

Oxidation and Reduction Reactions

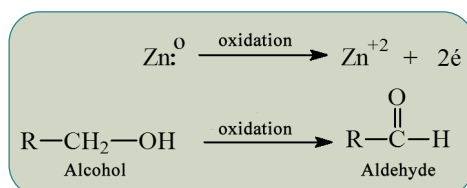
1

Oxidation Reactions

The oxidation of an organic molecule can be defined as increase in the amount of oxygen or decrease in the amount of hydrogen.

A decrease in the amount of electrons of atom or ion; or an increase in the value of a functional group is an oxidation reactions.

Oxidation and reduction refer to the loss or gain of electron of atoms or ions in inorganic (anorganic) chemistry respectively.



2

Oxidation Number (Ox. State)

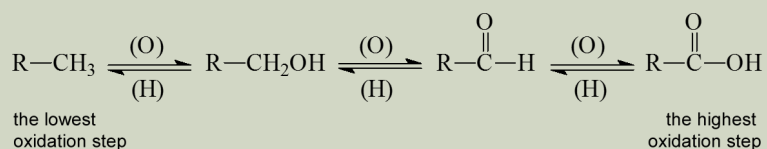
| Ox. step | Primary | Secondary | Tertiary | Quaternary |
|----------|--------------------|--------------------------------|--------------------|------------------|
| -4 | CH ₄ | | | |
| -3 | | RCH ₃ | | |
| -2 | CH ₃ OH | R ₂ CH ₂ | | |
| -1 | | RCH ₂ OH | R ₃ CH | |
| 0 | CH ₂ O | R ₂ CHOH | | R ₄ C |
| +1 | | RCHO | R ₃ COH | |
| +2 | HCOOH | R ₂ CO | | |
| +3 | | RCOOH | | |
| +4 | CO ₂ | | | |

The oxidation number of a free element is always 0. If an element loses the n number of electrons, it is considered to be oxidized by $+n$ value, and if it gains, it is considered to be reduced by $-n$ value. In organic molecules, the oxidation numbers of the "C" atoms can be calculated by considering each "H", -1 ; each "C", 0 ; each heteroatoms, $+1$ values for the 4 bonds of the "C" atoms.

3

Oxidation and Reduction

When an organic compound undergoes reduction, the reduction reactive oxidizes. When an organic compound undergoes oxidation, the oxidation reactive undergoes reduction. Oxidation and reduction reaction take place at the same time.



4

Applied in industrial and laboratory

Oxidation Methods

Oxidation in air or with pure oxygen. (These reactions can be accomplished by biologically catalyzing homogeneous or heterogeneous catalysts.)

Catalytic dehydrogenation at high temperature. (Vanadium oxides)

Oxidation with some inorganic substances except oxygen. (The most commonly used reagents: Sodium dichromate + H_2SO_4 (sulfochromic mixture), in neutral, basic or acidic medium KMnO_4 , concentrated nitric acid, hydrogen peroxide, ozone, some metallic oxide and peroxides, some oxygenated salts.)

Oxidation with some organic substances or peroxides and peracids.

5

Oxidation Reagents

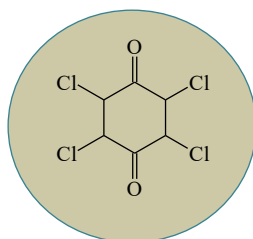
| | | | | | |
|------------------------|---------------------------------------|--|------------------|-------------------------------|---------------------------|
| O_2 | HNO_3 | SO_3 | Cl_2 | Ag_2O | MnO_2 |
| O_3 | RO-NO | $(\text{CH}_3)_2\text{S}^+-\text{O}^-$ | Br_2 | HgO | MnO_4^- |
| H_2O_2 | O-N_2 | SeO_2 | I_2 | $\text{Hg}(\text{OAc})_2$ | CrO_3 |
| t-BuO-OH | H_2NCl | | NBS | $\text{Pb}(\text{OAc})_4$ | CrO_2Cl_2 |
| R-COO-OH | $\text{H}_3\text{N}^+-\text{OSO}_3^-$ | | t-BuOCl | FeCl_3 | OsO_4 |
| | $\text{R}_3\text{N}^+-\text{O}^-$ | | | $\text{Fe}(\text{CN})_6^{3-}$ | IO_4^- |

6

Dehydrogenation (-2H):

