

REVIEW ON (AZO, FORMAZANE, SULFAZANE)- COMPOUNDS

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ABSTRACT:

Azo compounds represent the essential compound of organic reactions and the basic material for preparing many ligands, complexes, dyes, polymers, antioxidants, bioactive compounds and other biological compounds., this review involves azo compounds with its derivatives (Formazane and Sulfazane), also in this review ,we explained sulfazane as first time in first review about this compound as a new reaction fordiazo salt that prepared for the first time by (Dr. Nagham in year 2019) via many studies in this field, besides that ,this review includes :

Azo compounds.

Name and Properties.

General Methods of Preparation.

Other Alternative Methods of Preparation.

Mechanism of Preparation.

Reactions: (Classic Reactions like Azotation Reaction, Substitution Reactions), and Novel reactions(Sulfazane, formazane, Cyclization).

Formazane, Preparation, Reaction, Applications.

Sulfazane, Preparation, Reactions, Applications.

Cyclization Reaction of Azo Group, Preparation.

Applications.

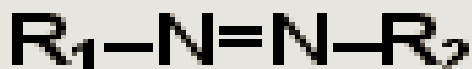
This review is part of previously reviews(2015 ,2019) that pointed it in references.

Keywords: *Azo ,Formazane, Sulfazane, imine, schiff base, new reaction, coupling, diazo salts, substitution.*

I. INTRODUCTION

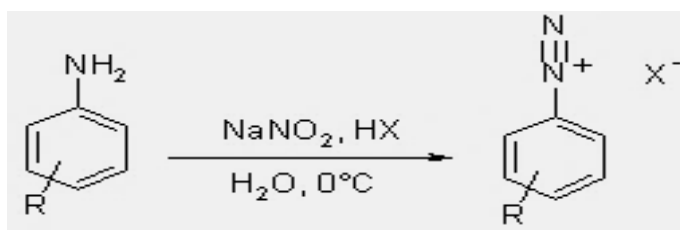
Azo Compounds

Azodyes include a nitrogen to nitrogen double bond as their chromophore (-N=N-). These dyes are generated through taking a diazonium salt and addition it to a strongly activated aromatic system. The history of dyeing can be divided into two great periods, the "pre-aniline," extending to 1856 and the "post-aniline" period. The former was characterized by a rather limited range of colors that were based on dye-producing animals and plants.

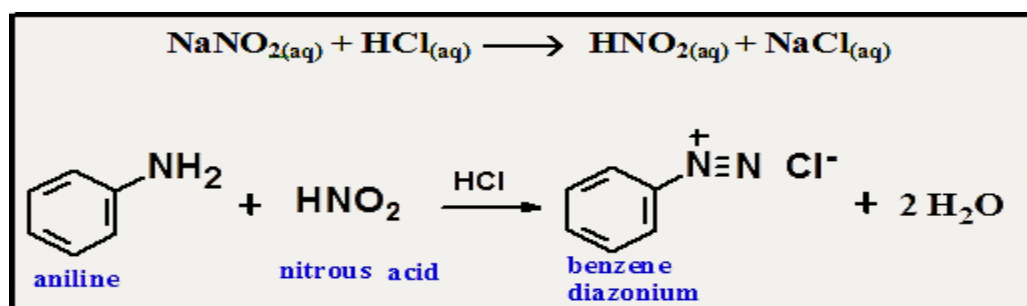


Properties of Azo Compounds:

- Azo compounds contain the $-N=N-$ group:
- In aromatic azo compounds, the R groups are arene rings; the structures of these are more stable than if the R groups are alkyl groups.
- This is because the $(-N=N-)$ group becomes part of an extended delocalized system involving the arene groups.
- The aromatic azo groups are highly coloured and are often used as dyes.
- Aromatic azo compounds are formed by a **coupling reaction** between a **diazonium salt** and a **coupling agent**.

**II. PREPARATION OF DIAZONIUM SALTS:**

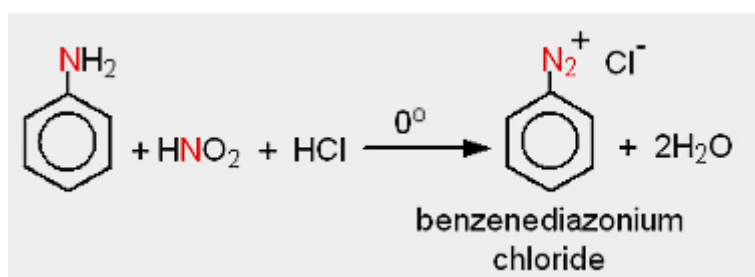
- The diazonium salts are very unstable; only stable diazonium salts are the aromatic ones, and these are not particularly stable due to presence of the benzene ring with its high electron density stabilizes the $(-\text{N}_2^+)$ group.
- Benzene-diazonium chloride is an example of a diazonium salt:
- In aqueous solution, Benzene-diazonium chloride decomposes above temperatures of 5°C and the solid compound is explosive; for this purpose, diazonium salts are created in ice-cold solutions and are used immediately.
- They are prepared in a **diazotation reaction**- a cold solution of sodium nitrate is added to a solution of aryl-amine in concentrated acid (below 5°C).
- The acid firstly reacts with the sodium nitrate to form an unstable nitrous acid
- The nitrous acid then reacts with the aryl-amine:

**Diazonium salts:**

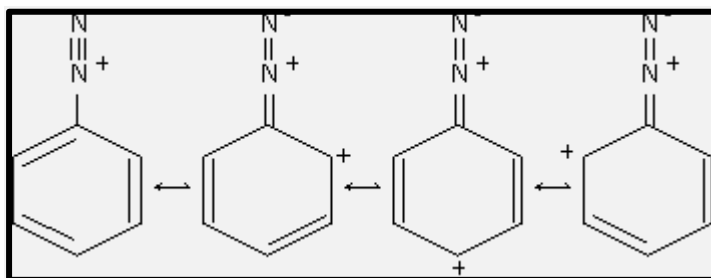
- Both aliphatic and aromatic primary amines can form diazonium salts. They do this by reacting with (nitrous acid), HNO_2 , at a temperature of $(0 - 5^\circ\text{C})$. The acid used to

generate the diazonium salt due to the instability of acid, it is always generated during a reaction, usually by the action of dilute sulphuric acid or hydrochloric acid on sodium nitrate NaNO_2 .

- Also alkyldiazonium salts are extremely unstable and always decompose to evolve the colourless unreactive nitrogen gas, amongst other products.
- The diazonium -cations of aromatic diazonium salts are somewhat more stable than their aliphatic counterparts. With phenyl-amine the benzene diazonium ion is formed.
- Although benzene diazonium salts can be isolated in the crystalline form., A structure for benzene diazonium chloride is:



- The greater stability of the benzene diazonium-cation compared with the alkyl diazonium-cation(aliphatic) is attributed to the diazo group being part of the delocalized system with the benzene ring and so the way in which the positive charge is distributed about the ring.



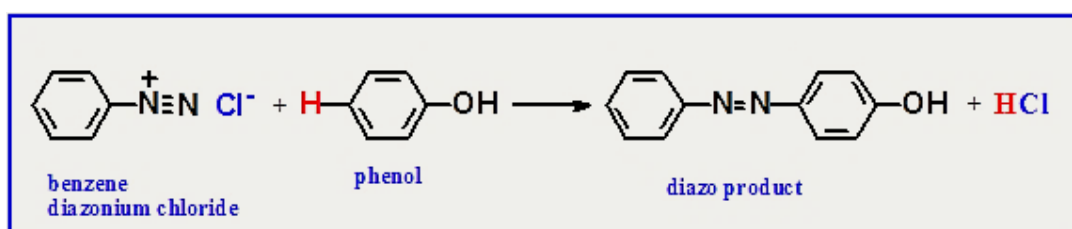
III. REACTIONS OF DIAZONIUM SALTS:

- A. Coupling Reaction.
- B. Substitution Reaction.
- C. Formation of Formazane.
- D. Formation of Sulfazane ((New Reaction that Invented by Prof. Dr. Nagham Aljamali in year 2019)).
- E. Cyclization Reaction((used in previously time but it developed by Prof. Dr. Nagham Aljamali in 2015)).

