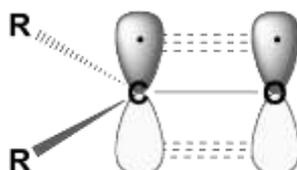


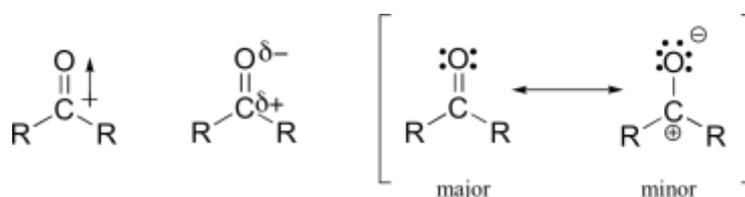
Carbonyl compounds (Aldehydes and ketones): Nucleophilic addition, Electromeric effect, Qualitative tests for Aldehydes and ketones.

❖ Aldehydes and Ketones: Nucleophilic Addition to C=O

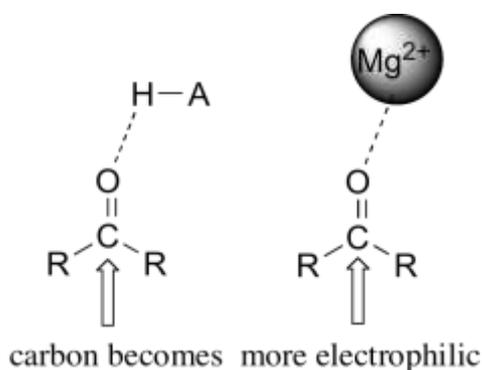
- Carbonyl carbons are **sp² hybridized**, with the **three sp² orbitals** forming overlaps with orbitals on the oxygen and on the two carbon or hydrogen atoms. These three bonds adopt trigonal planar geometry. The remaining unhybridized **2p orbital** on the central carbonyl carbon is perpendicular to this plane, and forms a 'side-by-side' p bond with a **2p orbital** on the oxygen.



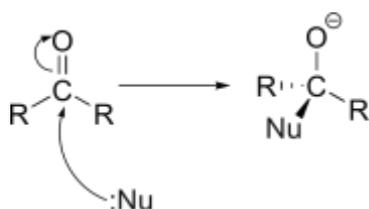
- The carbon-oxygen double bond is polar: oxygen is more electronegative than carbon, so electron density is higher on the oxygen side of the bond and lower on the carbon side



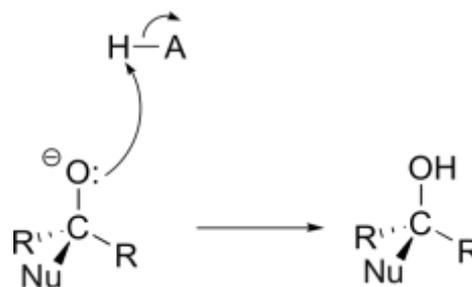
- The carbon, because it is electron-poor, is an electrophile: it is a great target for attack by an electron-rich nucleophilic group. Because the oxygen end of the carbonyl double bond bears a partial negative charge, anything that can help to stabilize this charge by accepting some of the electron density will increase the bond's polarity and make the carbon more electrophilic.



- The same effect can also be achieved if a Lewis acid, such as a magnesium ion, is located near the carbonyl oxygen.
- when a nucleophile attacks an aldehyde or ketone carbon there is no leaving group – the incoming nucleophile simply 'pushes' the electrons in the pi bond up to the oxygen.



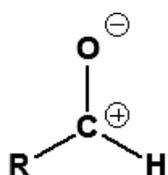
- After the carbonyl is attacked by the nucleophile, the negatively charged oxygen has the capacity to act as a nucleophile. However, most commonly the oxygen acts instead as a base, abstracting a proton from a nearby acid group in the solvent or enzyme active site.



- This very common type of reaction is called a **nucleophilic addition**.

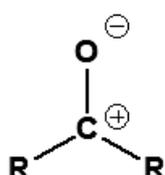
➤ Relative Reactivity of Carbonyl Compounds to Nucleophilic Addition

- In general aldehydes are more reactive than ketones because of the lack of stabilizing alkyl groups.
- The primary carbocation formed in the in the polarizing resonance structure of an aldehyde (discussed above) is less stable and therefore more reactive than the secondary carbocation formed by a ketone.



