

<b>Subject</b>	<b>Chemistry</b>
<b>Paper No and Title</b>	<b>Paper 5: Organic Chemistry -II</b>
<b>Module No and Title</b>	<b>Module 31: Diazonium coupling, Vilsmeier reaction and Gattermann-Koch reaction</b>
<b>Module Tag</b>	<b>CHE_P5_M31_e-Text</b>

<b>Principal Investigator</b>		<b>Co- Principal Investigator and Technical Coordinator</b>
<b>Prof A.K.Bakshi</b> Sir Shankar Lal Professor, Department of Chemistry University of Delhi		<b>Dr Vimal Rarh</b> Deputy Director, Centre for e-Learning and Assistant Professor, Department of Chemistry, SGTB Khalsa College, University of Delhi  <i>Specialised in : e-Learning and Educational Technologies</i>
<b>Paper Coordinator</b>	<b>Content Writer</b>	<b>Reviewer</b>
<b>Professor Diwan S Rawat</b> Department of Chemistry University of Delhi	<b>Professor Diwan S Rawat</b>  <b>Dr. Beena Negi</b> Assistant Professor Bhim Rao Ambedkar College, University of Delhi	<b>Prof. H. G. Krishnamurty</b> Professor emeritus Dept. of Chemistry, University of Delhi
<b>Anchor Institute : SGTB Khalsa College, University of Delhi</b>		

**CHEMISTRY**
**PAPER No. 5: Organic Chemistry - II**
**MODULE No. 31: Diazonium coupling, Vilsmeier-Haack  
reaction and Gattermann-Koch reaction**

## TABLE OF CONTENTS

1. Learning Outcomes
2. Gattermann-Koch Reaction
  - 2.1 Mechanism of Gattermann-Koch reaction
  - 2.2 Limitations of Gattermann-Koch reaction
3. Vilsmeier-Haack Reaction
  - 3.1 Reagents used in Vilsmeier-Haack reaction
  - 3.2 Structure of the Vilsmeier-Haack Complex
  - 3.3 Mechanism of Vilsmeier-Haack reaction
  - 3.4 Synthetic Applications of the Vilsmeier-Haack Reaction
4. Diazonium Coupling
  - 4.1 Diazo Compounds
  - 4.2 Diazonium Salt
  - 4.3 Coupling Reaction
  - 4.4 Uses of Diazo Compounds
5. Summary

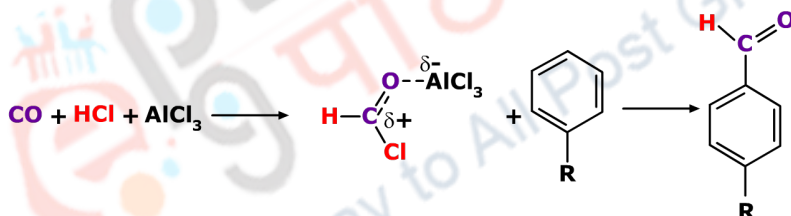
## 1. Learning Outcomes

After studying this module, you shall be able to

- Know about diazonium coupling
- Learn two name reactions Vilsmeier reaction and Gattermann-Koch reaction
- Learn the conditions under which these reactions occur
- Analyse the product formed in these reactions
- Learn the importance of these organic reactions

