing unstable 1º Carbocation and unable to rearrange itself to produce stabler carbocation.

15 Mark

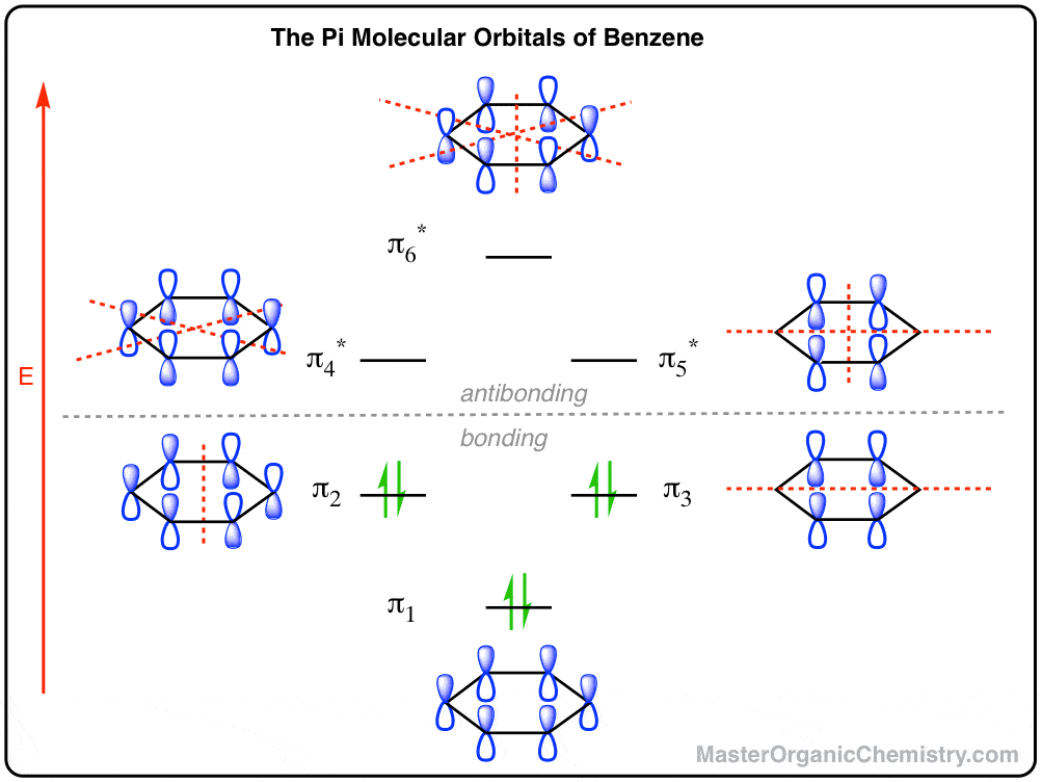
Easy

1. (a) Draw the π – molecular orbital diagram of Benzene. Predict whether the following compounds are aromatic, anti – aromatic or anti – aromatic: (i) Furan, (ii) Cyclopentadienyl cation. 5

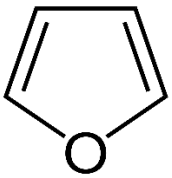
(b) Write notes on Synthesis of paracetamol. 5

(c) Nitration is also in absence of H_2SO_4 yet H_2SO_4 has no effect on benzene under the conditions employed. Show the mechanism of nitration of benzene. 5

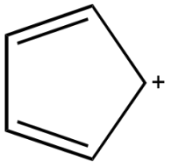
(a) π – molecular orbital diagram of Benzene