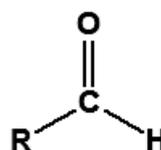
1° Carbocation

(Less Stable, More Reactive)



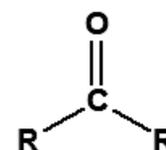
2° Carbocation

(More Stable, Less Reactive)



Aldehyde

Less Stabilization
More Reactive

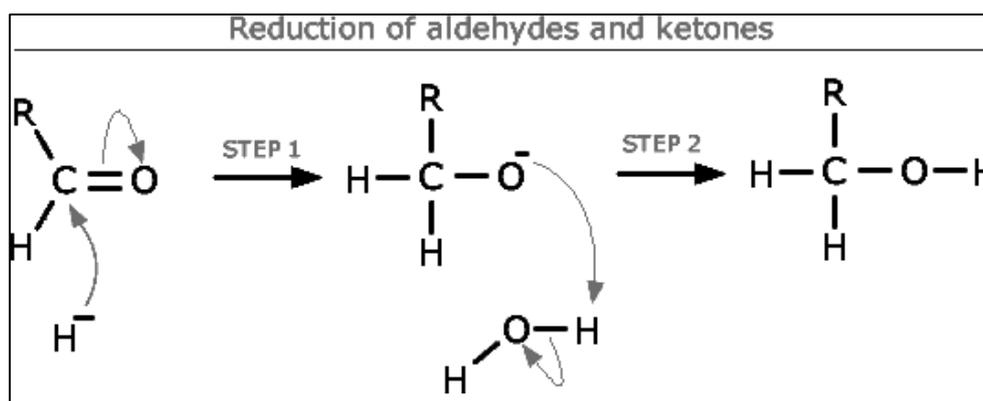
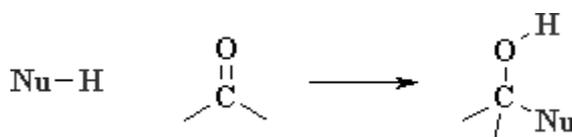


Ketone

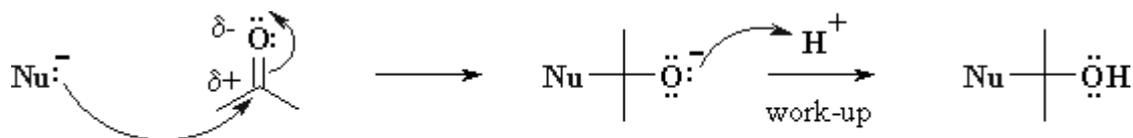
Less Stabilization
More Reactive

➤ Nucleophilic Addition

- There are three fundamental events in a nucleophilic addition reaction:
 - Formation of the new σ -bond between the nucleophile, **Nu**, to the electrophilic **C** of the **C=O** group
 - Breaking of the **π -bond** to the **O** resulting in the formation of an intermediate alkoxide
 - Protonation of the intermediate alkoxide to give an alcohol derivative



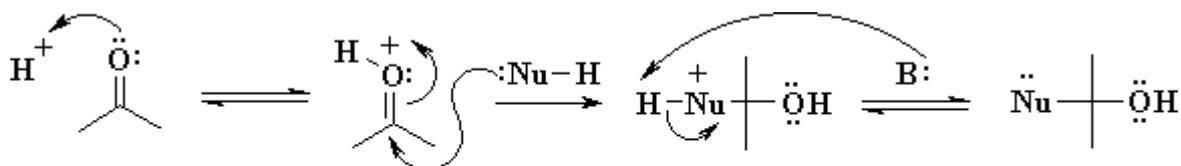
- **Strong nucleophiles** (anionic) add directly to the C=O to form the intermediate alkoxide. The alkoxides then protonated on work-up with dilute acid.



Nucleophilic Addition under **BASIC** conditions with stronger nucleophiles

Examples of such nucleophilic systems are: RMgX, RLi, RC≡CM, LiAlH₄, NaBH₄

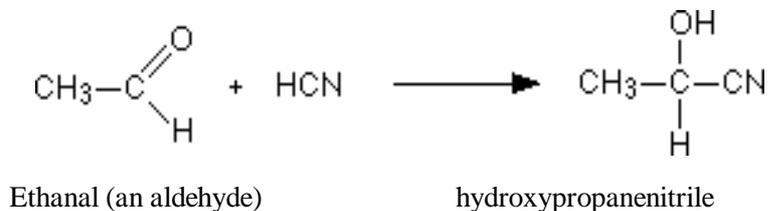
- **Weaker nucleophiles** (neutral) require that the C=O be activated prior to attack of the Nu. This can be done using an acid catalyst which protonates on the Lewis basic O and makes the system more electrophilic.