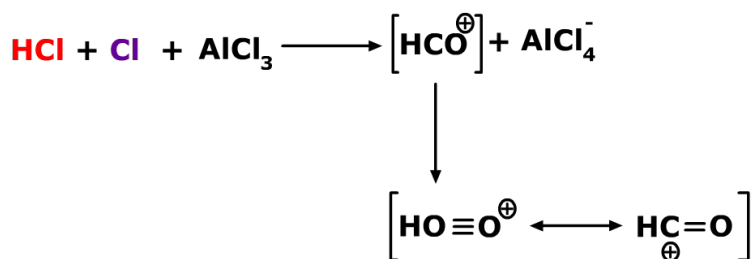
## 2. Gattermann-Koch Reaction

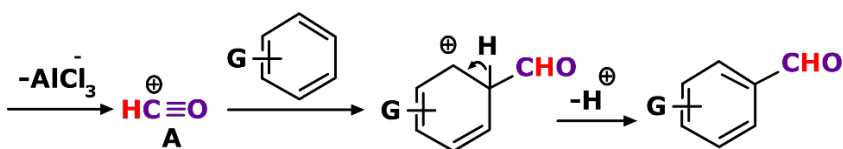
Gattermann-Koch is the name given to the reaction of an aromatic substrate with carbon monoxide and hydrogen chloride (gas) in the presence of a Lewis acid catalyst to form aromatic aldehyde. It is used for formylation of aromatic compounds. The reaction is carried out either under pressure or in the presence of CuCl.



### 2.1 Mechanism of Gattermann-Koch reaction

The reaction proceeds via generation of electrophile by the combination of carbon monoxide and AlCl<sub>3</sub>. The electrophile HCO<sup>+</sup> generated then reacts with the aromatic substrate in an electrophilic aromatic substitution reaction to yield the formylated aromatic compound.





Under high pressure conditions high yields are obtained in this reaction. To overcome the limitation of high pressure requirements, super-acidic catalysts have been developed, For example super acid generated from trifluoromethanesulfonic acid, hydrogen fluoride and boron trifluoride

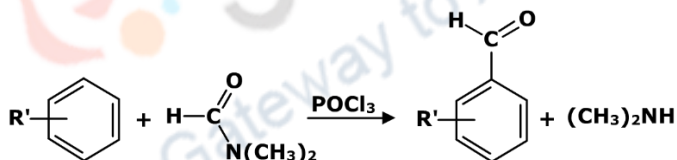
### 2.2 Limitations of Gattermann-Koch reaction:

The role of CuCl is not clear. It is known that CuCl combines with CO and this adduct may aid the reaction between HCl and CO.

Gattermann-Koch formylation method has many limitations. There are many other methods available for the formylation of aromatic compounds.

## 3. Vilsmeier- Haack Reaction

The reaction of electron-rich aromatic compounds with N,N-dimethylformamide (DMF) and phosphorus oxychloride ( $\text{POCl}_3$ ) to yield an aromatic aldehyde is called the Vilsmeier–Haack reaction.



### 3.1 Reagents used in Vilsmeier–Haack reaction

The Vilsmeier complexes employed in the formylation reactions are usually derived from N,N-disubstituted amide and  $\text{POCl}_3$ .

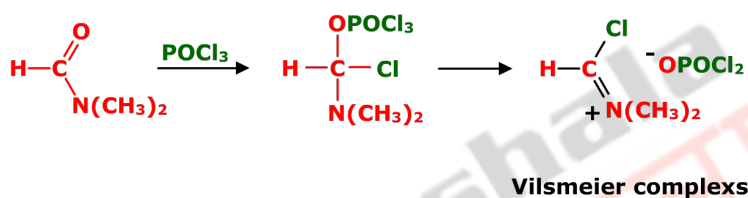
**N,N-disubstituted amides:** N-Methyl formanilide, N,N-dimethyl formamide, N-formylpiperidine and N-formylindoline have also been used other than DMF. Other amides such as N, N-dimethyl acetamide, N-methyl acetamide, N, N-dimethyl benzamide, etc. have been employed in the presence of  $\text{POCl}_3$  but these amides are prone to undergo self condensation.

**Acid chlorides:** Acid chlorides other than  $\text{POCl}_3$  have also been used in carrying out the Vilsmeier reactions. Some of these are  $\text{PCl}_5$ ,  $\text{SOCl}_2$ ,  $\text{COCl}_2$ ,  $\text{R/ArCOCl}$ ,  $\text{ArSO}_2\text{Cl}$ ,  $\text{Me}_2\text{NSO}_2\text{Cl}$ .