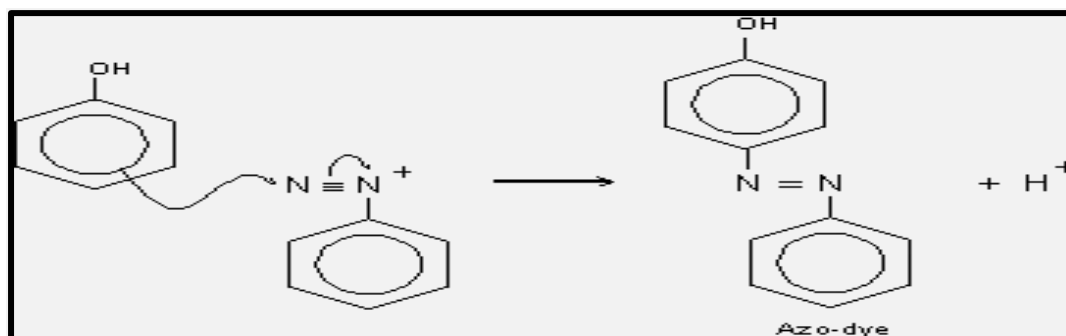
IV. NOW ALL REACTIONS OF DIAZONIUM SALTS IN DETAILS:

A. Coupling Reactions of Diazo-Salts:

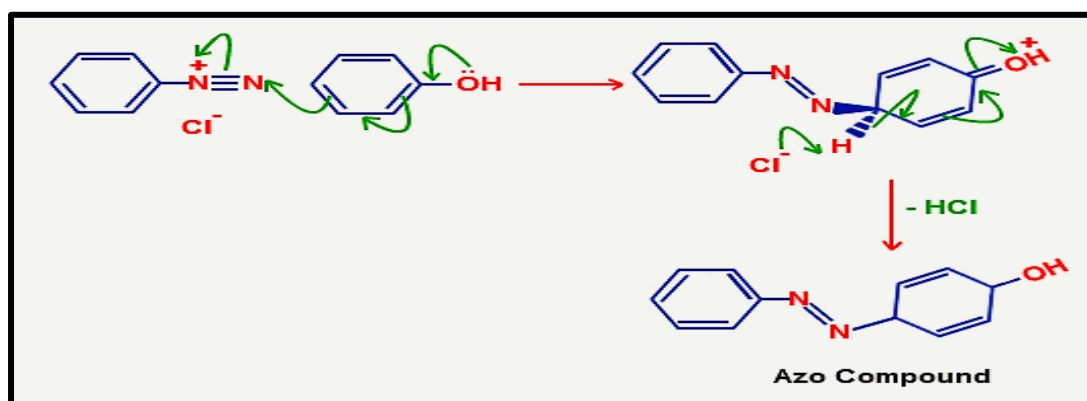
Coupling reactions act one of Diazo-salts reactions. In practice, a solution of a benzene diazonium salt is added to an alkaline solution of a phenol (or aromatic amine, like phenylamine). The benzene diazonium-cation behaves as an electrophile, but it is a weak electrophile and so the aromatic ring which it attacks must have attached to it an activating group such as (-OH or -NH₂). An electrophilic substitution reaction occurs to form an azo-dye.



Mechanism:

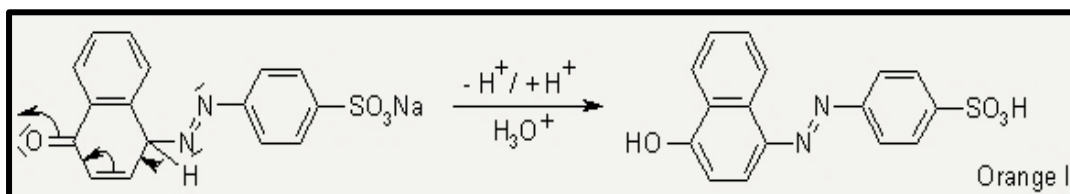


The electrophile chlorine activates the reaction and electrophilic substitution takes place on phenol. Substitution reaction takes place always in para position except when the position is already occupied. The mechanism for p-nitrobenzene diazoniumtetrafluoroborate in azo coupling with benzene or nitrobenzene.



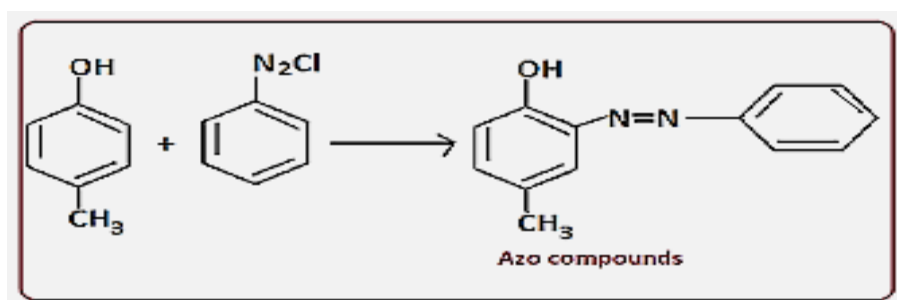
Aromatic diazonium ions acts as electrophiles in coupling reactions with activated aromatics such as anilines or phenols. The substitution normally occurs at the para position, except when this position is already occupied, in which case ortho position is preferred. The pH of solution is quite important; it must be mildly acidic or neutral, since no reaction takes place if the pH is too low.

Mechanism of Azo Coupling:

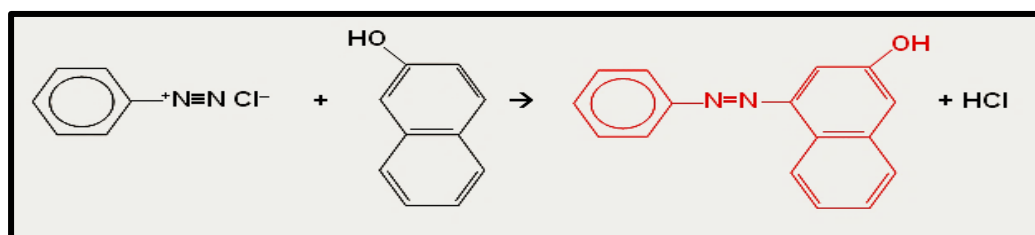


Diazo Coupling Reactions:

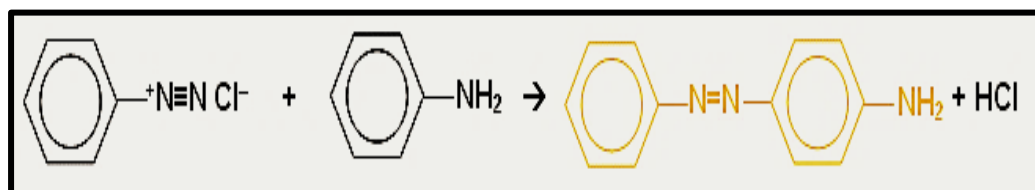
- In a diazo coupling reaction, the diazonium salt reacts with another arene (the coupling agent).
- The diazonium salt acts as an electrophile, reacting with the benzene ring of the coupling agent.
- When the ice-cold solution of the diazonium salt is added to a solution containing the coupling agent, a coloured precipitate of an azo compound is formed; many of these compounds are dyes.
- The coupling agent always reacts in the two or four position of the benzene ring (where one position is the functional group).
- The colour of the compound formed depends on the coupling agent that is being reacted with diazonium salt.
- When the diazonium salt is reacted with a phenol derivatives, a yellow/orange azo compound is formed:



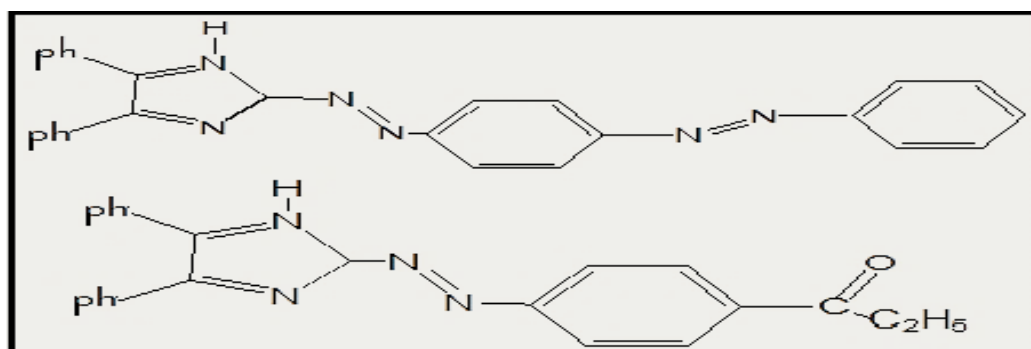
- With an alkaline solution of naphthalen-2-ol, a red azo compound is formed:



