

SYNTHESIS AND APPLICATIONS OF AZO COMPOUNDS: A MINI REVIEW

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ABSTRACT

The present mini review paper focus on trends in synthesis and uses of azo compounds in various fields such as dyeing of fabrics, acid-base titration indicators, pharmaceuticals, cosmetics, food, paints and many more. The major application of azo compound is to dyeing the fabric because of its wide range of colour shades ranging from yellow to orange, red, violet and sometimes dark brown also depending upon substituents present in structure. The $-N=N-$ (azo) group is the main functional group which is planked by two aromatic rings. This azo group is metabolise *in-vitro* as well as *in-vivo* in to two different aromatic amines hence use of azo compounds in pharmaceutical industries now a day widely increased.

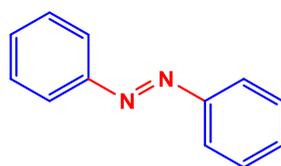
KEYWORDS: azo compounds, history of azo compound, synthetic methods, uses of azo compounds.

INTRODUCTION

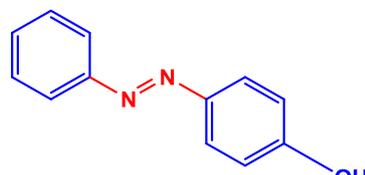
This is the present era of fashion, in every field we want alternative or better options in each and each thing starting from our basic needs such as food, clothes and shelter to our other priorities depending upon our affordability. Colour shades are not only the mood swingers of the plant kingdom but also animal kingdom. Some colours are made by nature to facilitates the life on earth and some are manmade. In case of synthetic colours azo compounds are most widely preferred due to

their vivid colour shade availability ranging from yellow, orange, and red to brown and so on. Azo compounds are basically organic compounds contains two or more aromatic rings coupled by azo ($-N=N-$) group on either side. Due to presence of this $-N=N-$ azo group, rings present on both sides shows elongation of conjugation and because of this they show different colour shade.^[1] Apart from this, azo compounds also used as antibacterial, antimalarial, antifungal, antioxidant, as well as antiviral agents.^[2]

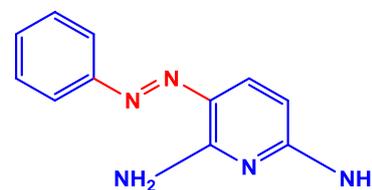
E.g.



Azo Benzene



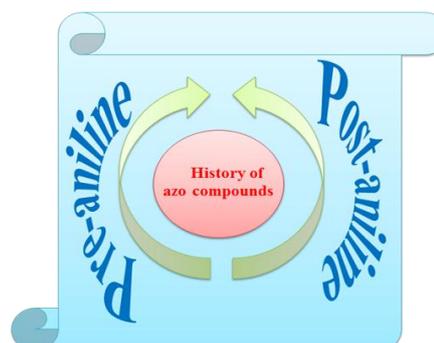
Solvent Yellow 7



Phenazopyridine

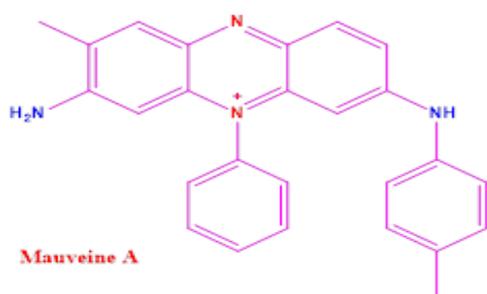
1. History in Brief

The history of azo compounds can be divided into two great eras Pre-aniline (before 1856) and Post-aniline (after 1856).

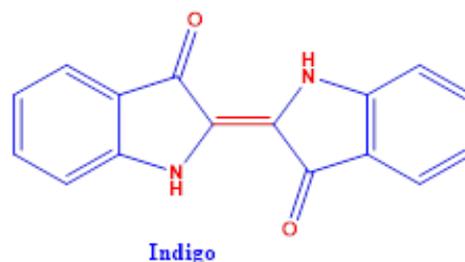


Pre-aniline era is categorized by limited range of colour shades, were colours obtained from plants and animals. Madder roots (found in Asia & Europe) are the great source of red colour whereas Indigo (found in India) plant is the source of blue colour which is still used today to dye the jeans. Along with these, animal source such as small shell fish nurez used for obtaining Tyrian purple colour. Some ancient samples also prove that there is an existence of series of reds and purples.^[3]

Post-aniline era is started after the availability of aniline which is obtain from coal-tar from 19th century (after 1856) and synthesized a dye Mauveine A this is the born period of synthetic colour. This is the starting of world of synthesitic dye.



In 1870 Adolph von Baeyer synthesizes the indigo and determines its structure, and from 1897 10,000 tons of indigo were manufactured per year in industry by replacing the agricultural production of colour.^[4]



Sir William Henry Perkin is the first azo compound developer in 1858^[5], then aliphatic azo compounds were reported in 1882 but they were unstable due to their rapid dissociation in to hydrocarbons and nitrogen.^[6-8] Then aromatic azo compounds are coming forward in focus due to their great resonance stability.^[9, 10]

After that azo pigments are in spotlight, first azo pigment (1885) is Para red which is used for paintings and store in canes. Following is the chronological order of azo pigments.^[1]

Azo Pigment Name	Year
Para red	1885
Lithol Red	1819
Red Lake C	1903
Pyrazolone (Hansa) Yellow	1909
Bon Red	1910
Diarylide Yellow & Orange	1911
2B Red	1931
Ni Azo Yellow	1947
Azo Condesate Yellow	1954
Benzimidazolones	1960
Opaque Azo Yellow, Orange & Red	1965
Quinoxilinedione	2000

Every azo pigment contains different types of different chromospheres and auxochrome that gives different colour, shade and stability.

Synthesis of azo compounds

In past there is only one method for preparation of azo compounds i.e. formation of diazonium salt and coupled

with electron rich aromatic ring (having $-\text{NH}_2$, $-\text{OH}$ etc groups).

This synthetic method is divided in to two steps 1) Synthesis of diazonium salt 2) Coupling of diazonium salt with electron rich aromatic compounds containing ($-\text{NH}_2$ or $-\text{OH}$ groups).