**Solvents:** When liquid amides are used as solvents, excess can be used, e.g DMF, dimethyl acetamide, N-methyl pyrrolidone, etc. Other solvents have also been used like benzene, toluene, chloroform, methylchloride, o-dichlorobenzene, dioxane and tetrahydrofuran.

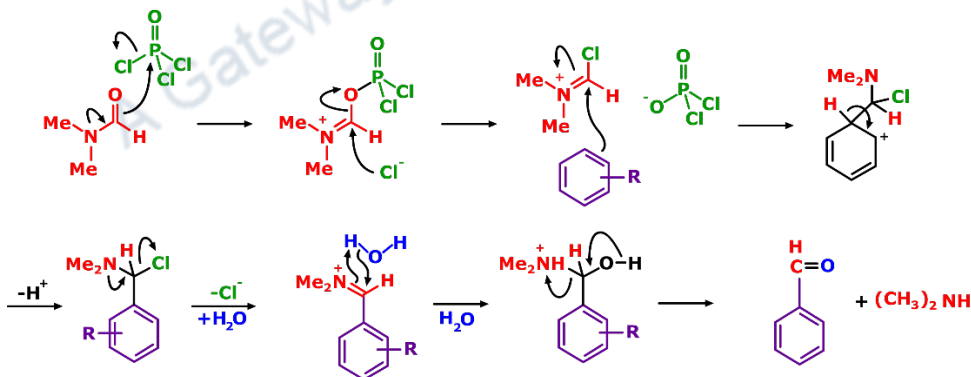
### 3.2 Structure of the Vilsmeier-Haack Complex

Phosphorous oxychloride reacts with tertiary amides to give adduct which exhibits salt like properties. These adducts so obtained are called as the **Vilsmeier complexes**.

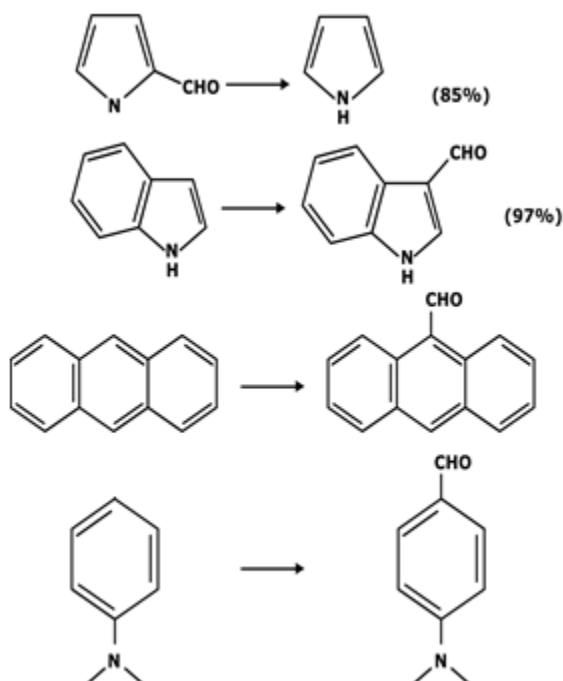


### 3.3 Mechanism of Vilsmeier-Haack reaction

The formylating agent is a chloromethyl iminium salt, also called the Vilsmeier complex that acts as the electrophile in an electrophilic substitution reaction with the aromatic substrate. The initial product of the electrophilic aromatic substitution step is unstable and easily hydrolyzes to yield the aromatic aldehyde as the final reaction product. With *mono*-substituted aromatic substrates the *para*-substituted aldehyde is formed preferentially.



V-H reaction is applicable only to electron rich aromatic compounds such as amines and phenols. Benzene and naphthalene are unreactive but anthracene gives 1-aldehyde (85%). N, N-dimethyl aniline gives 4-dimethyl amino benzaldehyde (80%). The method is particularly effective for compounds such as pyrroles which are not formulated by other procedures.