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



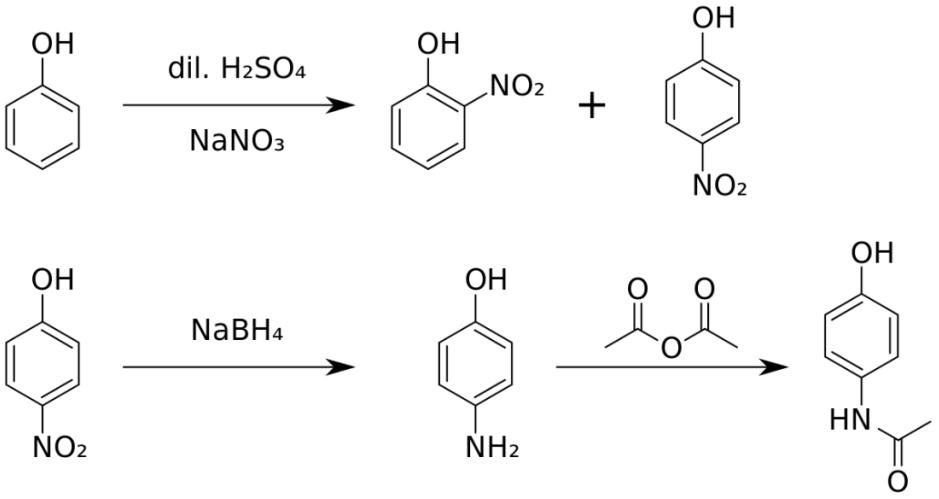
Cyclopentadienyl cation: Cyclopentadienyl cation is an aromatic heterocyclic system with positive charge. It is a 2π – electron system. [(4n + 2)π electrons, where n = 0]



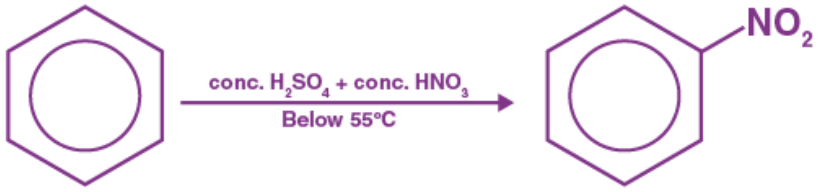
(b) Synthesis of paracetamol: Paracetamol is synthesized by nitration of phenol using sodium nitrate which yields a mixture of ortho and para nitro phenol, from which para nitrophenol (b. p. 279ºC) is separated out by steam distillation. Nitration in phenol is an electrophilic substitution and requires 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.

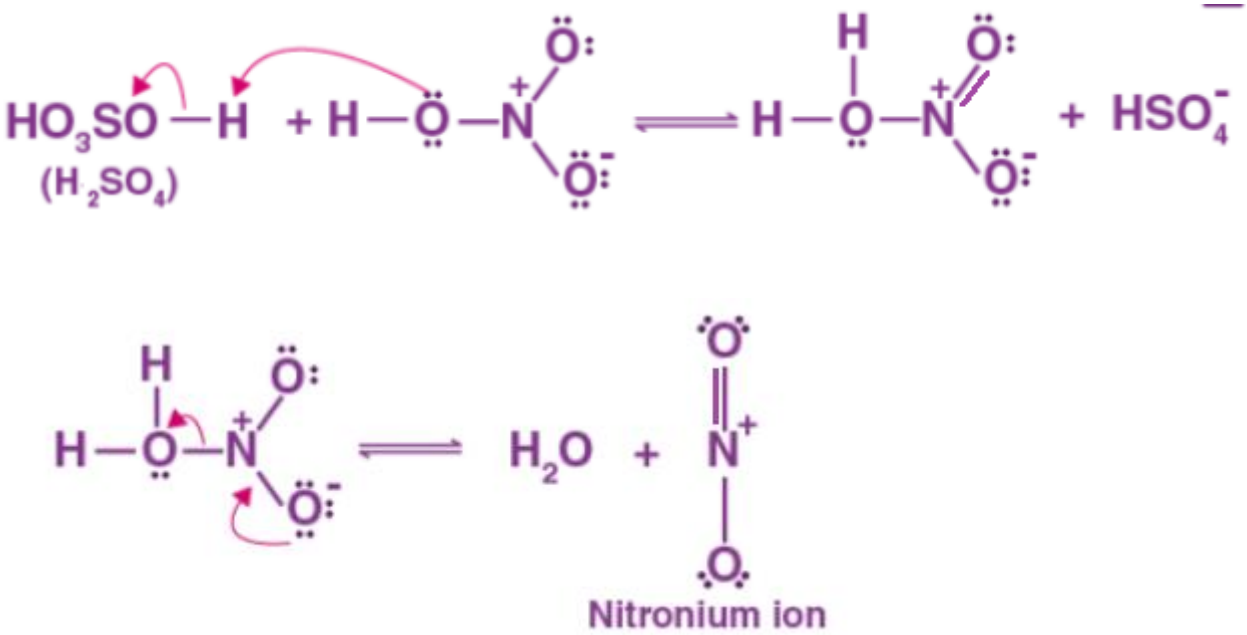


(c) Benzene reacts with concentrated nitric acid at 323-333K in the presence of concentrated sulphuric acid to form nitrobenzene. This reaction is known as nitration of benzene.