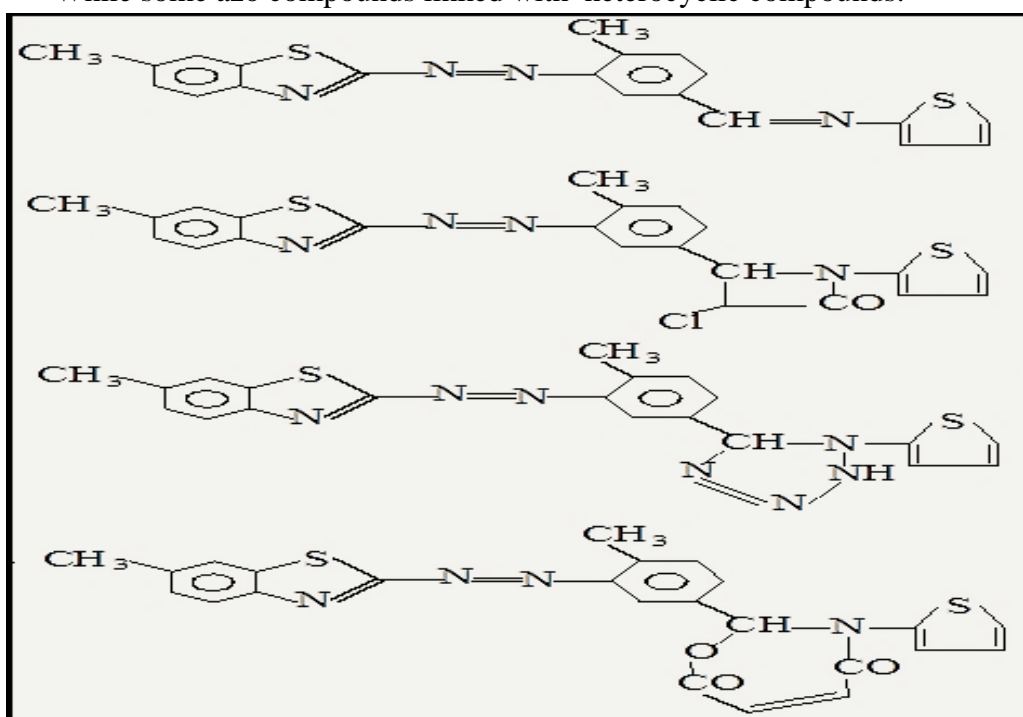
- A yellow dye is often formed when a diazonium salt is reacted with arylamines:



- Many different azo compounds can be formed by coupling different diazonium salts with
- Coupling of diazonium salts with phenols yields azo compounds, containing the azo group, (-N=N-). For example, an alkaline solution of phenol (the coupling agent) reacts with benzene diazonium chloride (an electrophile) to form a yellow azo-dye. Coupled with naphthalen-2-ol a bright red precipitate is formed.
- In azo compounds the -N=N- group is part of an extended delocalized electron system involving the aromatic rings, called a chromophore. The quantised molecular electronic energy levels are closer together in such delocalized systems and light from the visible region of the electromagnetic spectrum is absorbed (DE) when electrons are promoted from lower to higher levels. The azo compound then appears a colour corresponding to the unabsorbed visible light. Also, groups such as (-OH and -NH₂) are often attached to chromophores (also forming part of the extended delocalized electron system, so changing the DE values) to modify the colours of the molecules. Azo-dyes bind to fabrics in different ways. For cotton, many are insoluble and become trapped in the fibers. Others, called direct dyes, become attached to the fibers by hydrogen bonding and instantaneous dipole-induced dipole intermolecular bonding. Because intermolecular bonding is much weaker than covalent bonding, the dye molecules must be long and straight so that they can align closely with the cellulose fibers of cotton giving more opportunities for intermolecular attractions. There many studies explained azo coupling compounds involved one or more (-N=N-) group in same compound.

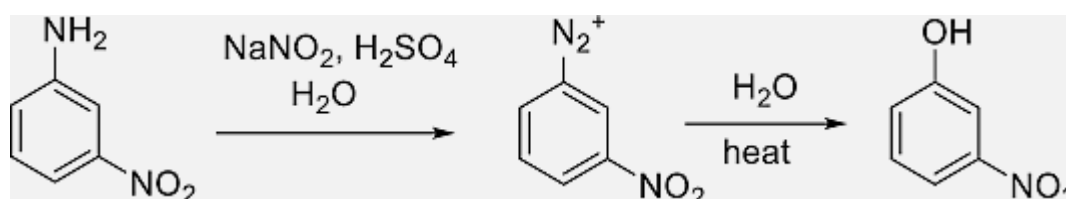


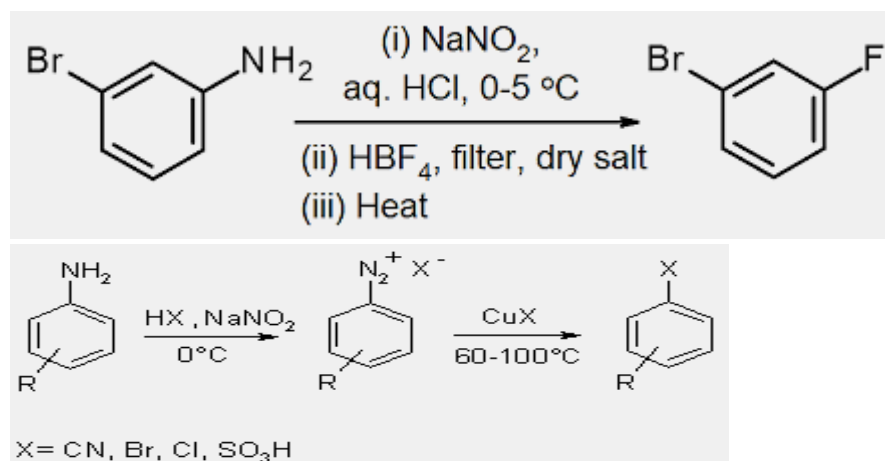
While some azo compounds linked with heterocyclic compounds:



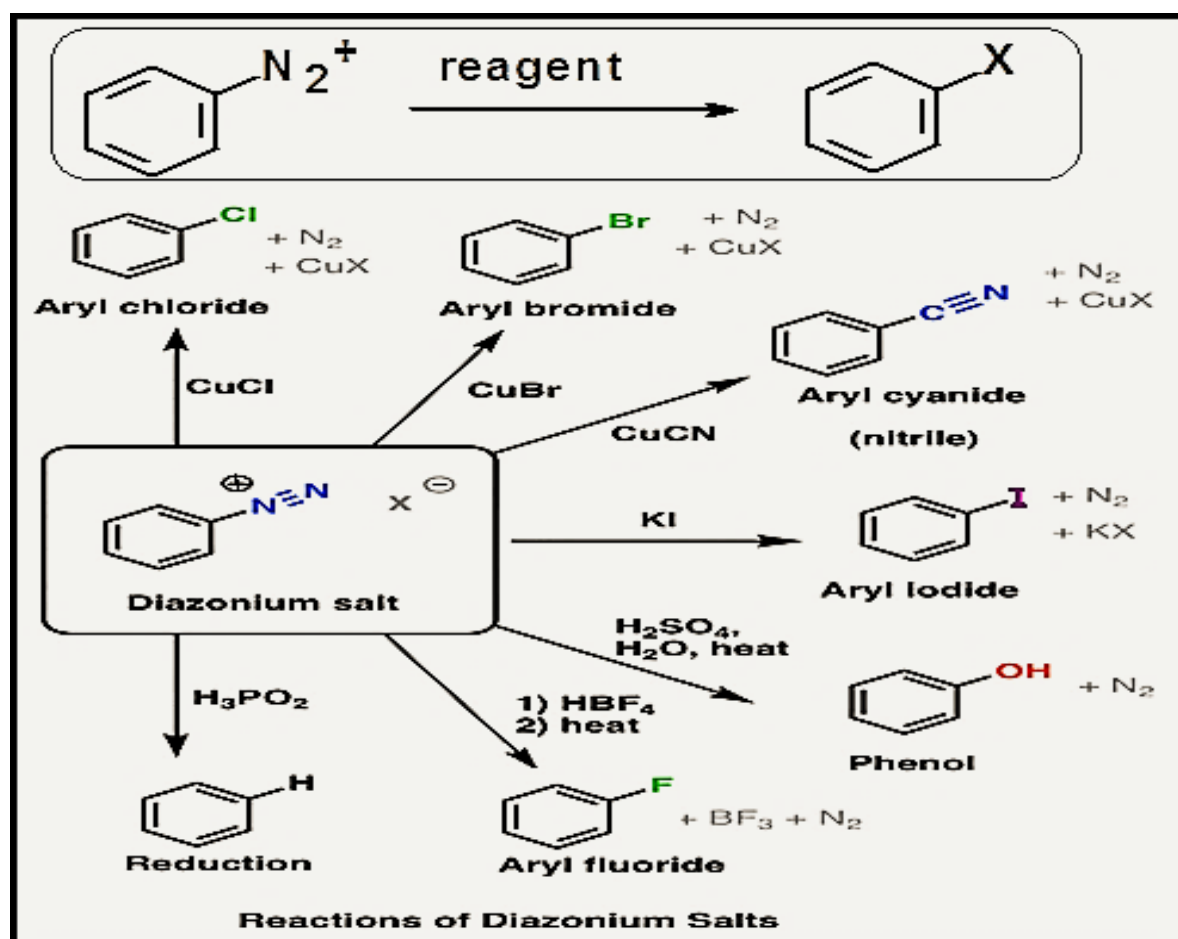
B. Substitution Reactions of Diazo- Salts:

Substitution reactions act one of Diazo-salts reactions .A generalized equation for a substitution reaction is shown below in which the reagent can be any reagent while (X any group):Examples for these reactions (substitution reactions) from the scheme :





All reactions in the Scheme:

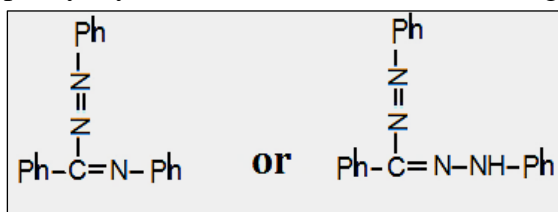


C. Formation of Formazane Compounds from Diazo-Salts:

Formation of formazane compound acts one of Diazo-salts reactions. The formazane derivatives have various applications in many fields in medicinal, chemical, pharmaceutical, biological, industrial and in coordination chemistry fields as a ligands in complexes with ions that due to their structures (involving more than two nitrogen atoms, azo group and imine group), their best significant attribute is their ability to prepare highly colored yields recognized as

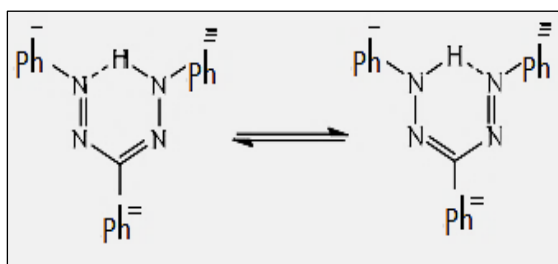
formazanecompounds upon reaction. This feature can be applied to detect biological decreasing systems. The formazane derivatives are currently widely applied each in chemistry and biology. This survey presents the various biological activities of formazane derivatives. This review report covered many applications which indicate that formazane derivatives exhibit multipurpose pharmaceutical and biological activities.

Formazane acts one of chemical organic compounds that involves the (-N=N-C=N-) or (-N=N-C=N-N) fragment according to type and structure of reactants from aromatic amine like (aniline, phenyl hydrazine, or like this), it has a long history as dye compounds.



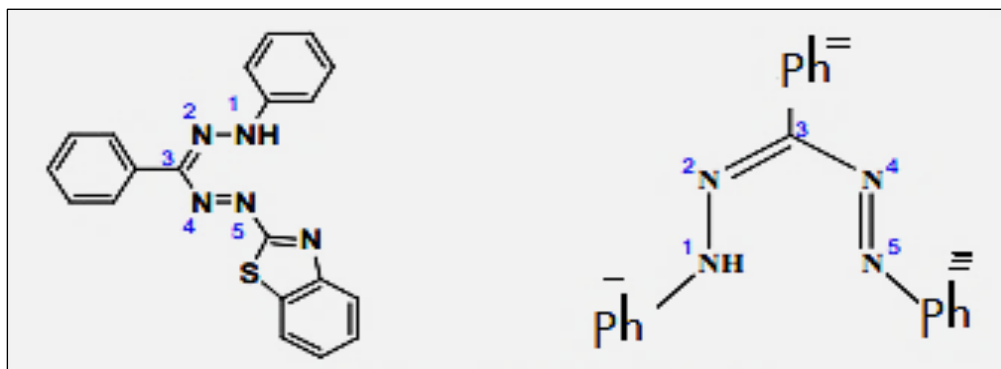
Formula of Formazane.

In recent chemical study the formazane not merely appears applications in the field of medicinal, biological and pharmaceutical researches besides are forerunners towards hetero cycles like thiadiazole- formazane, imidazole- formazane or any hetero cycle-formazane. The stability of formazane derivatives come from their structure that due to (more than two nitrogen atoms) which act (-N=N-C=N-) that leads to use the formazane compounds as a ligands in complexes. The solid state of formazane appears deep colors, extending from (red to a deep purplish-black) and involves the single and double bonds within the main chain of atoms: (-N=N-C=N-NH-), the types of their isomerism being dependent on the nature of the substituents, tautomerism in Figure 2.



Tautomerism in Formazane.

The formazane is a special redox structure representing as a proton acceptor or oxidant, this system is broadly used in altered branches of the natural sciences like medical field, pharmaceutical, immunology etc. The numbering system of formazane follows altered orders due to the common rule which heteroatoms (like N) with a charge in a ring should have the lowest possible number [9-15] in Tetrazolium; while in the formazane numbering starts from the amine group via convention.



Numbering in formazane.

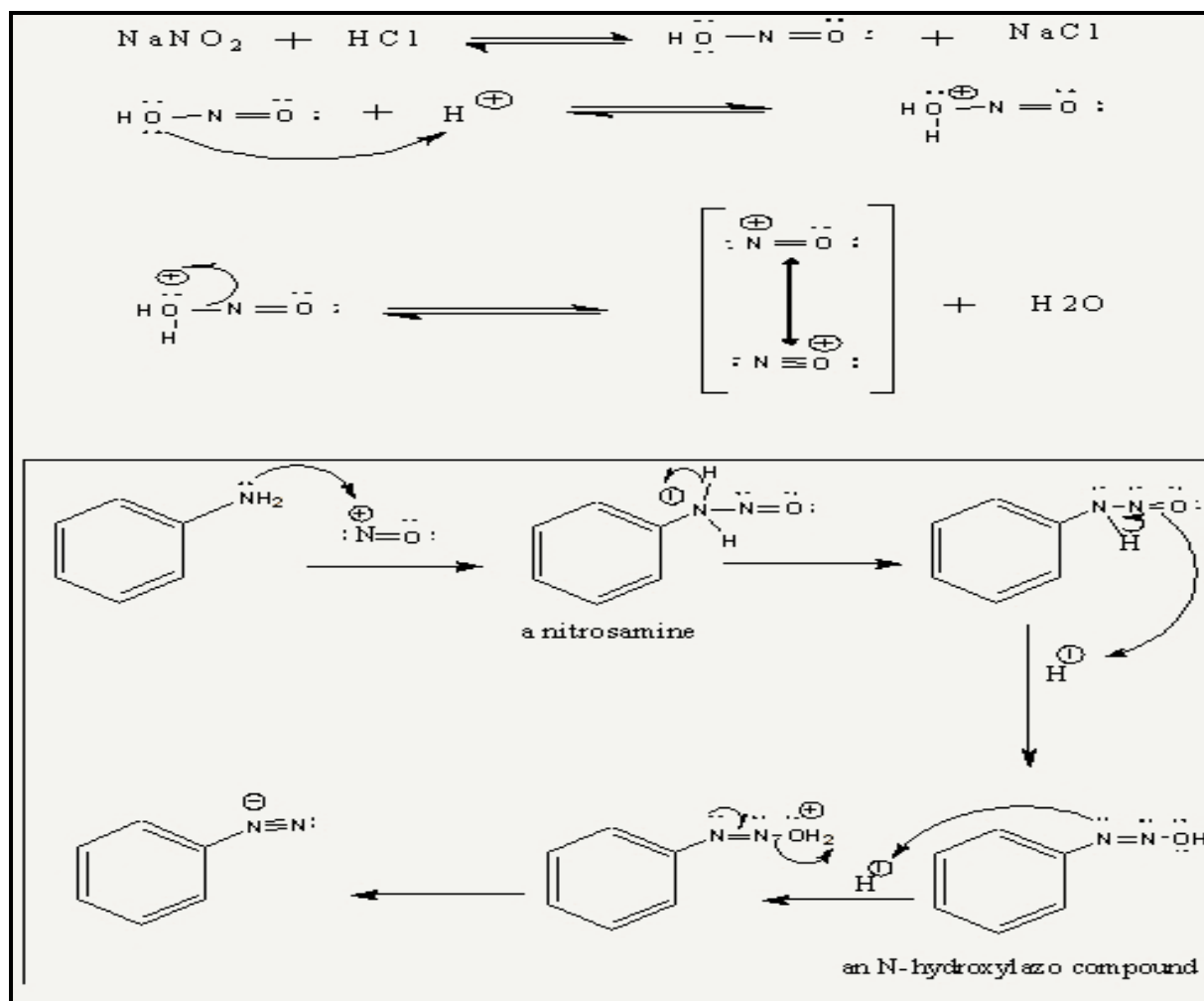
Preparation Methods of Formazane:

The general method of formazane synthesis is introduced according to procedures⁽²⁶⁻²⁸⁾. The method was applied to synthesize a series of formazane ligands which contain a large diversity of steric and electronic properties of the substituents. A synthetic procedure for the di-formazane system was developed in which the two formazane fragments are linked by a phenylene linker at meta and para-position:

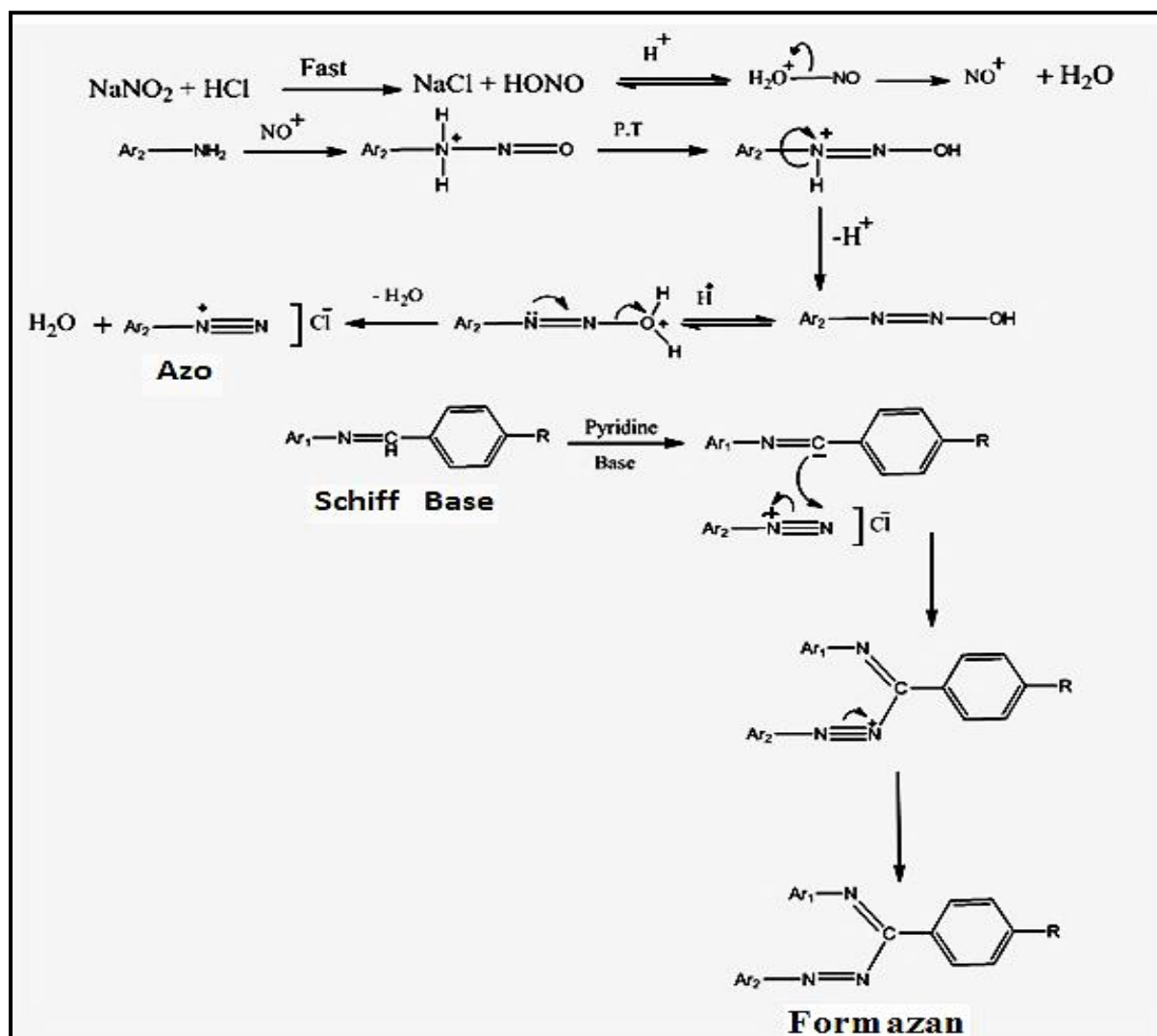
I. The First Step: Preparation of AzoCompound((Diazonium Salt)).

II. The Second Step :Preparation of Schiff Base (Imine Group)).

III. The Third Step :Preparation of Basic solution of Schiff Base (dissolved Schiff base in base medium like pyridine or (5 % sodium hydroxide) for (5 minutes) , then addition this mixture to azo salt after (24 hrs), filtration, dried , recrystallization, to yield formazane (colored compounds)., **Via Mechanisms⁽²⁶⁻²⁸⁾ , three steps ,Figures :**



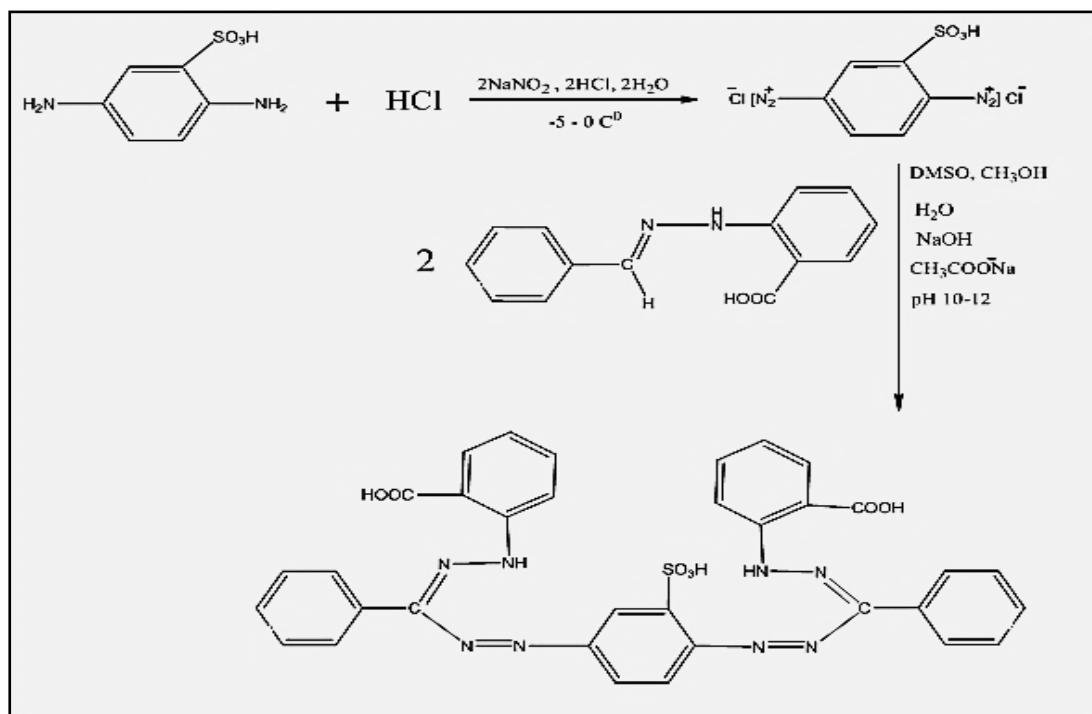
Mechanism of Diazonium salt –first step of formazane.



Mechanism of all steps of formazane.

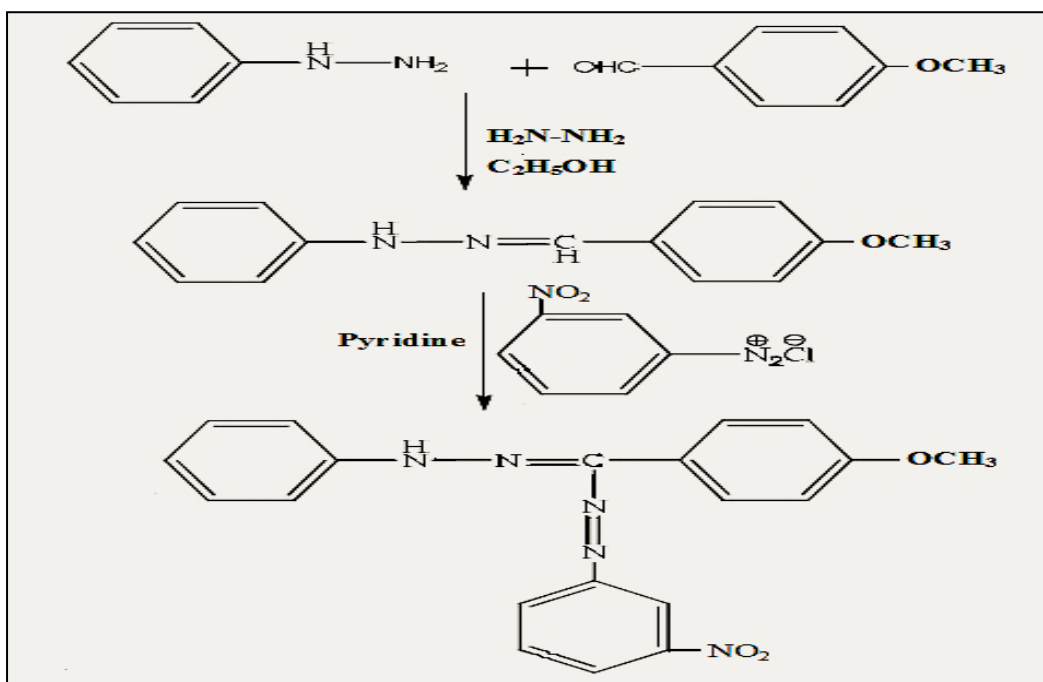
Alternative Methods of Preparation -Formazane:

1. By coupling between Diazonium Salt with Imine group :through using base medium like sodium hydroxide with sodium acetate.