## 4. Diazonium Coupling

### 4.1 Diazo Compounds

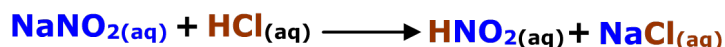
Compounds containing  $-N=N-$  group are known as diazo compounds. Their general structure is  $R-N=N-R'$

Here R and R' are preferably arene groups and the azo group is thus stabilised by becoming part of extended delocalised system. They are prepared by coupling reaction between a **diazonium salt** and a **coupling reagent**.

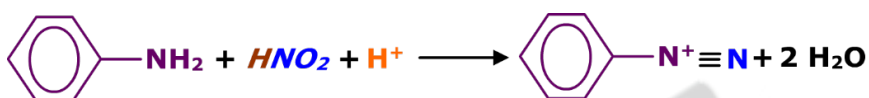
### 4.2 Diazonium Salt

Diazonium salts are prepared by adding cold solution of sodium nitrite ( $\text{NaNO}_2$ ) to arylamine solution in dilute acid below  $5^\circ\text{C}$  temperature. This process is called **diazotisation**. The diazonium salts are prepared fresh and used immediately.

The hydrochloric acid reacts with sodium nitrite to form unstable nitrous acid.

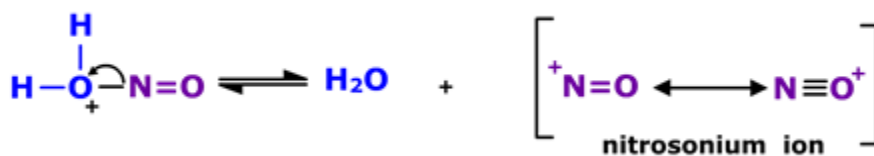


The nitrous acid formed *in situ* reacts with the arylamine to form diazonium ion.

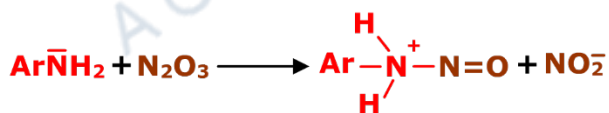


#### 4.2.1 Mechanism of diazotization:

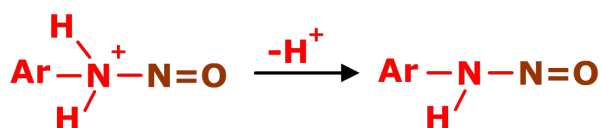
**Step 1: Formation or generation of  $\text{NO}^+$  (nitrosonium ion) or dinitrogen trioxide:** The nitrosonium ion formation takes place as follows where water is removed from nitrous acid



**Step 2: Attack of  $\text{NO}^+$  (nitrosonium ion) or  $\text{N}_2\text{O}_3$  on the amine**



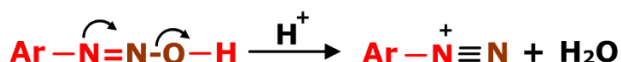
**Step 3: Loss of proton**



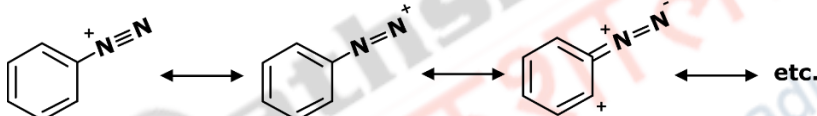
#### Step 4: Tautomerisation



#### Step 5: Loss of water and formation or generation of diazonium ion



**Stability of diazonium ion:** The aromatic diazonium salts are relatively more stable than aliphatic diazonium salts, as the electron rich benzene ring stabilises the  $-\text{N}^+\equiv\text{N}$  group. If the temperature rises above  $5^\circ\text{C}$ , the benzenediazonium chloride decomposes to form phenol and nitrogen gas is given off. The aromatic groups present stabilise the diazonium ion through donating electrons via delocalisation in comparison to aliphatic groups, as shown below.