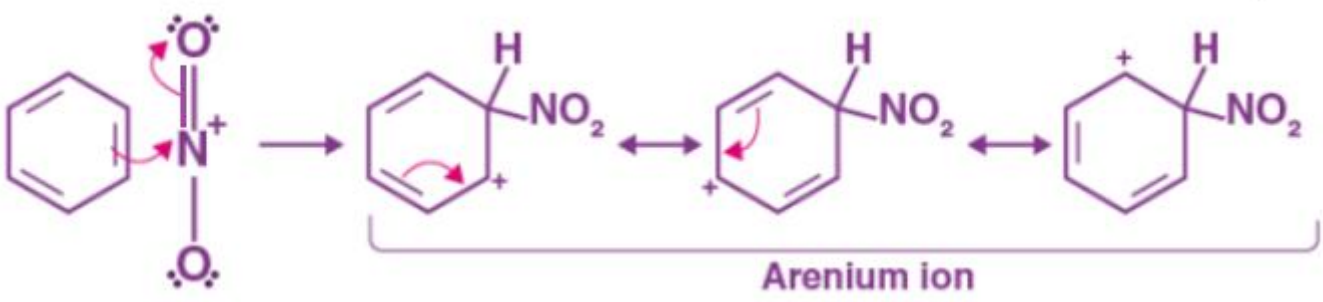


Mechanism of nitration of benzene:

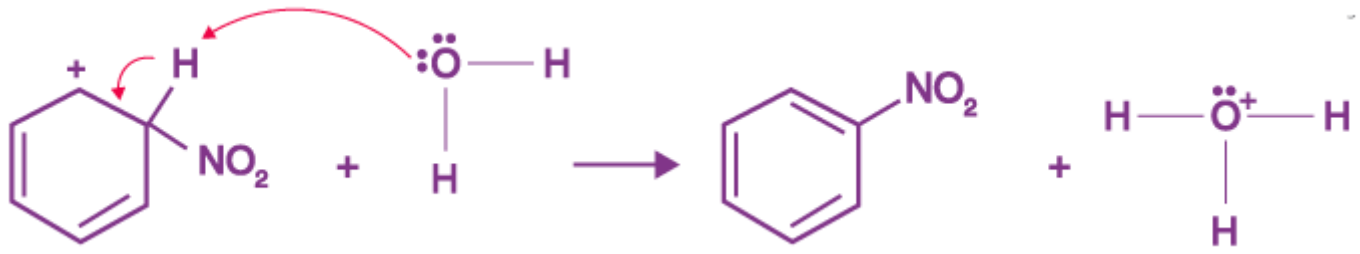
Step 1: Nitric acid accepts a proton from sulphuric acid and then dissociates to form nitronium ion.



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

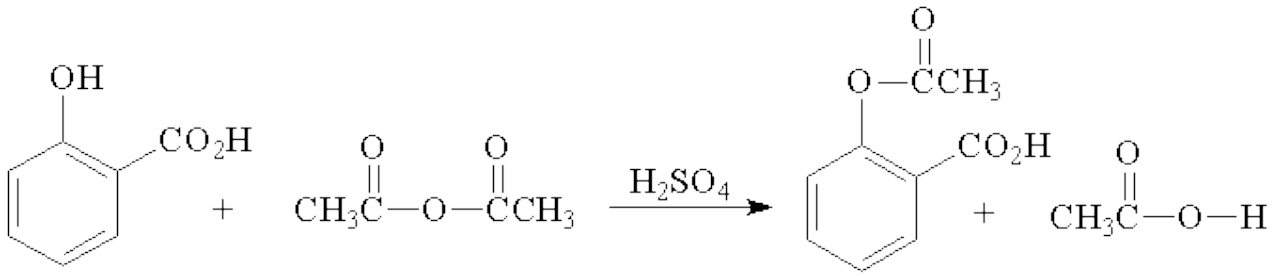
(b) Explain why – (i) p- nitrophenol has higher boiling point than o – nitrophenol.