Heat with Pt, Pd, S or Se

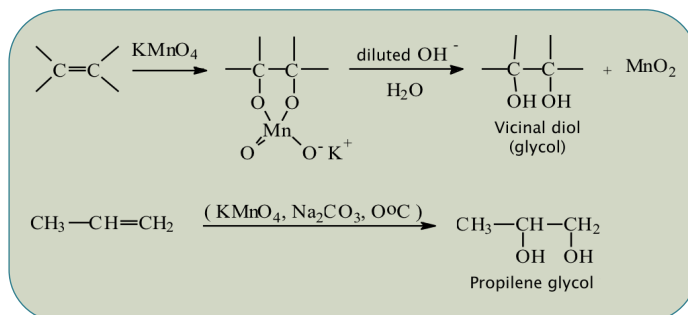
Substituted quinones (**e.g. Chloranil**)



7

Oxidation of Ethylenic Double Bond and Aromatic Side Chain with KMnO_4

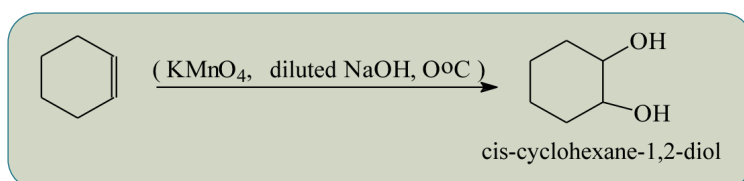
In dilute basic medium and in the cold ($0-5^\circ\text{C}$), KMnO_4 acts to dihydroxylate the double bond and glycols (1,2-diols) are formed.



8

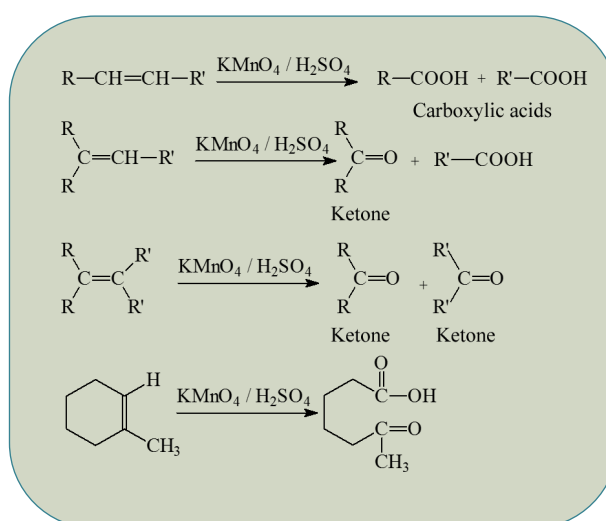
Oxidation of Ethylenic Double Bond and Aromatic Side Chain with KMnO_4

This reaction takes place as *cis*-addition in stereochemistry.
For example; *cis*-cyclohexane-1,2-diol is formed from cyclohexene.



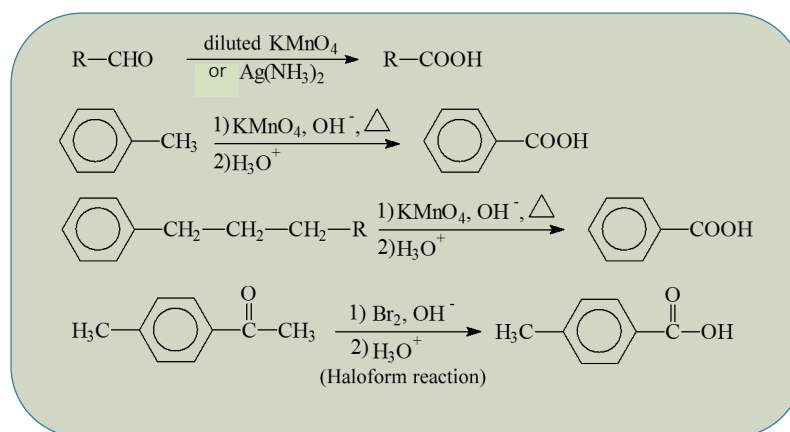
9

The acidic permanganate solution leads to ketone or carboxylic acid formation breaking the double bond according to the environment of the double bond carbon...



10

Oxidation in the side chain takes place in the benzylic carbone. Even if there are alkyl groups including multiple "C" atoms, it is always fragmented to benzoic acid...

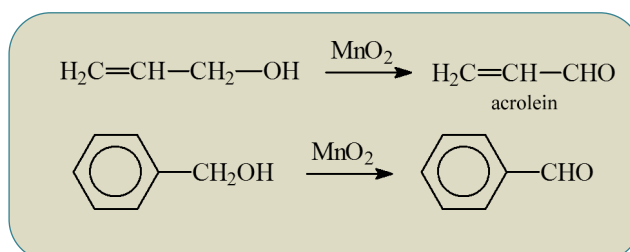


11

Moderate Oxidation with MnO₂

Freshly prepared MnO₂ is used in one step oxidation of allylic and benzylic alcohols.