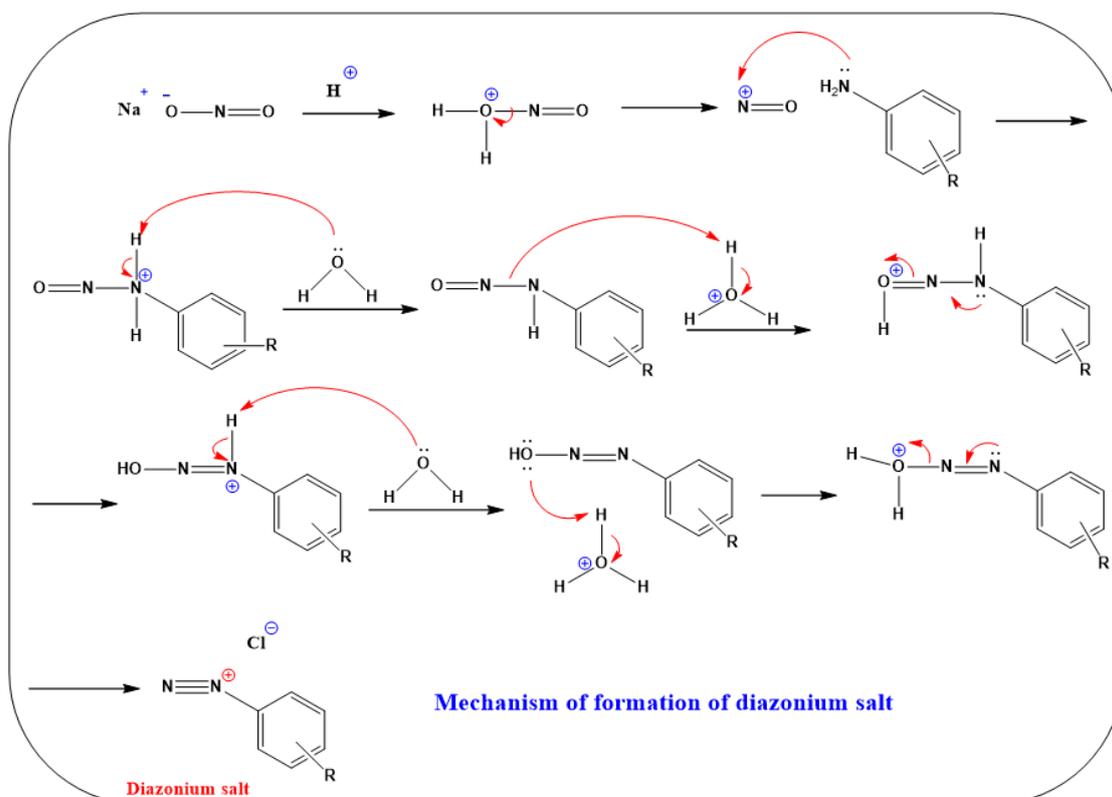


1) Synthesis of Diazonium salts

In this step Primary aromatic amines are dissolved in aqueous mineral acid (HX or H₂SO₄), is treated with sodium nitrite solution at lower temperature. The diazonium salts are unstable and slowly decomposes even at ice bath temperature, hence the diazonium salts were used immediately after preparation.

Following are the precautions were taken at the time of formation of diazonium salts.

- The diazotization must be carried out at low temperature 0-5°C to avoid formation of phenols.
- An excess of mineral acid should be used to prevent coupling reaction.
- Excess of nitrous acid be avoided because of it interferes with the reaction of the diazonium salt. Excess of nitrous acid can be removed by adding urea.
- As the diazonium ion decomposes in the presence of metals, the diazotization is carried out in wooden vats of rubber or glass-lined steel vessels.



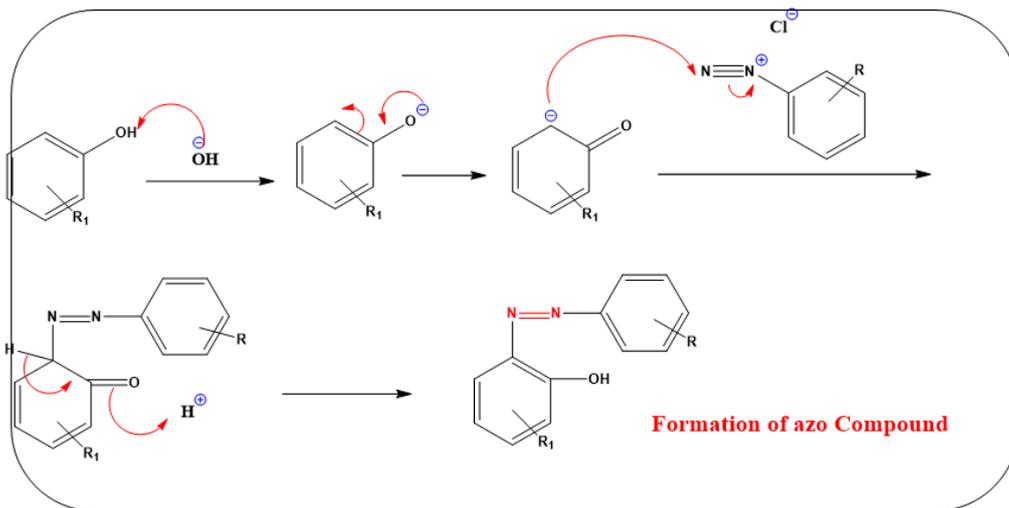
2) Coupling of diazonium salt with electron rich aromatic compounds containing (-NH₂ or -OH groups)

In coupling reaction, slightly alkaline medium is maintained for the effective coupling with electron rich aromatic compounds. The diazonium salt couples with number of coupling components such as phenols, naphthols and amines at the *ortho* and *para* positions with respect to the electron releasing group present in that aromatic compounds. In case of amine like aniline, α -naphthyl amine the coupling takes place at *para* to the amino group. Similarly amino naphthols couples at *ortho* to amino group under acidic medium or at *ortho* to hydroxyl group under alkaline medium.