(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 $KMnO_4$ (ii) Benzoic acid treated with lithium aluminium hydride. 4

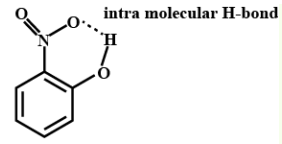
(a) Synthesis of Aspirin: The chemical name of Aspirin is 2 – acetoxybenzoic acid or acetylsalicylic acid. Asperin is an analgesic and used to get relief from pain without causing any significant disturbance in our nervous system.

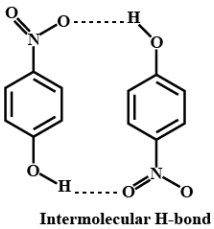
Synthesis: Aspirin is synthesised by treating salicylic acid with acetic anhydride in presence of a strong acid like H_3PO_4 which acts as catalyst. The result of this reaction is acetylsalicylic acid or aspirin and acetic acid is released as by product of the reaction. Aspirin is sparingly soluble in water and therefore gets precipitated on addition of water. Under this process the hydroxyl group (- OH) of the salicylic acid turns into ester group (- $OCOCH_3$).



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)





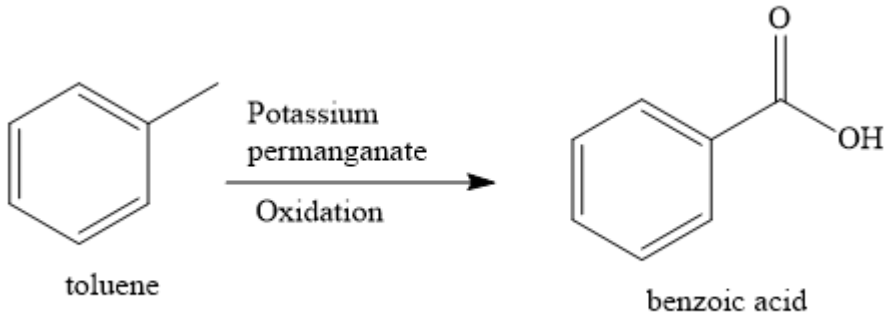
O-nitrophenol has intramolecular hydrogen bonding. P-nitrophenol has intermolecular hydrogen bonding. Intermolecular hydrogen bonding leads to a molecular association. This increases boiling point. Hene, O-nitrophenol has a lower boiling point than P-nitrophenol.

(ii) In aniline 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.

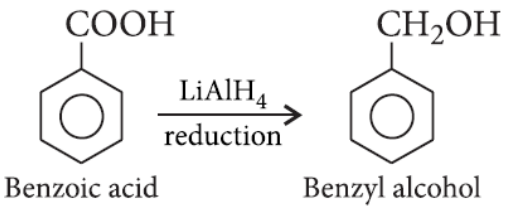
But in acidic medium (Nitrating mixture - $HNO_3(c) + H_2SO_4(c)$).

$NH_2+H^+ \rightleftharpoons NH_3^+$ 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 C_6H_5CHO, $C_6H_5COCH_3$, $C_6H_5CO\ C_6H_5$ in decreasing order of reactivity towards nucleophile addition reactions. Which of the species NO^+, CCl_4, CH_3, CN^- is an 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) $C_6H_5CHO > C_6H_5COCH_3 > C_6H_5CO\ C_6H_5$

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 C_6H_5CHO is more reactive towards nucleophiles than $C_6H_5COCH_3$ and $C_6H_5CO\ C_6H_5$.

(ii) The +I effect of alkyl group is weaker than +M effect of benzene ring. In other words, - CH_3 group reduces the positive charge on the carbonyl caused by – C_6H_5 group. Hence $C_6H_5COCH_3$ is more reactive towards nucleophiles than $C_6H_5CO\ C_6H_5$.

CN^- is an 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 O^- - N = O is an important ambident nucleophile.

$R – X + KNO_2 \longrightarrow$ RONO (major) + RNO_2 (Minor) +KX

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

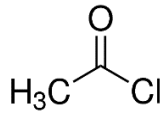
$RCl + OH^-(aq) \longrightarrow ROH + Cl^-(aq)$ [Hydrolysis reaction]

On the other hand, alcoholic KOH, contains ethoxy ions ($C_2H_5O^-$), which are more than OH^- ions. Consequently, ethoxy ion preferentially bring about dehydrohalogination to form alkenes.

$H_2C(H) - CH_2(Cl) + KOH\ (alc.) \longrightarrow H_2C = CH_2 + H_2O + KBr$

On the other hand, in haloarenes (Ar – 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.