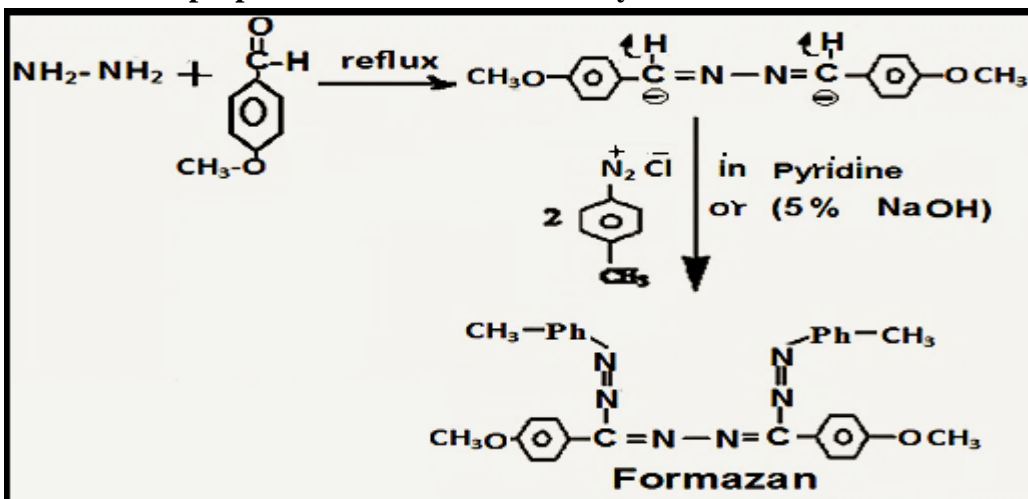


Mechanism - preparation of formazane via NaOH.

2. **By coupling between Diazonium Salt with Imine group through using base medium like pyridine:** Azo Compound ((Diazonium Salt)), then Preparation of Schiff Base (Imine Group)), then third step Preparation of Basic solution of Schiff Base (dissolved Schiff base in base medium like pyridine for (5 minutes) ,then addition this mixture to azo salt ,after (24 hrs) ,filtration, dried, recrystallization to yield formazane (colored compounds) ., Figures :



Mechanism - preparation of formazane via Pyridine.

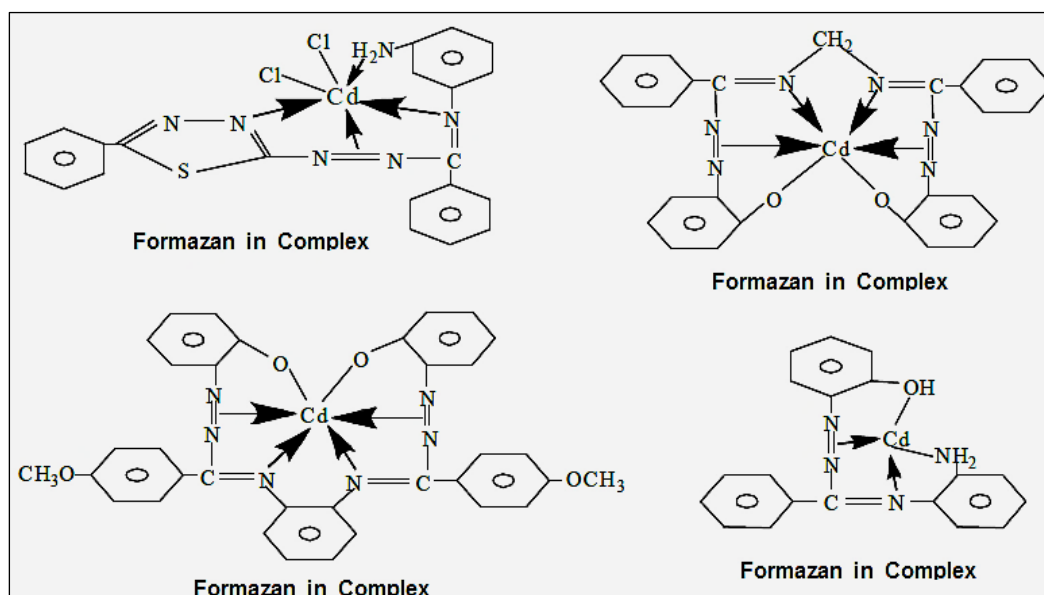


Mechanism - preparation of Bis - formazane via Pyridine.

Applications of Formazane Compounds:

Formazane in Coordination Chemistry in Complexes:

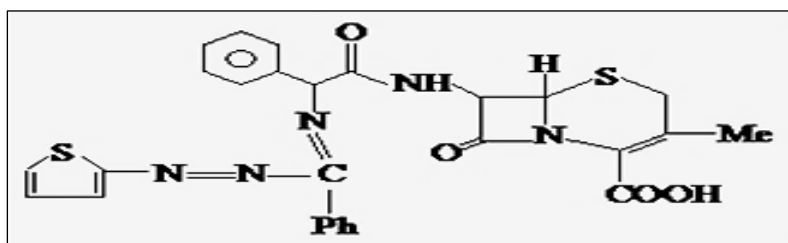
The complexes are formed and investigated as a solid-state and solution-state like the (Metal Ion)-complex reveals that formazane ligands appear a high flexibility in coordination chemistry.



Formazane in Complexes.

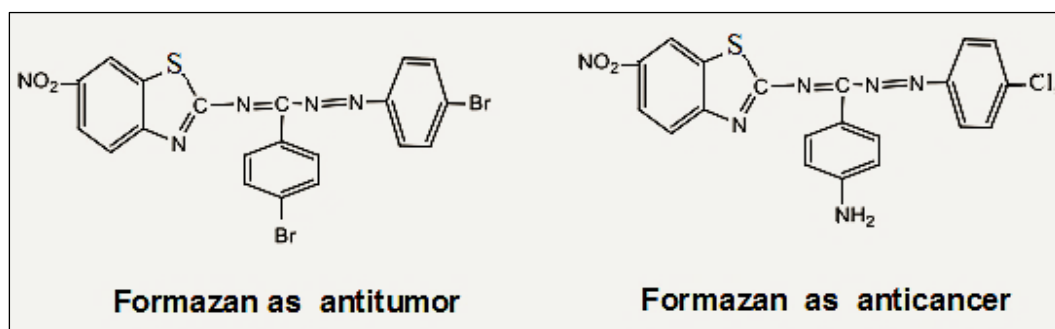
Applications of Formazane in Medical and Pharmaceutical Fields

A survey of literature reveals that many formazanes have been described to possess varied spectrum of natural activities. In the following a complete explanation of the currently reported pharmacological applications of numerous formazane derivatives which tested as antibiotics via preparation cephalixin -formazane drug.



Cephalixin -formazane drug.

The researchers scanned the cytotoxicity of formazane derivatives to a variation of human cancer cell lines involving (MCF-7 and MDA-MB-231), and found that it is cytotoxic to all tumor cells in a range of 5-100 μM . Whereas most of them showed IC₅₀ of 10-20 μM , A549 showed remarkable resistance (IC₅₀-100 μM) and MCF-7 showed high sensitivity (IC₅₀-5 μM)., Some formazane derivatives as examples for anticancer.

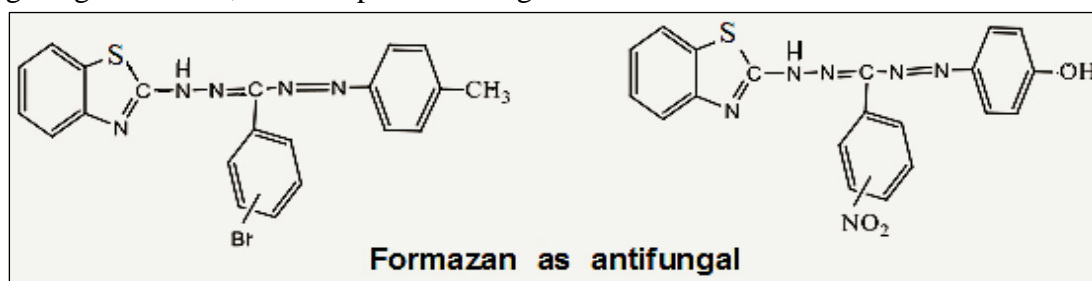


Formazane derivatives as anticancer.