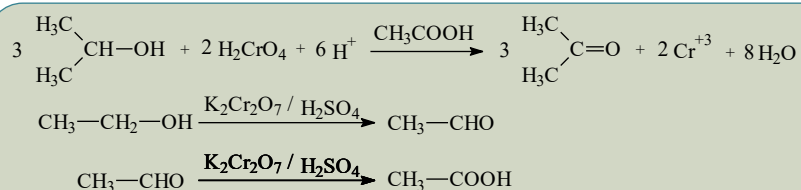
MnO₂ → Mn⁺⁺ is reduced and there is no oxidation to further steps.



12

Oxidation of the secondary alcohols with chromic acid (Obtaining of Acetone)

Acetone is obtained by the addition Chromic acid (H_2CrO_4), CrO_3 or $\text{Na}_2\text{Cr}_2\text{O}_7$ to H_2SO_4 . While Cr is reduced from **+6** to **+3**, related compound is oxidized.

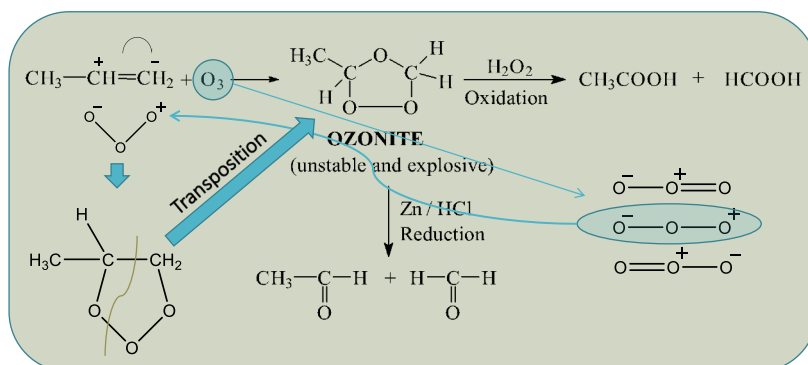


Other oxidation reagents including Cr (VI)

$\text{Na}_2\text{Cr}_2\text{O}_7$ (sodium bichromate), Na_2CrO_4 (sodium chromate), H_2CrO_4 (chromic acid), CrO_3 (chromic oxide), CrO_2Cl_2 (chromyl chloride)

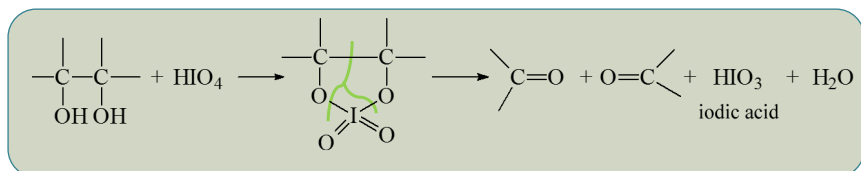
13

Oxidation of ethylenic compounds with O_3 (Ozonolysis)



14

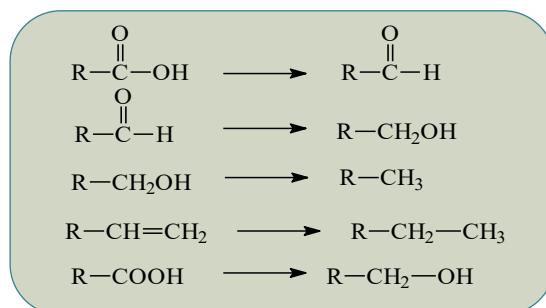
Oxidation with HIO_4 (Periodic Acid) in Vicinal Diols



15

Reduction Reactions

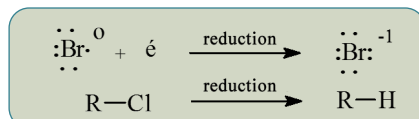
The reduction of an organic molecule can be defined as increase in the amount of hydrogen or decrease in the amount of oxygen. For example, the conversion of a carboxylic acid to aldehyde is the reduction. Because the amount of oxygen decreases.



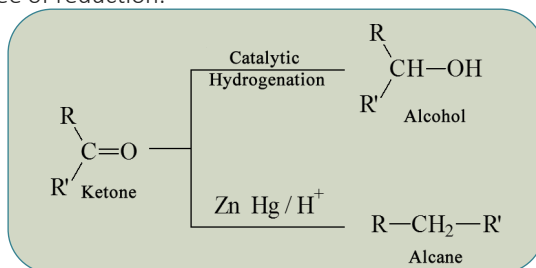
16

Reduction Reactions

An increase in the amount of electrons of atom or ion; or a decrease in the value of a functional group is a reduction reactions.