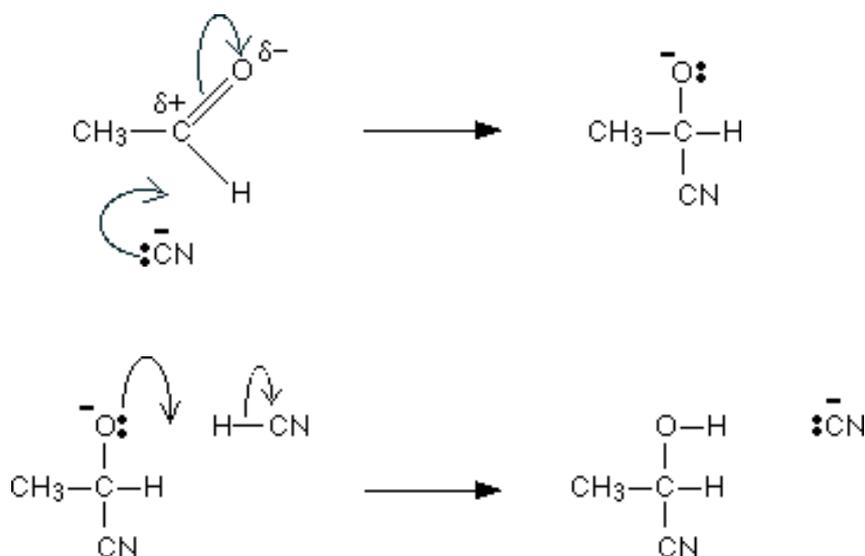
Nucleophilic Addition under **ACIDIC** condition with weaker nucleophiles

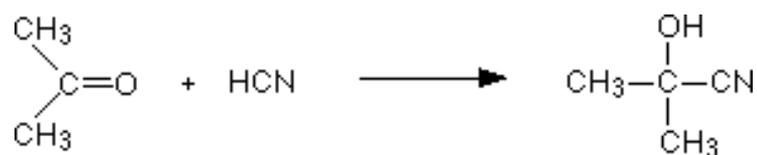
Examples of such nucleophilic systems are: H₂O, ROH, R-NH₂

➤ The reaction of aldehydes and ketones with hydrogen cyanide



The mechanism for the addition of HCN to ethanal

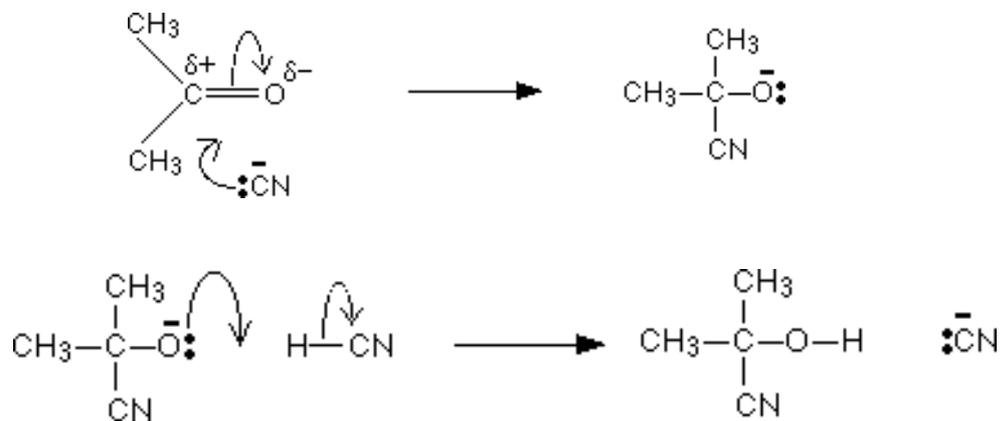




Propanone (a ketone)

2-hydroxy-2-methylpropanenitrile

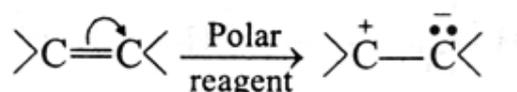
The mechanism for the addition of HCN to propanone



❖ Electromeric effect

□ About Electromeric effect mechanism:-

- In case of compounds containing multiple bonds (double or triple covalent bonds), the It-electron pair shifts completely towards more electronegative atom under the influence of attacking reagent.
- ❖ The complete transference of a shared pair of electrons of a multiple bond towards one of the atoms in the presence of an attacking reagent is known as **electromeric effect**.
- A multiple bond (double bond or triple bond) consist of sigma and pi-bond .Electron of pi bond are loosely held (due to the sideways overlapping) and easily polarizable .
- Therefore , when a compound having pi bond is approaches by a charged reagent (electrophile or nucleophile), the electron of bond are completely polarizable or displaced towards one of the constituent atom due to electrostatic attraction of repulsion.

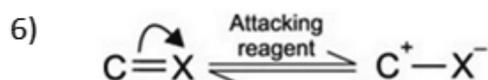


- The atom which acquire the electron pair become positively charged while the atom which leave/donate the electron , get the positive charge.