In the coupling reaction, the nitrogen of the diazonium group is retained in the product, in contrast to the replacement reaction, in which nitrogen is lost.

Trends in coupling

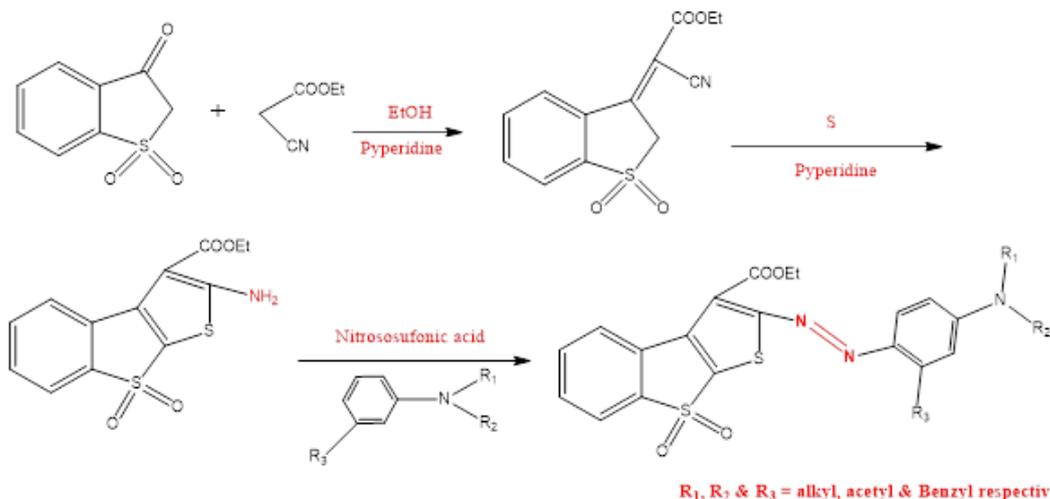
- In case of the presence of electron donating group in aromatic nucleus, the aromatic ring on which the attack takes place by diazonium ion, the coupling usually occurs at *para* to the electron donating group.
- Since the coupling reaction involves an electrophilic attack by the diazonium salt, coupling occurs at the position of high electron density. Thus, phenols and amines couples at a *para* position.
- The coupling between the diazonium salt and the coupling component not only depends upon the pH of the reaction medium but also upon the reactivity of the diazonium salt and coupling component.



Gewald reaction

Azo compounds are also prepared by using Gewald reaction. In this method benzo-thiophene-3 (2H) -one-1,1-dioxide allow to condense with ethyl cyanoacetate,

subsequently diazotized with nitrosyl sulphuric acid and coupled with substituted N,N-dialkyl aryl amines gives azo compounds.^[12]

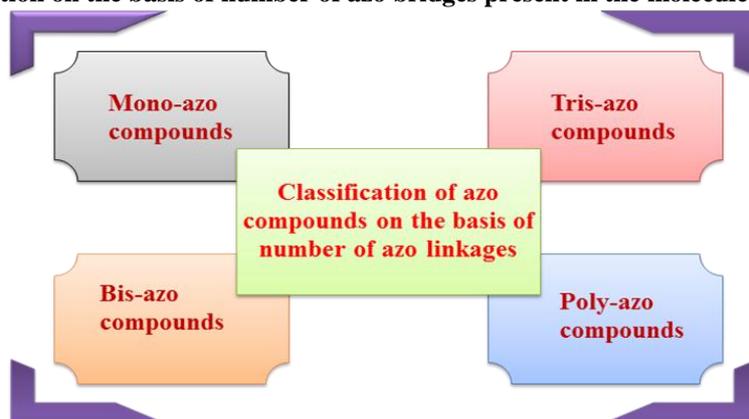


2. Types of azo compounds (azo dyes)^[13]

Azo compounds can be classified into various classes in two different ways. 1) Azo dyes can be classified on the basis of number of azo bridges present in the molecule,

such as mono azo-, bis azo-, tris azo- and poly azo dyes. 2) According to their applications i.e. acidic-, basic-, direct-, ingrain- and mordant azo dyes.

1) Azo dyes classification on the basis of number of azo bridges present in the molecule