There are many reduction reagent depending on the substance to be reduced and the degree of reduction.



17

Applied in industrial and laboratory

Reduction Reactions

Hydrogen (H_2) can reduce = and \equiv bonds in the alkenes and alkynes in company with metallic catalyser as Pt, Pd or Ni, unsaturated bonds of carbonyl groups ($\text{C}=\text{O}$) and $-\text{NO}_2$ group.

Nucleophilic hydride donors such as LiAlH_4 , NaBH_4 etc. are more carbonyl derivatives reducing compounds without affecting ethylenic unsaturated bonds.

The solutions of tin, iron, zinc metals with HCl are usually used for reduction of $-\text{NO}_2$ group to $-\text{NH}_2$ group.

Reductions can also be made with ethanol / Na and 2-propanol / Al mixtures

18

Reduction Reagents

Catalytic hydrogenation: H_2 + Pt, Pd or Ni

Hydrides: LiAlH_4 , AlH_3 , NaBH_4 , BH_3 , R_2BH

Metals: Li, Na, K, Zn, Mg

Others: NH_2NH_2 , R_3P , SO_3^{-2} , SnCl_2 , FeCl_2

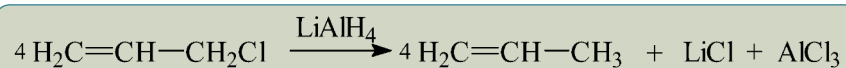
19

Reduction of Alkyl Halides, Carboxylic acid and Derivatives with LiAlH_4

LiAlH_4 is a strong reduction reagent. It is used to reduce many functional groups except isolated carbon-carbon double and triple bonds. It is a hydride (H^-) source.

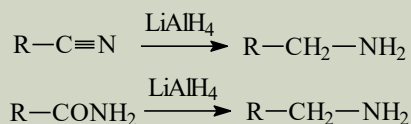
LiAlH_4 combines with all kinds of acidic proton and causes H_2 \uparrow out. Dry ethers or tetrahydrofuran (THF) are used as solvents as they also cause H_2 \uparrow out with water proton.

Preparation of hydrocarbons from halogenated derivatives:

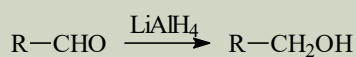


20

Preparation of Primary Amines by Action from Amides and Nitriles

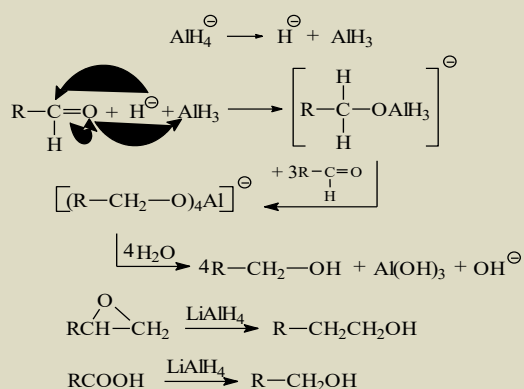


LiAlH_4 is converted to alcohols by reducing $\text{R}-\text{CHO}$, $\text{R}_2\text{C}=\text{O}$, $\text{R}-\text{COOH}$, RCOOR , $\text{RCH}(\text{O})-\text{CH}_2$, RCOCl molecules.



21

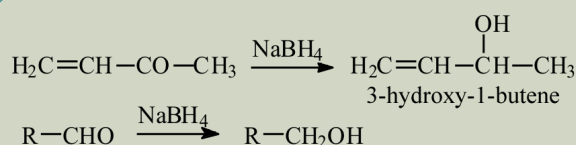
Reaction Mechanism of LiAlH_4



22

Reduction of Carbonyl Derivatives with NaBH_4

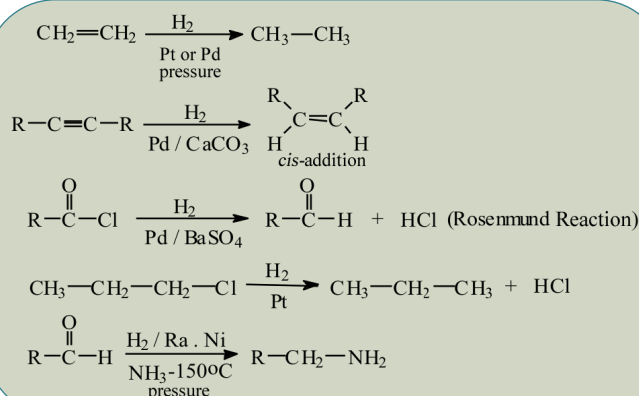
NaBH_4 is a weaker reduction agent than LiAlH_4 . It is used to reduce aldehydes and ketones majorly. The reduction process with NaBH_4 can be carried out in an aqueous medium or alcohol.