□ Characteristics of electromeric effect

- 1) It is a **temporary effect** and comes into play in the presence of an attacking reagent.
- 2) It takes place in case of compounds having multiple bonds which may be polar or nonpolar.
- 3) Due to the cleavage of a pi-bond, the electrons transferred leave their original orbital and attains a new position.
- 4) Electromeric effect is usually denoted as E effect (+E and -E effect)
- 5) the transfer of electrons taking place is represented by a curved

arrow as :- ( or ).



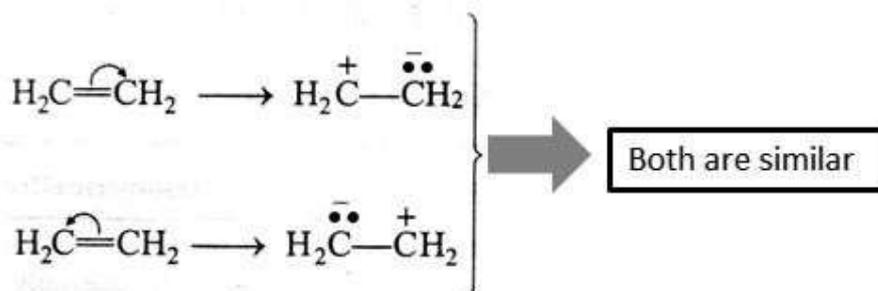
- Since C loses its share in the electron pair to X, C acquires a positive charge and X a negative charge. The structure formed is more stable as the normal structure and is formed only at the time of reaction under the requirement of attacking reagent.
 - If the attacking reagent is withdrawn without the reaction being allowed to take place, electron distribution reverts to its normal state.
- 7) This effect is of common occurrence during addition of polar reagents on $\text{>C}=\text{C}<$, $\text{>C}=\text{O}$, $\text{-C}\equiv\text{N}$ bonds.
 - 8) In cases where Inductive effect and Electromeric effect simultaneously operate, usually Electromeric effect predominates.

□ Direction of shift of electron pair:-

□ The direction of shift of electron pair can be decided on the basis of following point:-

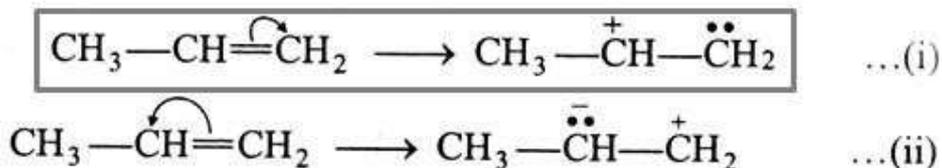
- a) When the group linked to a multiple bond are similar, the shift can occur to either direction.

▪ Example :- In "Ethylene" the shift can occur to any of the carbon atom.

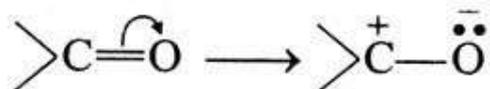


- b) When the dissimilar groups are linked on the two 'ends of the double bond, the shift is decided by the direction of inductive effect.

▪ Example :- In "Propylene" the shift can be shown in the following ways.



- Due to electron repelling nature of methyl group, the electronic shift occurs according to Equation (i) way and **not** by Equation (ii) way.
- c) In the case of carbonyl group, the shift is always towards oxygen, i. e., more electronegative atom.



- d) In cases where Inductive effect and Electromeric effect simultaneously operate, usually Electromeric effect predominates.
- Since the Electromeric effect takes place only at the time of attacking reagent, it always facilitates the reaction and never inhibits it.

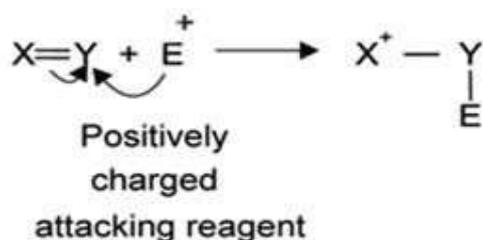
Types of Electromeric Effect

Like inductive effect, electromeric effect is of two types:-

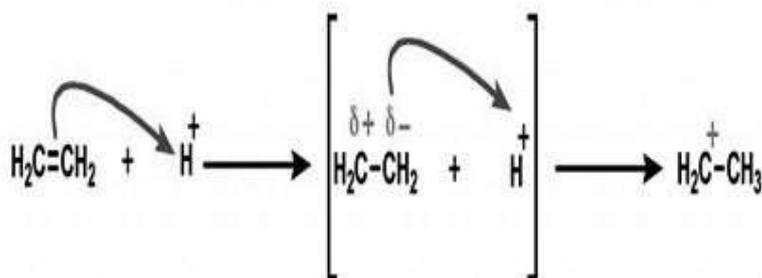
- 1) +E effect
- 2) -E effect

1) +E effect

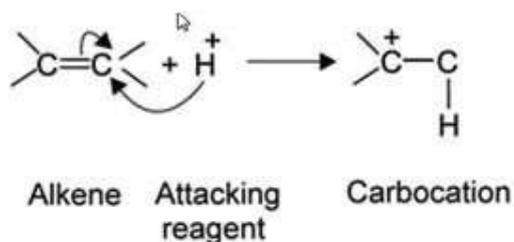
If a lone electron pair shifts towards the attacking reagents, it is known as +E effect.