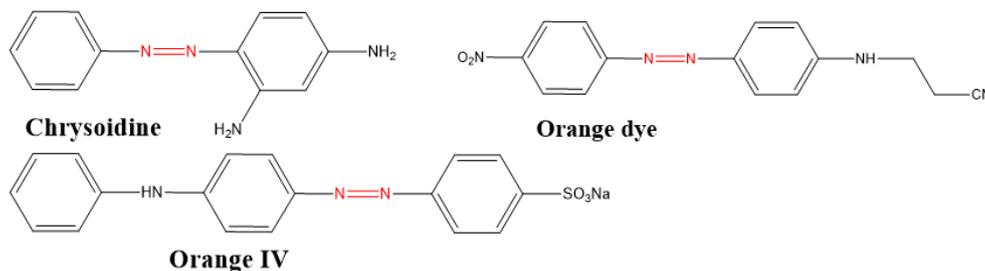


a. Mono-azo compounds

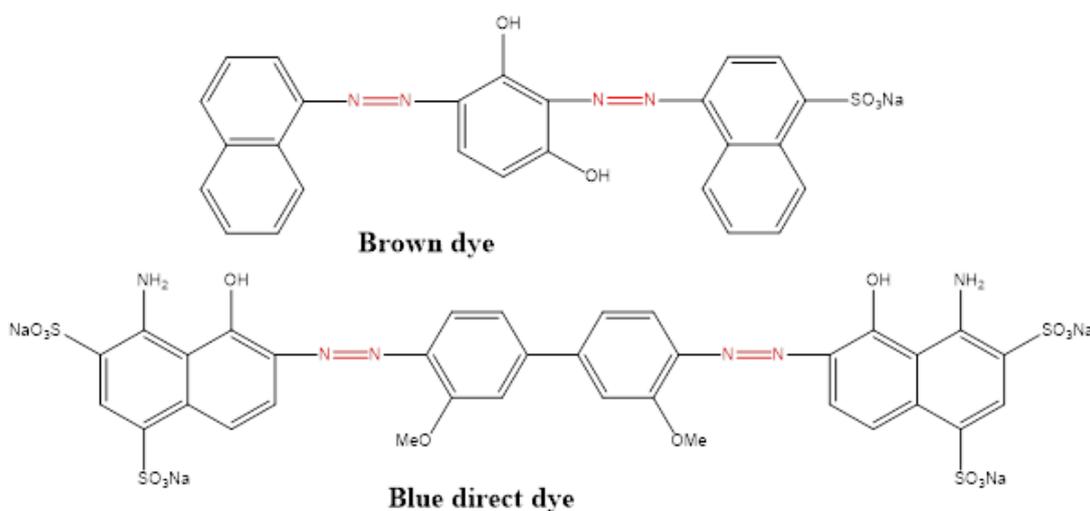
Mono azo compounds are the synthetic compounds that must contains only one azo ($-N=N-$) bond. **e.g.**

Chrysoidine, Mordant Black 17, orange dye for cellulose acetate, polyamides, polyesters, and polyacrylonitrile.

e.g. Yellow basic dye, yellow dye

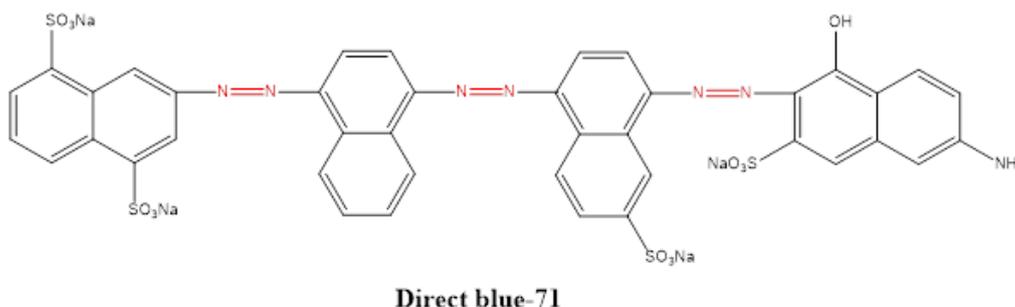
**b. Bis-azo compounds**

Bis azo compounds are the synthetic compounds that must contains two azo ($-N=N-$) bonds. **e.g.** Orange direct dye, Brown dye, Blue direct dye etc.

**c. Tris-azo compounds**

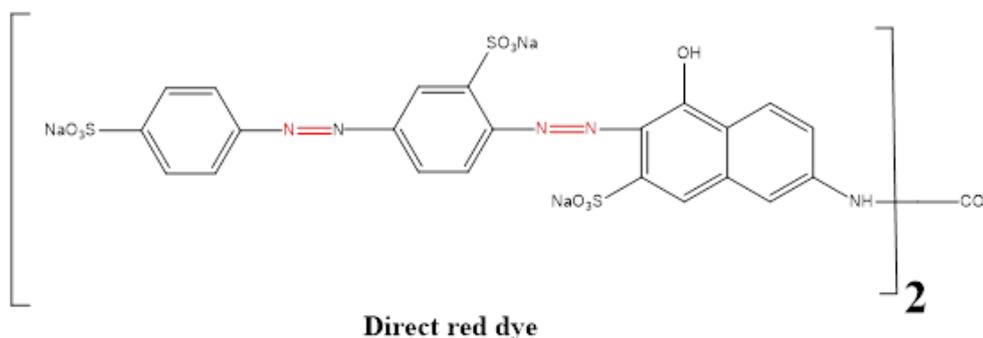
Tris azo compounds are the synthetic compounds that must contains three azo ($-N=N-$) bonds. **e.g.** Direct Blue, Direct Black 38.

e.g. Direct blue 71,

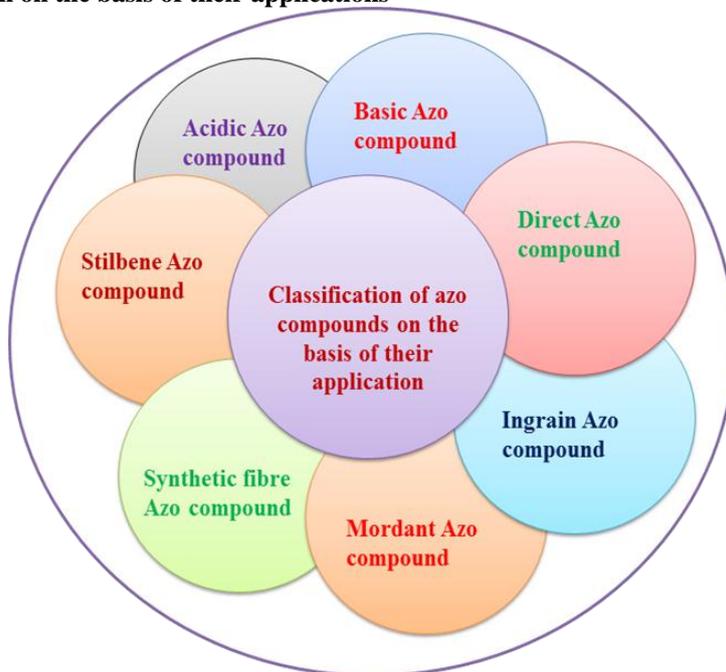
**d. Poly-azo compounds**

Poly azo compounds are the synthetic compounds that must contains more than three azo ($-N=N-$) bond.

e. g. Direct red dye



2) Azo dyes classification on the basis of their applications



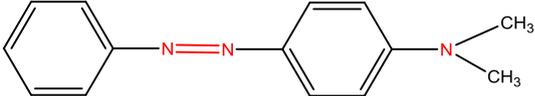
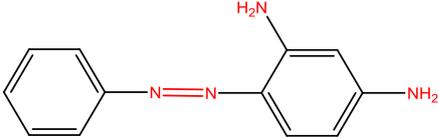
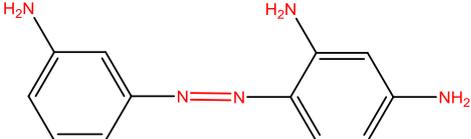
a. Acidic azo dyes: The acidic azo dyes are characterized by the presence of an acidic group e.g. $-\text{SO}_3\text{H}$, $-\text{COOH}$, and phenolic, which makes the dye more soluble and also serves as reactive point for mixing the dyes to fiber. There are some important acid azo dyes listed below.