23

Catalytic Reduction (Hydrogenolysis)

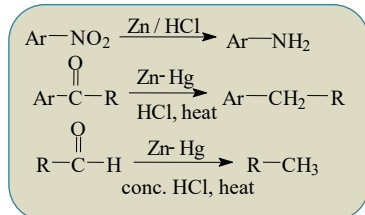
Hydrogenolysis is called that is opened by hydrogen and a metal catalyser the bond in the ethylenic and acetylenic unsaturated structures and the bond between carbon and heteroatom. These metals are platinum (Pt), rutenium (Ru), palladium (Pd) and nickel (Ni).



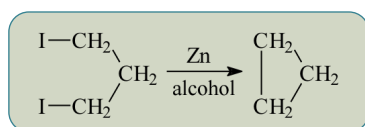
24

Examples of Reduction using Metal / Acid System

It is used Zn, Fe, Sn / HCl, H₂SO₄ and SnCl₂, FeSO₄. When metal is treated with acid, the hydrogen gas is formed on the rise.



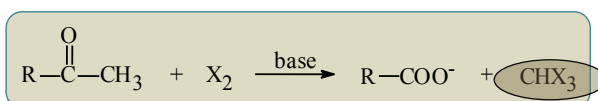
Zn also reduces in aqueous and alcoholic medium.



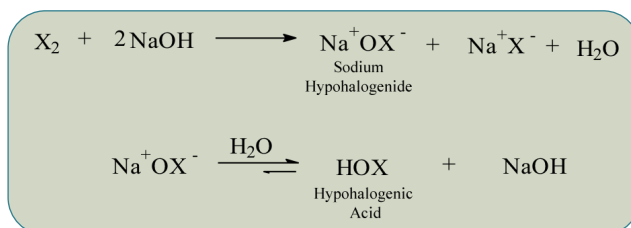
25

Haloform Reaction

The halogenation of the α -C atom of many ketone compounds can be carried out in the form of total halogenation in a basic medium. So methyl ketones [CH₃-CO-] contain three halogen atoms in α -C and are formed trihalomethyl ketones.



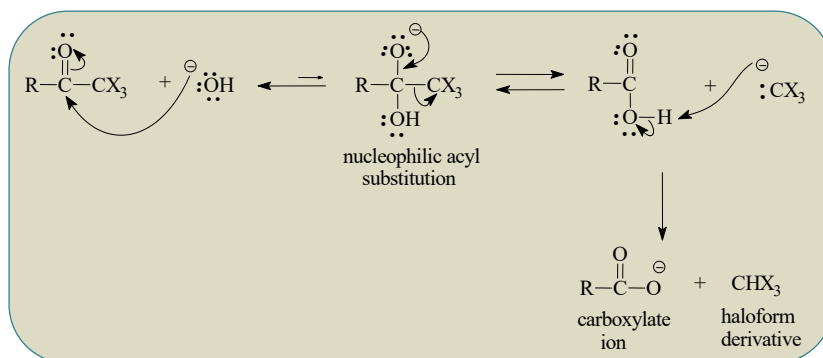
The haloform reaction takes place via the hypohalogenide derivative of halogens in basic medium.



26

Reaction Mechanism

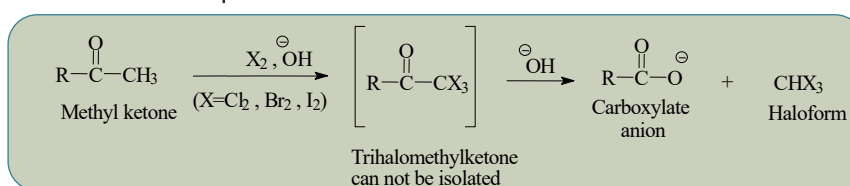
The trihalomethyl group of the resulting compound forms a leaving group for the nucleophilic acyl substitution, resulting in the formation of the carboxylated aryl which is displaced by the basic OH^- group of the medium. However, the immediate rapid proton exchange completes the formation of the haloform derivative with the carboxylate anion.