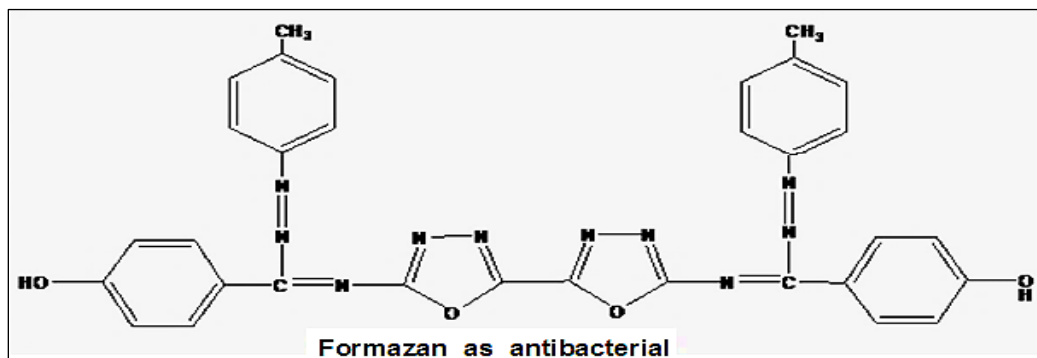
Formazanes are applied to screening of antitumor drugs, determination of activity of tumor cell and sperm practicality. In other studies, the researchers prepared also a similar series of formazane derivatives and the results of their analysis for antitumor activity that these compounds have good activity against cancer and tumors.

Applications of Formazane in Biological Fields:

Some formazanes possess antimicrobial activity., in many studies prepared the formazane derivatives and tested their antibacterial with antifungal activity via the agar diffusion method. All the formatted formazanes were screened in vitro for their antibacterial activity against various microbes like Bacillus .S, E- coli, P. aeruginosa and antifungal activity against Candida albican gave good results, like compounds in Figures:



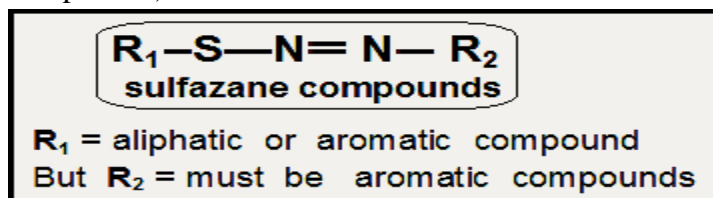
Formazane as antifungal.



Formazane as antibacterial.

D. Formation of Sulfazane Compounds from Diazo-Salts:

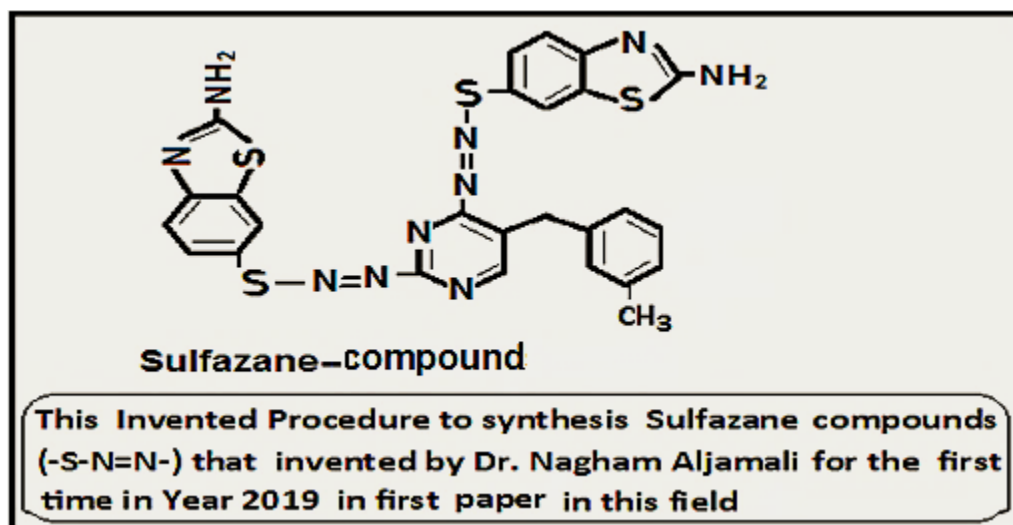
Formation of sulfazane compound acts one of Diazo-salts reactions (Nevel and Innovated compound). Sulfazane Compounds was synthesized and invented for the first time^(25, 34, 40) in year 2019 by (Prof. Dr. Nagham Aljamali) who synthesized these compounds via many steps of conjugated process of azo group with thiol group in basic medium and special condition to format (S-N=N-), besides that she concluded by many studies that these compounds have (high stability, colors, solid compounds, medical applications as anticancer, biological applications as antibacterial and antifungal compounds).



General Structure of Sulfazane Compounds

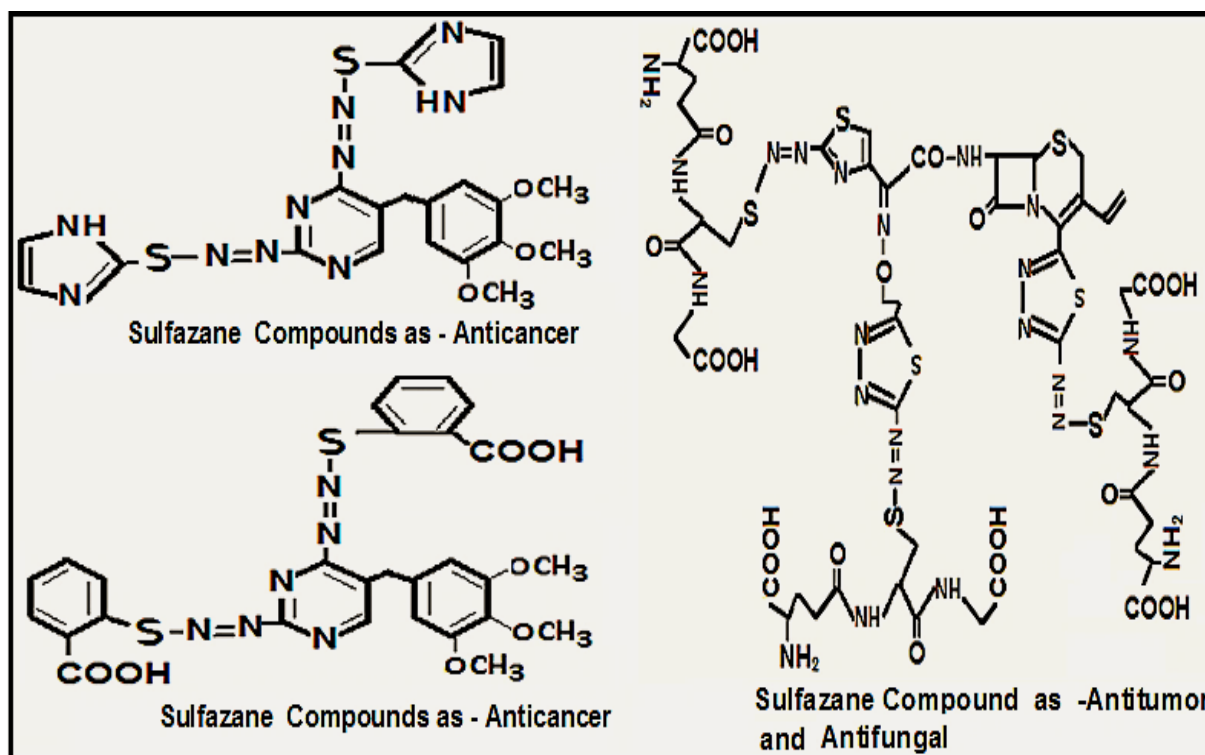
Preparation Method of Sulfazane Compounds:

Thiol compounds in basic medium (Pyridine, or piperidine, or 5% NaOH, or basic alcoholic solution,..) in three steps reacts with solution of Diazo salt via same steps according to invented procedures^(25,34, 40) in papers (Author Dr. Nagham et al, years 2019, 2020), after (2 days), filtered, washed, dried, recrystallized to yield sulfazane compounds like:



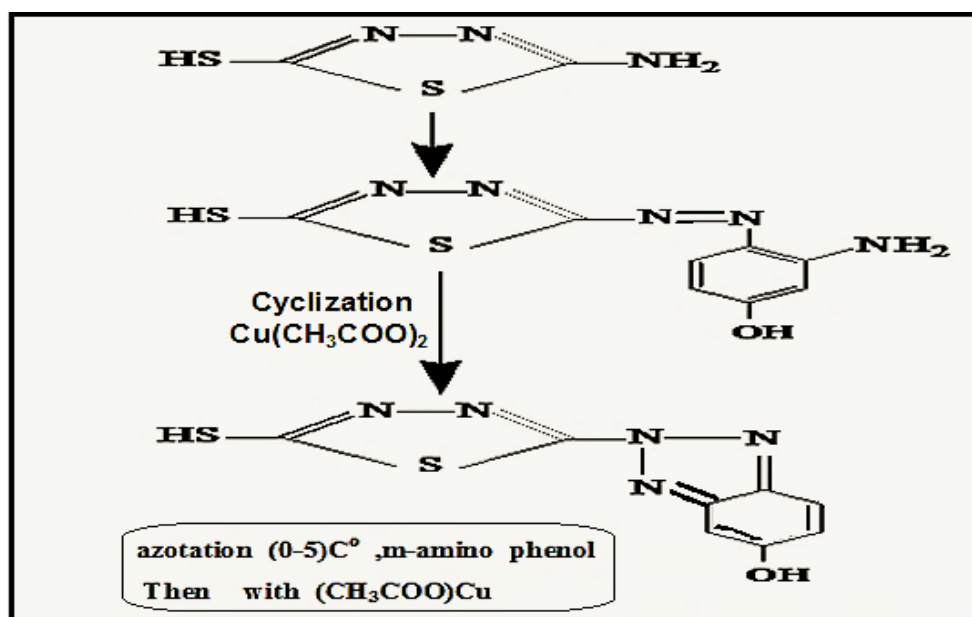
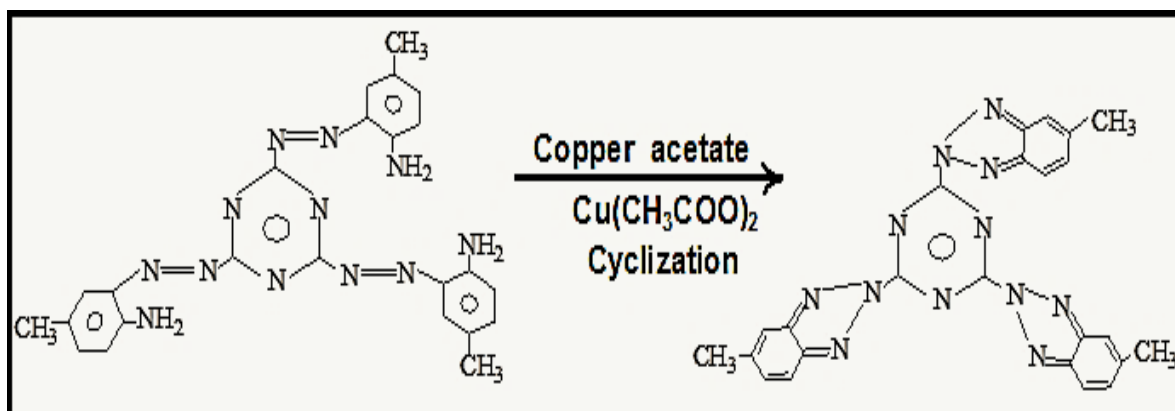
Applications of Sulfazane Compounds:

There are studies^(24,26-30) carried out by (Dr. Nagham in years 2019, 2020 ,and go on in future...),these studies improved various applications in biological, pharmaceutical, medical fields besides to applications in coloring process(due to its coloring properties and stability) and other applications in synthetic chemistry field:



Sulfazane Compounds in Medical and Pharmaceutical Fields ((reference .41))

E. Cyclization Reactions of Azo compounds: Azo group (-N=N-) reacts as intra-molecular cyclization reaction with amine group in ortho-position in same azo compound in presence of copper acetate to formation cyclic compound that involved three nitrogen atoms:

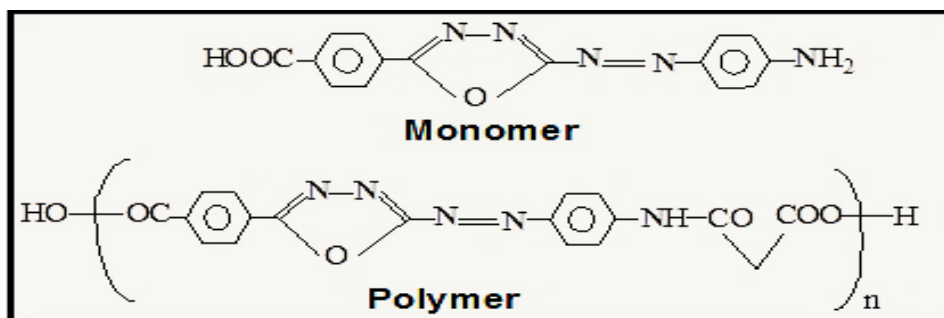


Cyclization reaction by using copper acetate in pyridine.

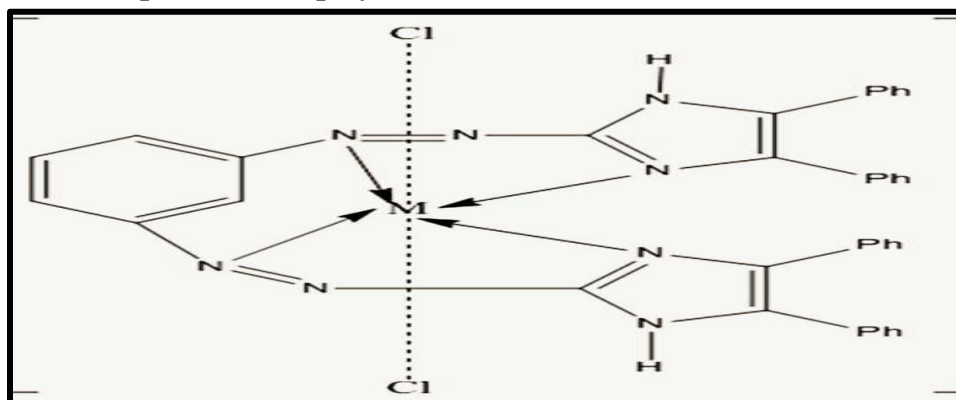
Also there are other cyclization agents like pipyridine, FeCl_3 , and other for this purpose.

Applications of Azo Compounds:

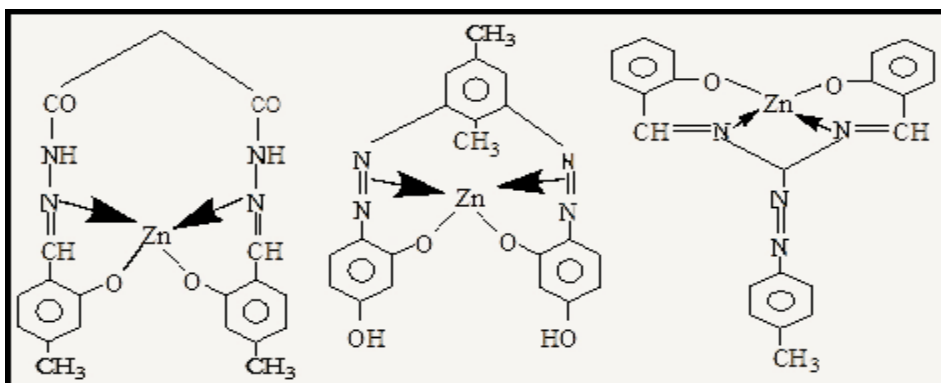
There are numerous applications in different fields of azo compounds like in medical, pharmaceutical, synthetic chemistry, biological, industrial fields like:



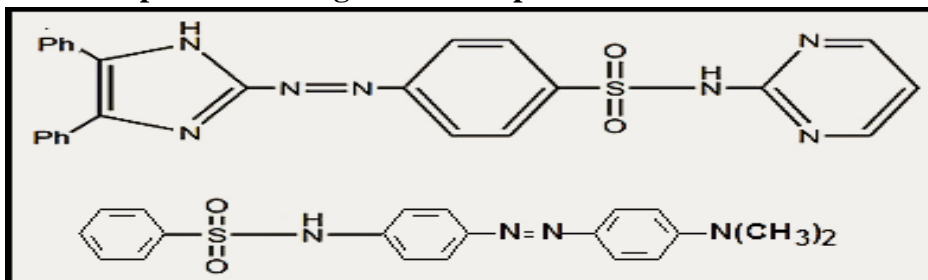
Azo Compounds as a polymer and Monomer



Azo Compounds as a complex



Azo Compounds as a ligands in complexes



Azocompounds as antibacterial and antifungal

CONCLUSIONS

Diazonium salts are light sensitive with break down under near [UV](#) or violet light. This property has led to their use in document reproduction. In this process, paper or film is coated with a diazonium salt. After contact exposure under light, the residual diazo is converted to a stable [azo dye](#) with an aqueous solution of coupler., Also formazane and sulfazane are coloured, stable compounds, besides to various applications in many fields.

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