Sub-Class	Structure
Methyl orange	
Methyl red	
Orange-I (α -naphthol) Orange-II (β -naphthol)	

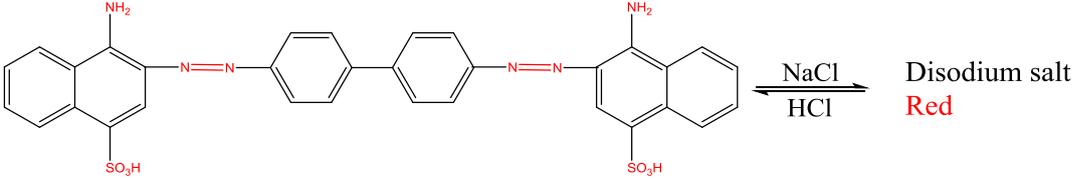
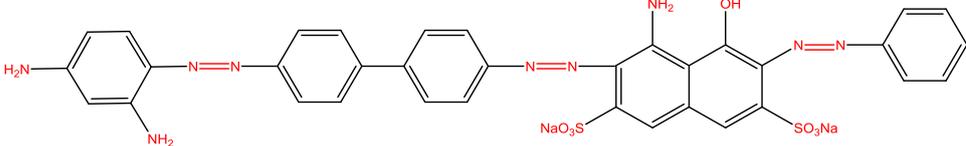
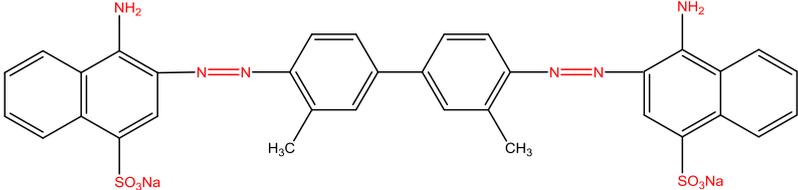
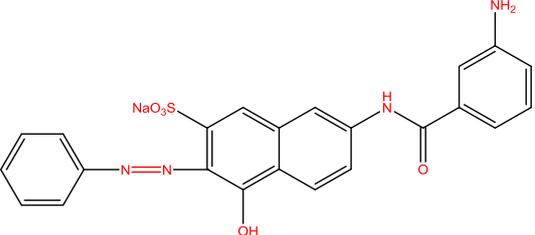
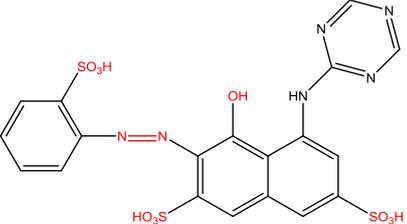
Orange-IV	
Fast red A	
Ponceau 2R	
Orange G	
Acid red 97	
Chrome blue Black R	
Carbolan dyes	

b. Basic azo dyes: In these dyes $-NH_2$ or $-NR_2$ groups are present as the dye auxochrome. There are some important basic azo dyes which are given as follows.

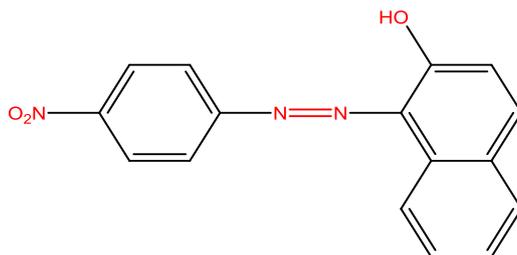
Sub-Class	Structure
Aniline yellow	

Butter yellow	
Chrysodine G (2,4-diaminoazobenzene)	
Bismarck brown (Phenylene brown)	

c. Direct azo dyes: The azo dyes required mordant for dyeing cellulosic fibres i.e. cotton, linen, paper etc. However, there are certain azo dyes which can also dye directly without mordant; such azo dyes are called as direct or substantive azo dyes. Some important direct azo dyes are listed below.

Sub-Class	Structure
Congo red	
Direct deep black	
Benzopurpurin	
Rosanthere O	
Procion dyes	

d. Ingrain azo dyes: An important dye belonging to this group is para red or nitraniline red. It is applied by dipping the fabric in an alkaline solution of 2-naphthol, drying it and then passing it through a cold solution of diazotised *p*-nitraniline.



e. Mordant azo dyes: Chromium is the most widely used metal in mordant azo dyes; the dyes so formed are called azo chrome mordant dyes. The various azo dyes that need mordants are:

Sub-Class	Structure
Diamond black F	
Chromotrope 2B	
Ingralans	
Erichrome black T	

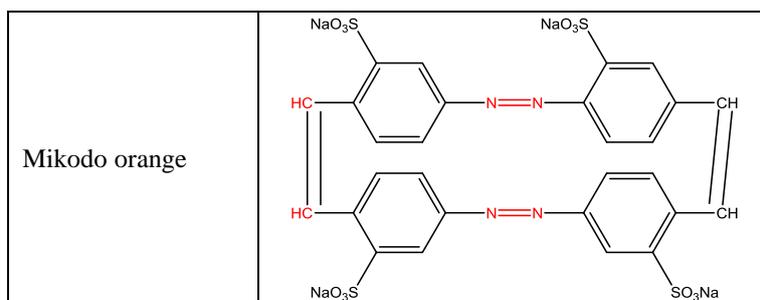
Erichrome black A	
Erichrome red B	

f. Synthetic fibres dye: Many dyes have been prepared for the synthetic fibres, synthetic fibres may be dyed with the acidic, basic or disperse dyes.