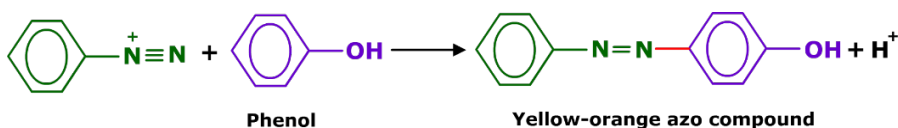


### 4.3 Coupling Reaction

If the benzenediazonium chloride is reacted with another compound containing a benzene ring, called a coupling agent (such as phenol or aromatic amine), an azo compound is produced. The diazonium salt acts as an electrophile in a coupling reaction. Many of the products of coupling reactions are important dyes. A coloured precipitate of azo compound is formed immediately on reaction of diazonium salt with amines or phenols.

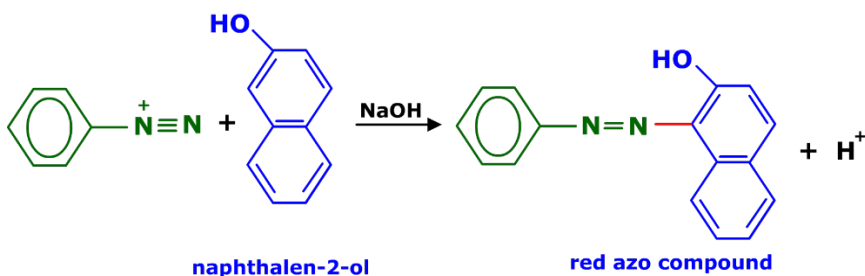
#### 4.3.1 Examples of coupling reactions:

(a) Benzenediazonium salt and alkaline phenol gives a yellow orange azo compound

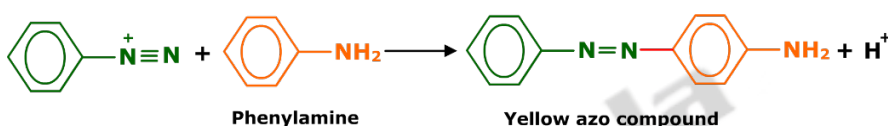


(b) Benzenediazonium salt and alkaline naphthalen-2-ol gives a red azo compound.





(c) Benzenediazonium salt and phenylamine gives a yellow azo compound.



#### 4.3.2 Mechanism of coupling reaction:

The mechanism involves an initial attack of coupling agent (phenols or anilines) on an electrophilic diazonium ion, followed by loss of a proton. The product is normally a *trans*-diazo compound rather than *cis*.



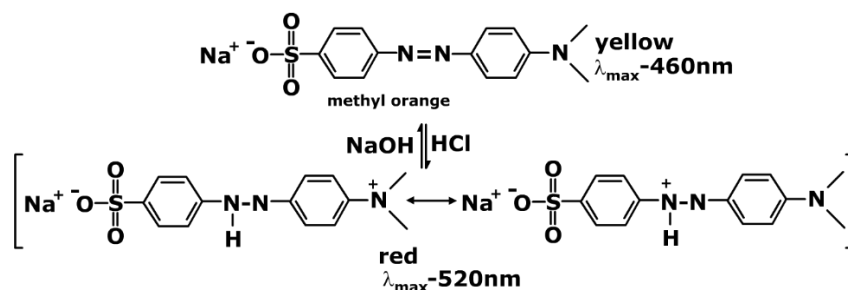
### 4.4 Uses of Diazo Compounds

Diazo compounds are used as pH indicators and dyes.

#### 4.4.1 pH Indicators

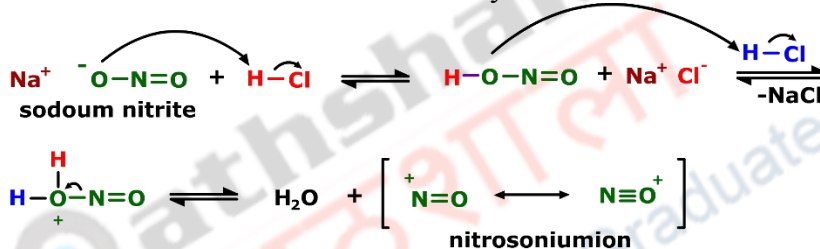
Methyl yellow, methyl orange, methyl red, congo red and alizarine yellow are some typical azo compounds used as pH indicators.