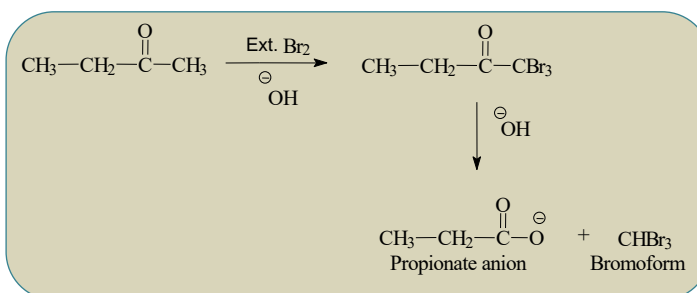
27

Haloform Reaction

General Reaction Equation



Example



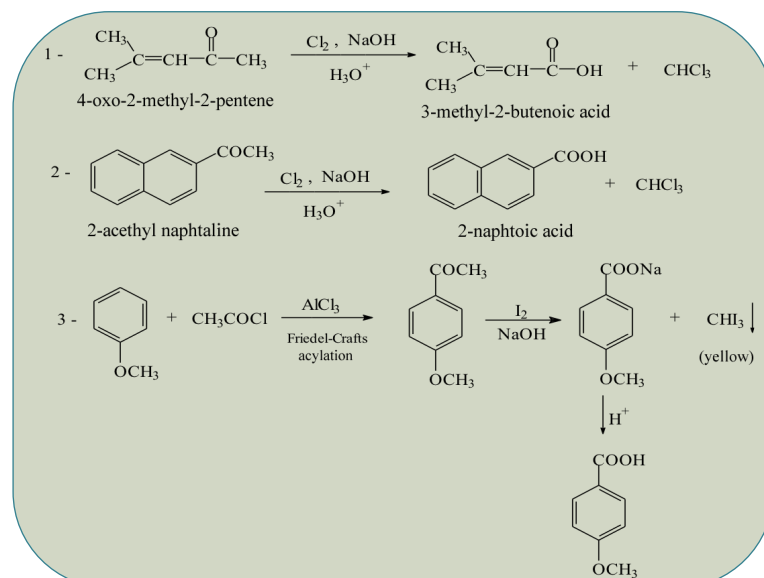
28

$$\text{C}_6\text{H}_5\text{COCH}_3 \xrightarrow[\text{OH}^-]{\text{Ext. I}_2} \text{C}_6\text{H}_5\text{COCl}_3 \xrightarrow{\text{OH}^-} \text{C}_6\text{H}_5\text{COO}^- + \text{CHI}_3 \downarrow$$

Benzoyl chloride Benzoate anion Iodoform

$$\text{R}-\overset{\text{OH}}{\underset{|}{\text{CH}}}-\text{CH}_3 + \text{I}_2 \longrightarrow \text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{CH}_3 + 2 \text{HI} \xrightarrow[\ominus \text{OH}]{\text{Ext. I}_2} \text{R}-\overset{\text{O}}{\parallel}{\text{C}}-\text{O}^\ominus + \text{CH}_3 \downarrow$$

Example Haloform Reactions

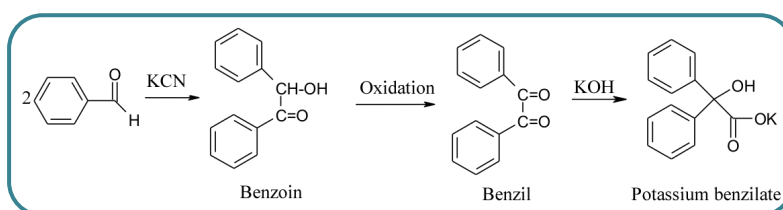


Benzilic Acid Synthesis

Benzilic acid synthesis can be seen as a method of obtaining α -hydroxy carboxylic acid. The benzilic acid is synthesized by the action of benzaldehyde.

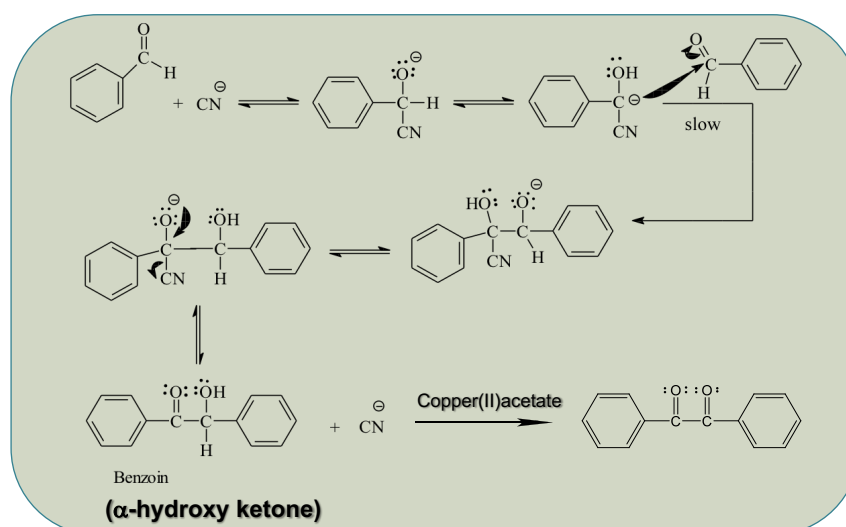
When the benzaldehyde molecule is boiled with KCN in alcoholic medium, the two molecule benzaldehyde gives the benzoin molecule as a condensed molecule.