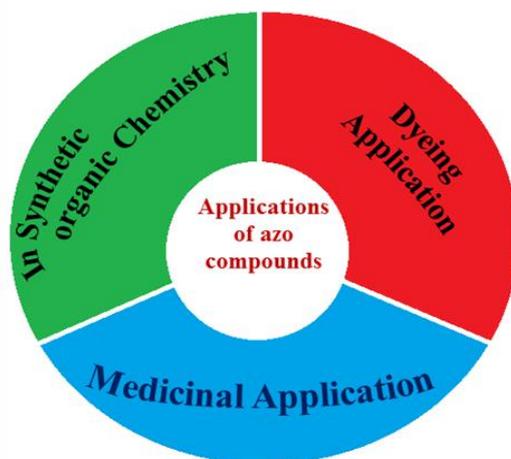
Sub-class	Structure
Red azo dye (dye rayon and nylon red)	
Yellow disperse dye (used for terylene)	
Asrtazone red GTL A cationic dye (used for polyacrylonitrile fibres)	

g. Stilbene fibres dye: These are yellow and orange direct azo dyes and are for cellulosic fibres, though these dyes possess azo group, they are not obtained by the process of diazotization and coupling.

Sub-class	Structure
Naphthalene yellow	



3. Applications of azo compounds

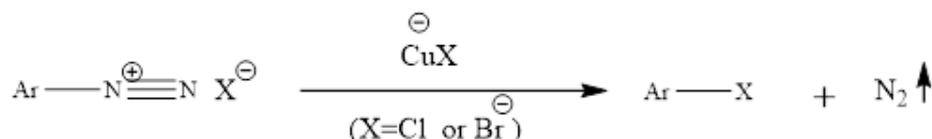


A) In synthetic Organic chemistry

1) Sandmeyer reaction^[14]

Replacement of the diazonium group by halide (mostly –Cl or –Br) carried out by mixing the solution of freshly

prepared diazonium salt with cuprous halide (mostly cuprous chloride or cuprous bromide) is known as Sandmeyer reaction.

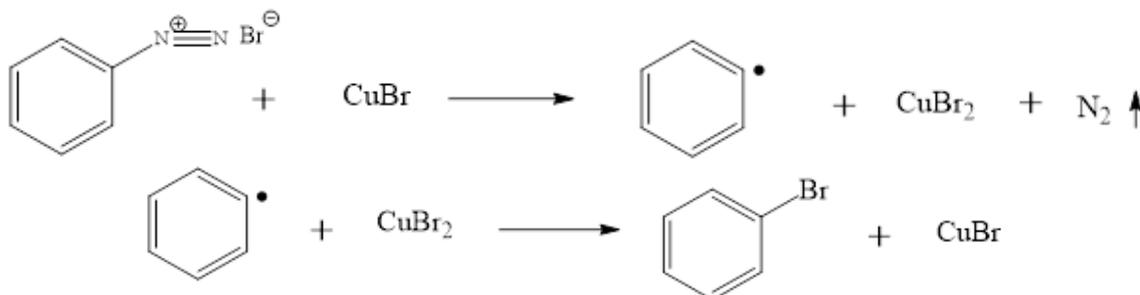


At room temperature or occasionally at elevated temperatures, nitrogen steadily evolved, and after several hours the aryl chloride or aryl bromide can be isolated from the reaction mixture.

the aryl nitrogen bond produces an aryl radical and the cupric halide.

The Sandmeyer reaction is believed to proceed by a free radical mechanism. Cuprous salts catalyze the free radical substitution by halides and some other anions for nitrogen in arenediazonium salts. Homolytic cleavage of

Abstraction of halogen from the cupric salt by the aryl radical leads to the halo aromatic while regenerating the catalyst. Because the halogen substitution takes place at a specific carbon atom. This regiospecific method is often the best approach for the preparation of chloro and bromo aromatic compounds.



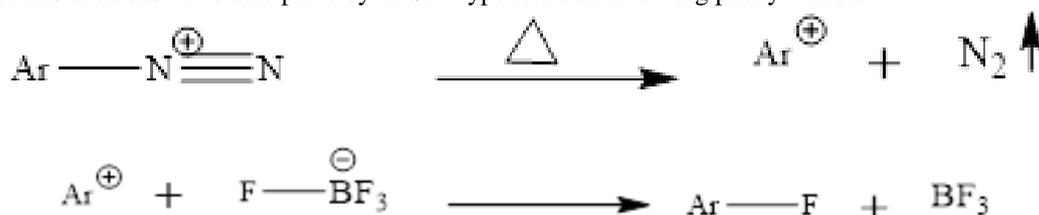
Sometimes the synthesis is carried out by a modification known as the Gatterman reaction, in which copper powder and hydrogen halide are used in place of the cuprous halide.

2) Balz-Schiemann reaction^[14]

Sandmeyer reaction and Gatterman reaction are the best reactions for introduction of Cl or Br atom to aromatic nucleus. But for introduction of F atom the Balz-Schiemann reaction is used. In this arenediazonium salt is heated in presence of BF_4^- forming arenediazonium fluoborate which decomposes to form fluoro compound. This reaction is known as Balz-Schiemann reaction.



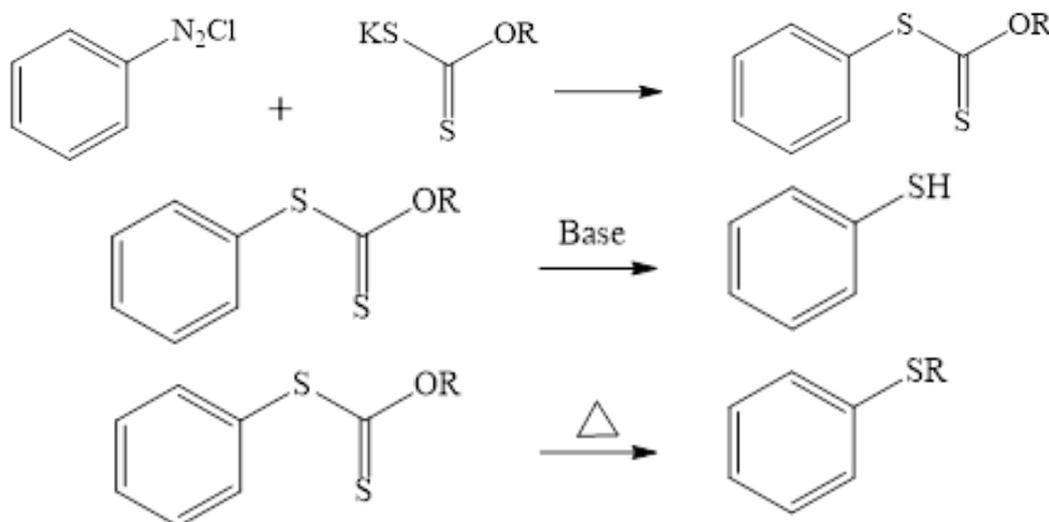
The reaction has been shown to take place by an $\text{S}_{\text{N}}1$ type reaction involving phenyl cation.