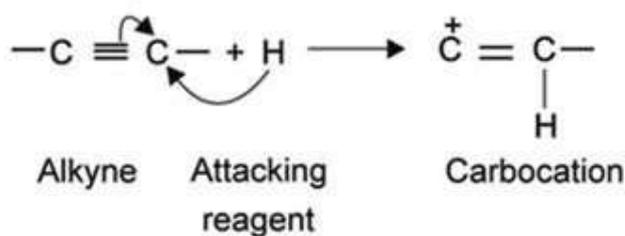
Example :- 1



Example :- 2

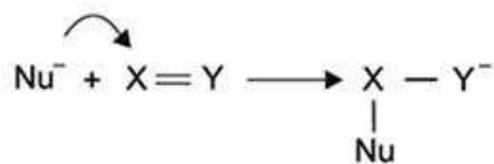


Example :- 3

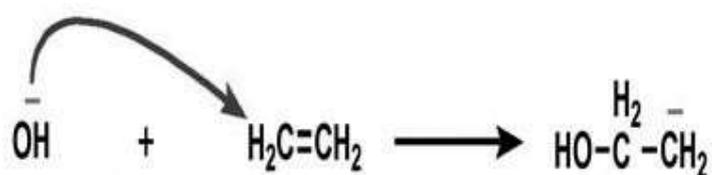


2) -E effect:-

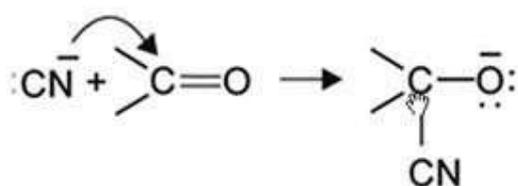
- If a lone electron pair shifts away from the attacking reagent, it is known as — E effect.



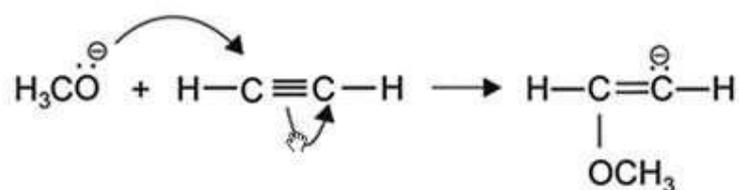
Example:-1



Example:-2



Example:-3



□ Differences between inductive effect and electromeric effect

<u>Inductive effect</u>	<u>Electromeric effect</u>
1) It is a permanent effect	1) It is a temporary effect
2) The presence of multiple bond is not essential	2) The presence of a multiple bond is essential.
3) The polarity of bond is essential	3) The polarity of bond is not essential.
4) Partial charge separation takes place	4) Complete charge separation takes place
5) No ions are formed	5) Ions are formed.
6) Attacking reagent is not Required	6) Attacking reagent is required
7) The displaced electrons do not leave their molecular orbitals . however, distortion of electron position cloud take place	7) The displaced electrons leave their orbitals and attain a new position
8) It involves mere displacement of electrons	8) It involves complete transference of π –electrons

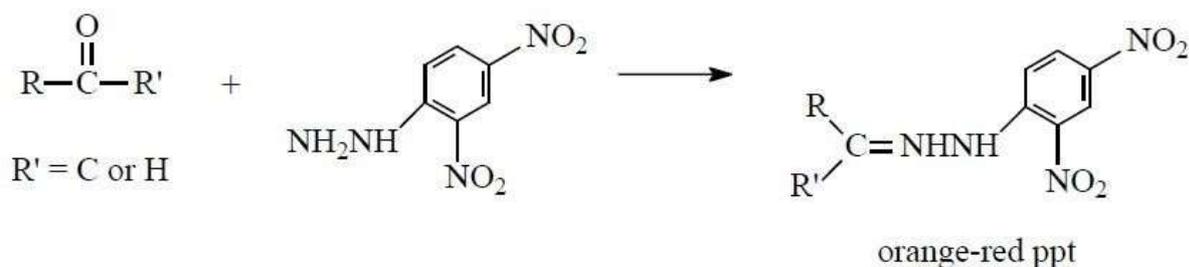
❖ Qualitative tests for Ketones and Aldehydes