As a very common example, methyl orange is used as an acid-base indicator in titrations. In case where the solutions are more basic than pH 4.4, methyl orange exists almost predominantly as the yellow coloured negative ion. In case of solutions that are more acidic than pH 3.2, it exists in the protonated form as a red coloured dipolar ion. Due to this, methyl orange can be used as an indicator for titrations that have their end points in the pH 3.2 to 4.4 range. In concentrated basic solution, methyl orange appears orange in colour.

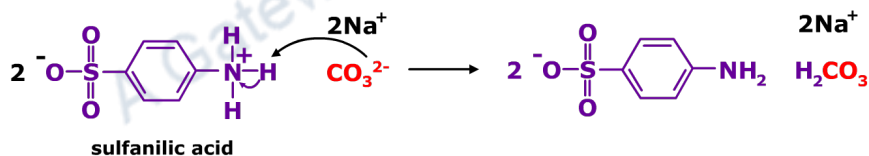


The pH indicator Methyl orange is prepared by the reaction of diazonium salt of sulfanilic acid and *N,N*-dimethylaniline.

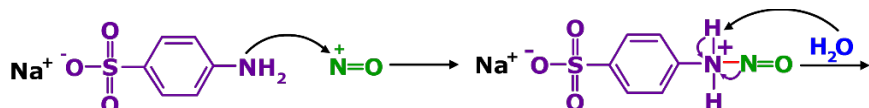
**Formation of nitrosonium ion:** In order to obtain the nitrosonium ion ( $\text{NO}^+$ ), sodium nitrite has to be treated with hydrochloric acid.



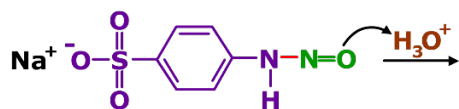
**Preparation of the diazonium salt of sulfanilic acid:** Sulfanilic acid is insoluble in acid solutions. The first step is to dissolve sulfanilic acid in basic solution (such as sodium carbonate). It then reacts instantly with nitrous acid.



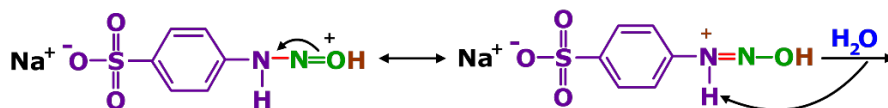
**Attack of nitrosonium ion on sodium salt of sulfanilic acid:**



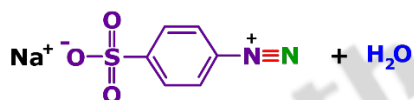
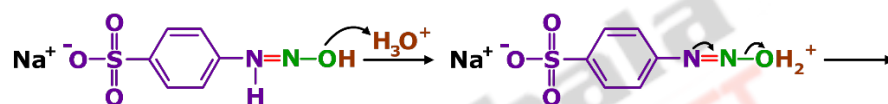
**Protonation:**