3) Leuckart Thiophenol Reaction

The Leuckart Thiophenol Reaction allows the preparation of thiophenols and corresponding thioethers from anilines or their corresponding diazonium salts.

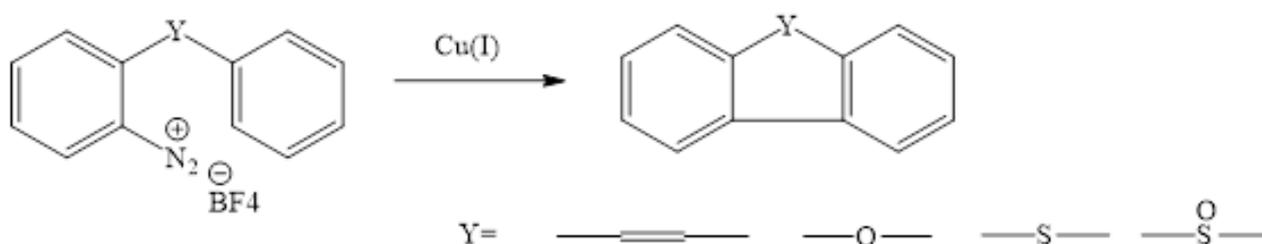
The first step is the reaction of an aryl diazonium salt with a potassium alkyl xanthate to give an aryl xanthate, which affords an aryl mercaptan upon basic hydrolysis or an aryl thioethers upon warming.

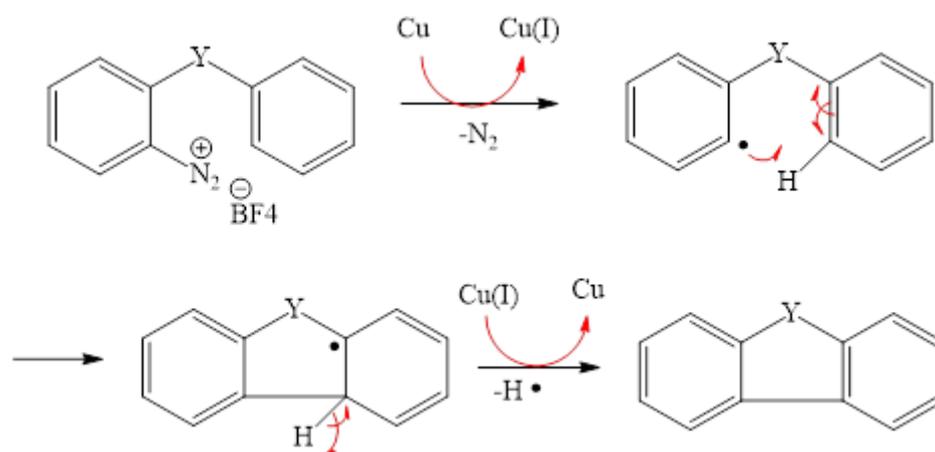


4) Pschorr Reaction

The Pschorr Reaction allows the preparation of biaryl tricyclics by intramolecular substitution of one arene by

an aryl radical. This radical is generated in situ from an aryl diazonium salt by copper catalysis. Although excess copper salts are used, the yield is normally moderate.





B) Dyeing applications

Azo dyes are most important class of dyes because they are strong, easy to prepare from cheap, readily available starting materials. They cover the whole shade range and have good fastness properties.

Azo dyes has been widely used for development of theoretical organic chemistry as they are used for developing and then testing, theories of color and constitution, indicator action and acid-base equilibrium. All azo dyes contain at least one, but more usually two, aromatic residues attached to the azo group. They exist in the more stable *trans* rather than the *cis* form. Both nitrogen atoms are SP^2 hybridized so that the carbon-nitrogen bond angles are 120° .

Azo dyes formation is one of the qualitative tests for detection of primary aryl amines. Particularly primary amines are reacts with nitrous acid in controlled temperature condition resulted into formation of diazonium salt, this diazonium salt is couples with aromatic nucleus containing strongly electron releasing group which activates the ring towards electrophilic aromatic substitution.

Azo compounds are widely used in various industries such as in leather industry to give desirable colour to leather, in paint and printing industries, in optical industries to colour the optics and in laser industries to give colours to lasers.

C) Medicinal application

There are various applications of azo compounds in medicine as well as in pharmaceuticals, such as antibacterial (Prontosil – the first azo compound used in medicine), antiviral, antifungal, antioxidants, anticancer, ant diabetic, anti-inflammatory, drug-carries and in cellular staining. Some of the azo compounds use in cancer chemotherapy.^[15] As stated by Nurul Asma Razale et. al. (2023), the azo compound boost Chromogenic activity, which is widely used in heavy metal detection. Synthesis of an azo compound that could detect heavy metal built up by body could be useful.^[16] Durga Prasad Mishra et. al. (2024) reported

that, azo metal complexes of some azo compounds with Mn and Ni shows significant antibacterial and antifungal activity against broad spectrum of microorganisms. The efficacy depends on length and nature of azo linkage, metal ion and substituents (electro donating or electron withdrawing).^[17] Azo compounds are also used in cellular staining to visualize cellular components and metabolic processes.^[18] Azo compounds containing heterocyclic compound moiety shows enhancement in the biological and pharmaceutical activities results in the formation of new biocompatible drug with wide range of activity.^[19] Substituents present on aromatic rings of azo linkage on either side shows variety of medicinal applications such as presence of electron withdrawing group enhances the antimicrobial activity against gram-negative bacteria.^[20] Schiff bases of azo compounds and azoxy based schiff bases shows antiproliferative activity and cytotoxic effect against HeLa cell lines, but Schiff bases shows better results as compared to azoxy based Schiff bases.^[21] Azo compounds having thiophene moiety in their linkage gives cytotoxic activity, some derivatives exhibits good antitumor activity vs. Ehrlich Ascites carcinoma tumor cells.^[22]