- Aldehydes and ketones share the carbonyl functional group which features carbon doubly bonded to oxygen.
- In the case of **ketones** there are two carbon atoms bonded to the carbonyl carbon and no hydrogens.
- In the case of **aldehydes** there is at least one hydrogen bonded to the carbonyl carbon, the other attachment may be to a carbon or a hydrogen.
- In all cases the carbon(s) that are attached to the carbonyl group may be **aliphatic** (not part of an aromatic ring) or **aromatic** (part of an aromatic ring).
- **Aldehydes** and **Ketones** both undergo a reaction type known as nucleophilic addition. Under less acidic conditions, in this type of reaction a nucleophile (a species that can donate a pair of electrons, in other words a Lewis base) donates a pair of electrons toward the carbonyl carbon forming a single bond to it. At the same time the double bond between the carbonyl carbon and oxygen becomes a single bond as one bonding pair of electrons in the double bond moves to become an unshared pair on the oxygen. The oxygen now has one bond to it and it holds three pairs of unshared electrons, so it has a negative charge. Consequently, the oxygen picks up a proton from somewhere (possibly one that was attached to the nucleophilic atom that attacked the carbonyl carbon) and becomes an -OH group.

1) 2,4-Dinitrophenylhydrazine (2,4-DNP) Test (Test for both Aldehydes and Ketones)

- Both **aldehydes** and **ketones** will react with a number of nitrogen containing compounds through nucleophilic addition and subsequent loss of water to give reaction products that have a **carbon-nitrogen double bond**. These reactions are useful in distinguishing **aldehydes** and **ketones** from other functional groups, but cannot be used to distinguish between a ketone and aldehyde.
- 2,4-dinitrophenylhydrazine can be used to qualitatively detect the carbonyl group functionality of an **aldehyde** or **ketone** functional group. A positive test is signaled by a yellow/red precipitate, known as a **dinitrophenylhydrazone**

DNP Test:



- **Standards**

- Cyclohexanone, Benzophenone, and Benzaldehyde

- **Procedure**

- Add a solution of 1 or 2 drops or 30 mg of unknown in 2 mL of 95% ethanol to 3 mL of 2,4- dinitrophenylhydrazine reagent. Shake vigorously, and, if no precipitate forms immediately, allow the solution to stand for 15 minutes.

- **Positive test**

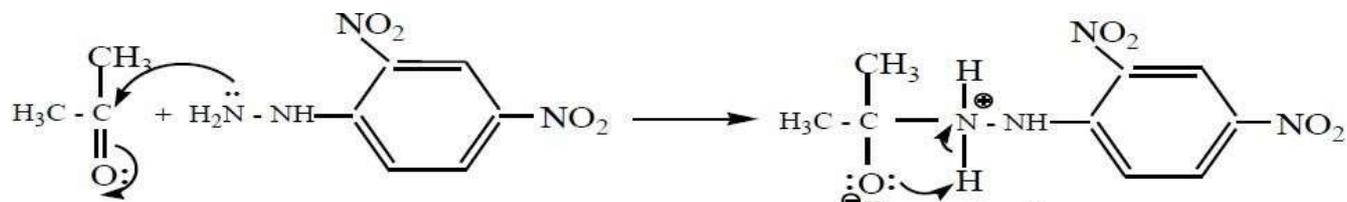
- Formation of a precipitate is a positive test.

- **Complications**

- Some ketones give oils which will not solidify.
- Some allylic alcohols are oxidized by the reagent to aldehydes and give a positive test.
- Some alcohols, if not purified, may contain aldehyde or ketone impurities.
- However, the 2,4-dinitrophenylhydrazine is itself orange-red; thus the color must be judged with caution.

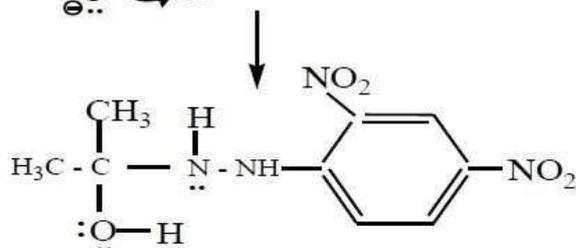
✓ 2,4-dinitrophenylhydrazine with acetone (less acidic solution):