Benzil molecule with α -diketone structure is formed by oxidation of benzoin. The benzilic acid salt is formed by the molecular rearrangement (**conversion reaction**) of this structure in the alkaline solution.



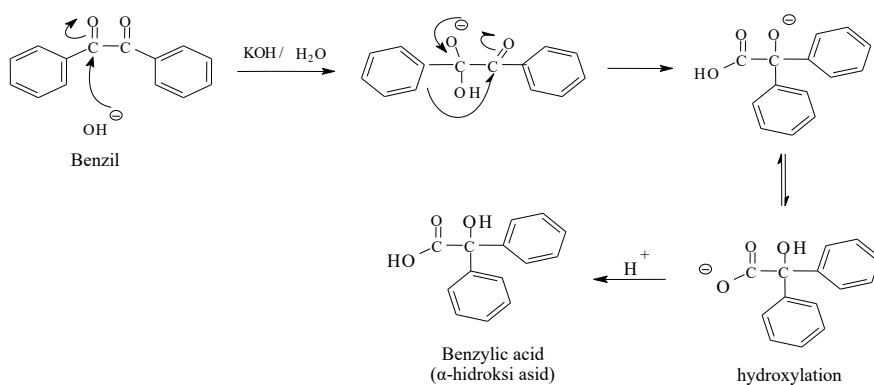
31

General Reaction Equation



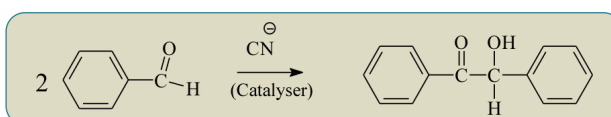
32

General Reaction Equation



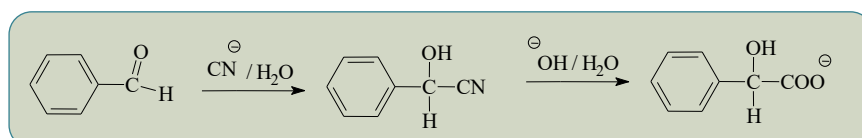
33

Benzilic Acid Synthesis (summary)



As a side product in the formation of benzoin:

- 1- Cannizzaro product can be formed.
- 2- Cyanohydrine derivative can be formed. Hydrolysis of this derivative then gives α -hydroxy carboxylic acids.



34

Benzilic Acid Synthesis (summary)

Many condensation reactions are generally catalyzed with bases. However, differently, the benzaldehyde is catalyzed with the cyanide ion using KCN. Benzyl gives benzilic acid, which is α -hydroxyl carboxylic acid, with strong bases. The reaction is carried out in hot and aqueous ethanolic medium with the aid of concentrated sodium or potassium hydroxide. In order for this reaction to occur;

Diketone is required.

The yield decreases with the introduction of alkyl groups instead of phenyl.

OH^- attack is toward carbonyl ($\text{C}=\text{O}$), which has less electron density.

OH^- is not catalyser.

35

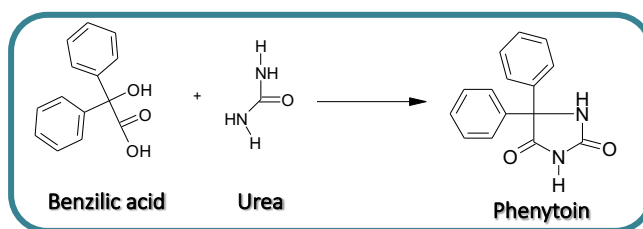
Conversion Reactions

Rearrangement

Transposition

Conversion or transposition reactions are formed by a new arrangement in the molecule to form a more stable thermodynamic structure of the result molecule. As a result, when compared to the starting molecule, they are referred as transposition or conversion reactions to be rearrangement or a change in the molecule skeleton.

The benzylic acid obtained in this way is a pharmaceutically important substance and is used, for example, in the synthesis of anticonvulsant (antiepileptic) drugs. For example; benzilic acid and urea are used in the synthesis of an anticonvulsant compound is called phenytoin.