**Tautomerization:**

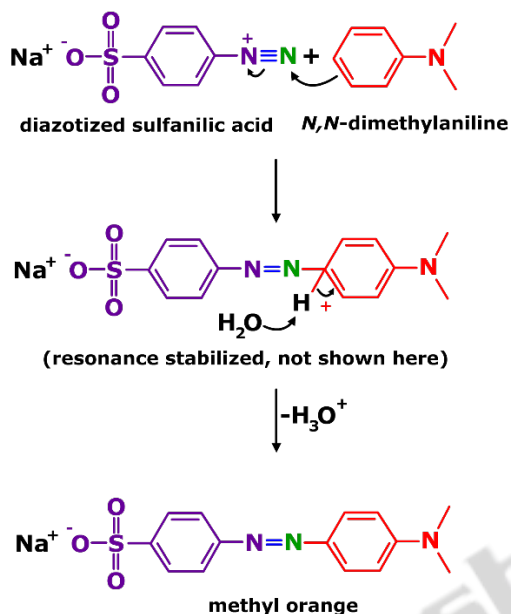


**Loss of water molecule:**



diazotized sulfanilic acid

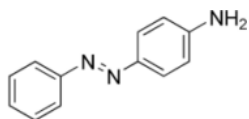
**Addition to *N,N*-dimethylaniline:** The diazonium salt so obtained is allowed to react immediately with dimethylaniline in the same solution in which it was precipitated. As a result, the initial product obtained from the coupling is bright red acid form of methyl orange, which is known as helianthin. In the presence of base, helanthin is converted to the main product, i.e., orange sodium salt, known as methyl orange.



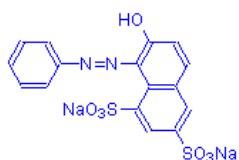
#### 2.4.2 Azo dyes

Azo dyes are compounds that contain two aromatic fragments connected by N=N double bond. Azo compounds are stable so the dyes do not fade. Using different diazonium salts and coupling agents one can make different colours. The colours of azo dyes include different shades of yellow, red, orange, brown, and blue. Dyes are used to give colors to substances, especially fabrics. In general, coloured substances appear coloured because they absorb radiation in the visible region of the spectrum. The energy absorbed causes changes in electronic energy thereby the electrons are promoted from a ground state to an excited state. The electrons excited in this case are the outer bonding electrons or lone pairs. Chromophores, functional groups that absorb light, and are responsible to give color to these dyes. The most common chromophores are azo, nitro, and carbonyl groups. Auxochromes, are the functional groups that are integral part of dyes and are responsible for intensifying the color. The most common auxochromes are hydroxyl, amino, sulfonate, and carboxylate groups.

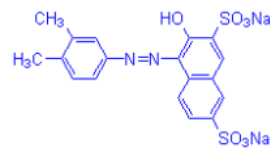
**Example of azo dyes:** Aniline Yellow, Orange G, Xylidine, Alizarin Yellow R, Bismark Brown Y and Congo Red are examples of some dyes containing azo linkages, which are synthesized by coupling reaction.



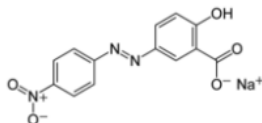
Aniline Yellow



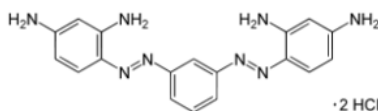
Orange G



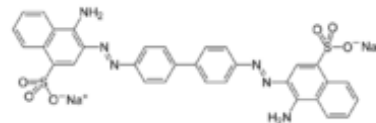
Xylidine



Alizarin Yellow R



Bismark Brown Y



Congo Red

## 5. Summary

- Diazo compounds (containing  $-N=N-$  group) are commonly used as pH indicators and dyes
- Aromatic diazonium salts are normally prepared from arylamine,  $\text{NaNO}_2$  and  $\text{HCl}$ . Successful diazotisation requires
  - (a) Keep temperature below  $5^\circ\text{C}$ , the solution should be acidic and the solution should have a slight excess of nitrous of acid
  - (b) The diazonium salt need not be isolated and reactions can be carried in solution
  - (c) The reaction of diazonium salt with aromatic nuclii is known as coupling reaction. The overall reaction is an case of aromatic electrophilic substitution.
  - (d) Aromatic azocompound are of immense value in research and industry (azo dyes)
- The reaction of electron-rich aromatic compounds with  $\text{DMF}$  and  $\text{POCl}_3$  to yield an aromatic aldehyde is called the Vilsmeier–Haack reaction.
- Phosphorous oxychloride reacts with tertiary amides to give adduct known as Vilsmeier complexes.
- The reaction of an aromatic substrate with  $\text{CO}$  and  $\text{HCl}$  in the presence of a Lewis acid catalyst to form aromatic aldehyde is known as Gattermann-Koch reaction.