Step I

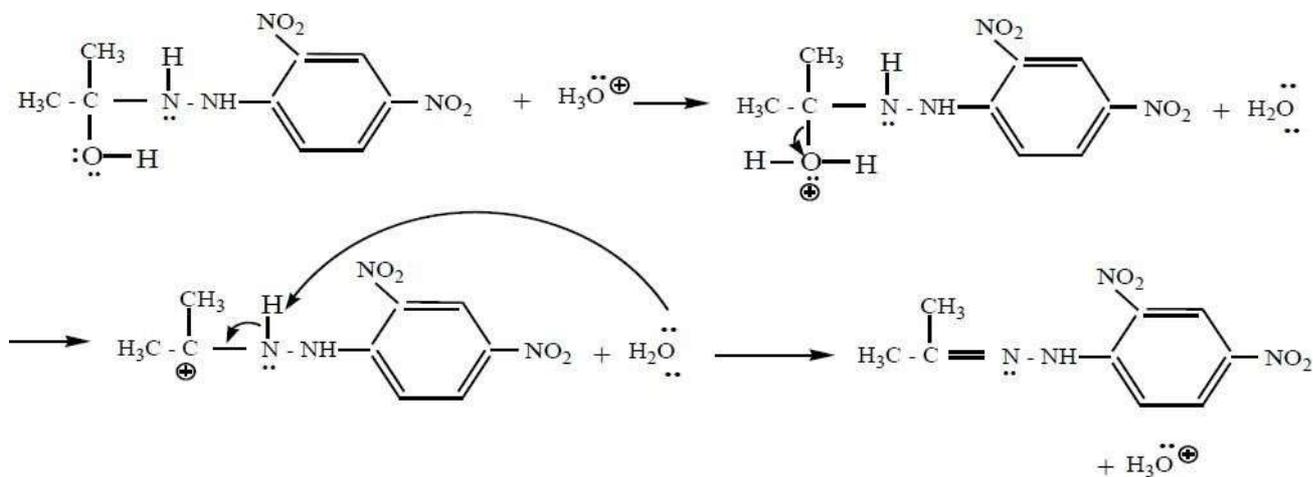


Nucleophilic addition of 2,4-DNP to acetone.

The curved arrows show electron movement as bonds are formed and broken.

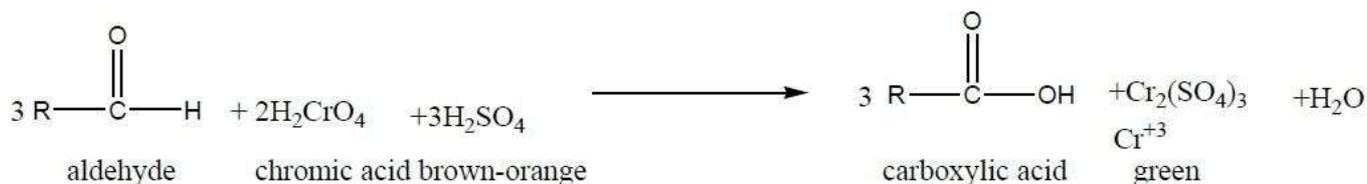


Step II



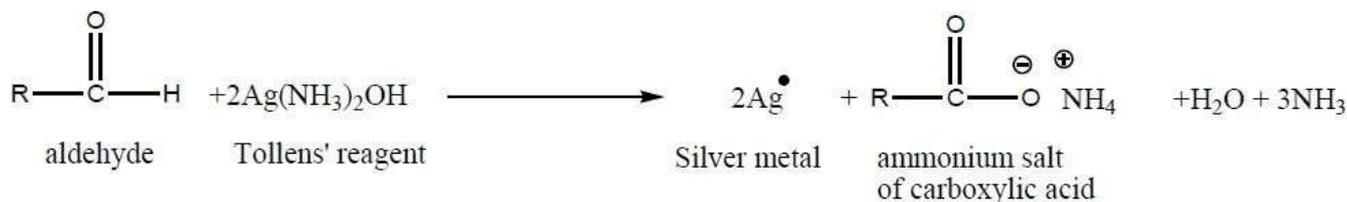
2) Chromic Acid Test (Tests for Aldehydes)

- These reactions are usually referred to as nucleophilic additions.
- **Aldehydes are oxidized by chromic acid, ketones are not.**
- When an aldehyde is oxidized by orange brown chromic acid the chromic acid is reduced to Cr^{3+} , which is green.
- Consequently, chromic acid can distinguish between aldehydes and ketones.
- It is also true those other functional groups; primary and secondary alcohols for example, can be oxidized by chromic acid, causing the formation of a green color.
- **Procedure:** Dissolve 10 mg or 2 drops of the unknown in 1 mL of pure acetone in a test tube and add to the solution 1 small drop of **Jones reagent (chromic acid in sulfuric acid)**. A positive test is marked by the formation of a green color within 5 seconds



3) Tollen's' Test (Tests for Aldehydes)

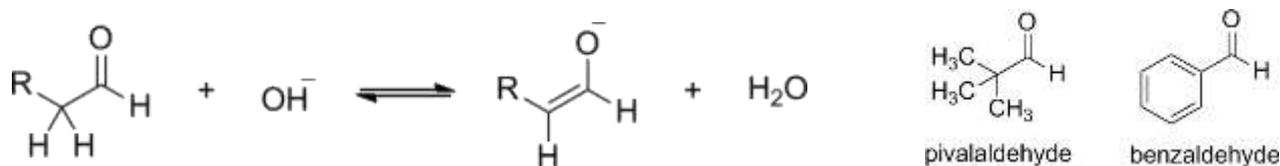
- **Aldehydes** are also oxidized by **Tollen's' reagent**, a substance that contains Ag^+ .
- The silver ion is, concomitantly, reduced to metallic silver.
- Silver ion is a weak oxidizing agent; aldehydes are very easily oxidized and are essentially unique in being able to reduce silver ion to silver metal.