36

Calculation of Yield in Synthesis Reactions

The yield of products produced in synthesis reactions of organic compounds is lower than calculated theoretically. For this reason, **practical yield** must also be calculated besides **theoretical yield**.

Theoretical Yield

At the end of the synthesis reaction, is the amount in grams of the product that should be theoretically obtained.

Practical Yield

At the end of the synthesis reaction, is the amount in grams of completely pure and dry product that obtained.

37

Reasons why practical yield is lower than theoretical yield

Reversibility of reactions.

Spending of the starting substance by giving other side (parasite) reactions beside the product.

The reagents used are volatile and all of the calculated starting substance has not entered the reaction.

The resulting product has side reactions due to some physical and chemical effects or decrease of the amount by decay up to be taken from the reaction medium.

The reagents used are not in the desired purity.

Mechanical losses that may occur during product purification.

38

Yield Calculation

$$\% \text{ Yield} = \frac{\text{Practical Yield}}{\text{Theoretical Yield}} \times 100$$

When the yield calculation is made, it should be determined which of the starting substances is the Basic Substance. (Limiting reagent)

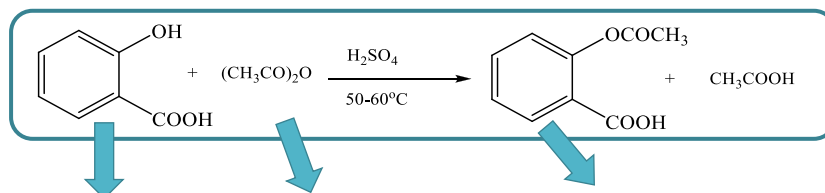
Totally spent (consumed) substance by entering all into the reaction

After the limiting reagent is detected, the yield calculation is made on this substance. Because, in order to be able to calculate the yield, the starting substance selected must be completely reacted so that mistakes are prevented.

39

Example 1 (Calculation of yield over weight in aspirin synthesis reaction)

1.3 g salicylic acid and 2 g (1.9 ml) acetic anhydride were reacted to yield 1.6 g aspirin. Calculate the yield of the reaction according to these data.



M.W. = 138.12 g/mole

1.3/138.12=0.0094 mole

M.W. = 102.09 g/mole

2/102.09=0.0195 mole

M.W. = 180.15 g/mole

1.6/180.15=0.0089 mole

40

Solution

All of 0.0094 mol substance react, so **salicylic acid is basic substance**. Yield calculation is made over this substance.



Calculation of theoretical yield:

From 138.12 g salicylic acid 180.15 g Aspirin is obtained
 From 1.3 g salicylic acid X g Aspirin is obtained

$X = 1.3 \times 180.15 / 138.12 = 1.69 \text{ g} = \text{Theoretical yield}$
 The amount obtained in practice = 1.6 g = **Practical yield**

| | |
|----------------|------|
| 1.69 g product | %100 |
| 1.6 g product | % X |

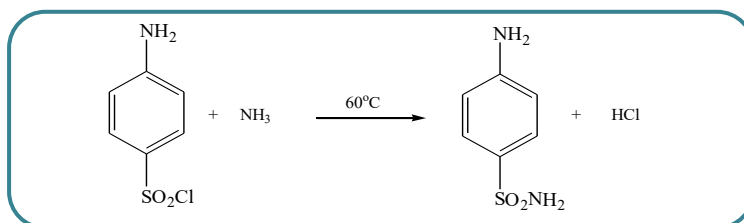
$X = 1.6 \times 100 / 1.69 = \%94.6$

Result : In this reaction, aspirin was synthesized with %94.6 yield.

41

Example 2 (Calculation of yield over mole in *p*-aminobenzenesulfonamide synthesis reaction)

191.6 g *p*-aminobenzenesulfonyl chloride and 500 ml ammonia were reacted to yield 135.7 g *p*-aminobenzenesulfonamide. Calculate the yield of the reaction according to these data.



p-Aminobenzenesulfonyl chloride
 M.W. = 191.69 g

p-Aminobenzenesulfonamide
 M.W. = 172.21 g

42

Solution

p-Aminobenzenesulfonyl chloride M.W. = 191.69 g

$$191.6/191.69 = 0.9995 \text{ mole}$$

p-Aminobenzenesulfonamide M.W. = 172.21 g

$$135.7/172.21 = 0.7880 \text{ mole}$$

$$\% \text{ Yield} = \frac{\text{Practical Yield}}{\text{Theoretical Yield}} \times 100$$

$$\% 78.84 = \frac{0.7880}{0.9995} \times 100$$

Result: In this reaction, *p*-Aminobenzenesulfonamide was synthesized with %78.84 yield.

43

See You
In Laboratory...

44