Question: Why does Benzaldehyde not respond to Fehling's test and Tollen's test?

Answer:

- The rate-limiting step of the Fehling's test reaction with aldehydes is the formation of the corresponding enolate:



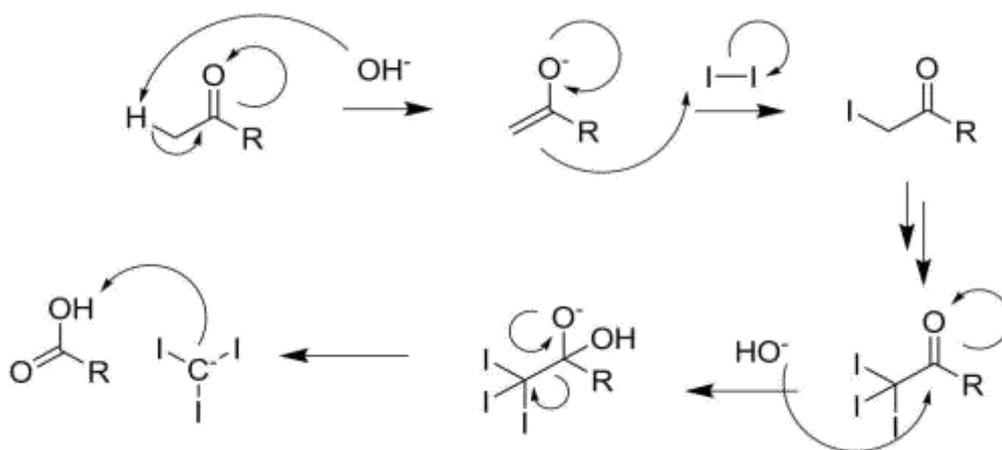
- The subsequent reaction of the enolate with **copper(II)** proceeds through a single electron transfer mechanism.
- **Aldehydes that lack alpha hydrogens**, such as **Benzaldehyde** or **pivalaldehyde** (2,2-dimethylpropanal) cannot form an enolate and thus do not give a positive Fehling's test result under usual conditions.
- In Benzaldehyde, the carbonyl group is an electron withdrawing group so the carbonyl group pulls the electron from the electron-rich benzene ring.
- Due to this, the polarity of the **C-H bond** in the carbonyl group is reduced because the **C-H bond** now has a higher electron density. Thus, the **C-H bond** becomes stronger (the lesser the polarity of a bond, the stronger the bond).
- So **Fehling's solution** (comparatively a weaker oxidizing agent than **Tollen's reagent**) can't oxidize Benzaldehyde (an aromatic aldehyde). However, Fehling's solution can oxidize an aliphatic aldehyde.

4) Iodoform Test for Methyl Ketones

- Methyl ketones, but not other ketones, are oxidized by iodine in aqueous sodium hydroxide.
- The ketone is oxidized to a carboxylic acid; yellow iodoform also forms. It is the yellow iodoform that is indication of a positive test.
- Acetaldehyde, but not other aldehydes, gives this test owing to its structural similarity to methyl ketones.
- It is also true that ethanol (oxidized to acetaldehyde) and secondary alcohols that can be oxidized to methyl ketones give this test.
- **Procedure:** If the substance to be tested is water soluble, dissolve 4 drops of a liquid or an estimated 50 mg of a solid in 2 mL of water in a large test tube. Add 2 mL of 3 M sodium hydroxide and then slowly add 3 mL of the iodine solution. Stopper the test tube and shake vigorously. A positive test will result in the brown color of the reagent disappearing and the yellow iodoform solid precipitating out of solution. If the substance to be tested is insoluble in water, dissolve it in 2 mL of 1,2-dimethoxyethane, proceed as above, and at the end dilute with 10 mL of water.
- **Reaction:**



- **Reaction Mechanism:**



Question: Does acetic acid give a positive result with the iodoform test?

Answer:

- Acetic acid contains a $-\text{COMe}$ group, so theoretically, it should give a positive result in the iodoform test (i.e. a yellow precipitate of CHI_3 being formed).
- But practically no carboxylic acids give a positive result towards iodoform test, because the $\text{C}=\text{O}$ in the COOH has delocalisation over the group, so it doesn't respond.