DISCUSSION

Azo compounds are well known for its colouring property due to their vivid colour and versatility of applications in number of various fields such as dyeing the fabrics, in synthetic organic chemistry and in pharmaceutical industries as anti-bacterial, anti-viral, anti-proliferative and for many more applications. Many researchers reported that the above mentioned properties depend on the structure and functional group present in it, in addition to this some were reported the SAR (Structure and Activity relationship) for some azo molecules including the metal complexes of azo ligands.

In the synthesis of azo compounds diazotization method is preferentially adopted for most types of azo compounds. The application of azo compounds not only show hopeful outputs but also gives some challenges like impact on environment. Most azo compounds have potential health risk when they are exposed to environment as it is and therefore they needs developing

eco-friendly compounds before exposure to our eco system. Reduction of azo compounds by azoreductase enzyme is the best method to cleave the azo compound in to two primary aromatic amine which are less harmful. Apart from these some azo compounds are also used as food additives, therefore the new challenge is to design and synthesize the biocompatible and biodegradable azo compound.

CONCLUSION

In the present mini review, the author spotlight the history of azo compounds, classification of azo compounds on the basis of number of azo linkages and on the basis their use. The author again discusses the applications of azo compounds in various fields such as in synthetic organic chemistry, in dyeing of fabrics and also in medicinal and pharmaceutical fields.

Upcoming research work should focus on introducing the new green methods of synthesis of azo compounds from eco-friendly starting compounds with biocompatibility. This new methods can open the various applications as a new era for azo compounds in number of industries like synthetic organic chemistry, pharmaceutical industries, medicinal field, food industries, dyeing industries etc. This mini review may be a road map for the chemists who are working on azo compound chemistry.

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Conflict of interest

The author declared no conflict of interest.

REFERENCES

- Said Benkhaya, Souad M'rabet and Ahmed El Harfi, Classification, properties, recent synthesis and application of azo dyes, *Heliyon*, 2020 Jan 31; 6(1): e32071, doi:10.1016/j.heliyon.2020.e03271
- Md. Nasim Khan, Digvijaysinh K. Parmar and Debasis Das, Recent applications of azo dyes: A paradigm shift from medicinal chemistry to biomedical sciences, *Mini-Reviews in medicinal Chemistry*, 2020; 21(9): 1071-1084. 10.2174/1389557520999201123210025
- Gung, B.W., Taylor, R.T. *J. Chem. Ed.*, 2004; 81: 1630.
- Decelles, C. *J. Chem. Ed.*, 1949; 26: 583.
- A. Thakuri, M. Banerjee, A. Chatterjee, Microwave-assisted rapid and sustainable synthesis of unsymmetrical azo dyes by coupling of nitroarenes with aniline derivatives, *Iscience*, 2022, 25.
- F. Eltaboni, N. Bader, R. El-Kailany, N. Elsharif, A. Ahmida, Chemistry and applications of azo dyes: A comprehensive review, *Journal of Chemical Reviews*, 2022; 4: 313-330.
- R. shinde, N. Korde, R. More, Green synthesis, characterization, and biological activity of aryl azo schiff bases, *Journal of Applied Organometallic Chemistry*, 2021; 1: 165-173.
- R. Sarathi, L. Renuga, N.L. Devi, Sheeba, E.S. Esakki, S.M. Sundar, Photocatalytic Degradation of Malachite Green Dye by Metal Oxide Nanoparticles - Mini Review, *Journal of Chemical Reviews*, 2023; 5: 15-30.
- M.O. Heragy, A.A.M. Moustafa, E.S. Elzanfaly, W.A. Al-Shareef, A.S. Saad, Miniaturized solidstate sensor for inline monitoring of the microbial biodegradation of a biohazardous textile azo dye (Direct Red-81), *Talanta Open*, 2022; 6: 100146.
- S. Zafar, D.A. Bukhari, A. Rehman, Azo dyes degradation by microorganisms—An efficient and sustainable approach, *Saudi Journal of Biological Sciences*, 2022; 29: 103437.
- Areeg M Fadhel and Abbas Ali Slih Al Hamdani, Historical Background, Literature Review on the Synthesis and Applicability of Azo-Dye Compounds: An Extensive Review, *Advanced Journal of Chemistry A*, 2024; 7(6): 687-724.
- Sabnis R., Rangnekar D., Sonawane N. 2-Aminothiophenes by the Gewald reaction. *J. Heterocycl. Chem.*, 1999; 36: 333–345.
- O. D. Tyagi and M. Yadav *Text book of Synthetic dyes*, 1st, 1990; 110.
- S. M. Mukherji, S. P. Sing and R. P. Kapoor, *Organic Chemistry*, IInd ed., 791-792.
- Md Naseem khan, D K Parmar and Debasis Das, Recent applications of azo dyes: A paradigm shifts from medicinal chemistry to biomedical sciences, *Mini-Reviews in medicinal chemistry*, 21(9): 1071-1084.
- Nurul Asma Razali and Zuhair Jamain, Synthesis, chemical application and biological application of azo based molecules containing different terminal group:A review, *Journal of Molecular Structure*, 2023; 1284: 135329.
- Durga Prasad Mishra, Prafulla Kumar Sahu, Biswajeet Achary, Satya Prasad Mishra and Seturam Bhati, A review of the synthesis and application of azo dyes and metal complexes for emerging antimicrobial therapies, *Results in Chemistry*, 2024; 10: 101712.
- Yousaf ali, Shafida Abd Hamid and Umer Rashid, Biomedical applications of aromatic azo compounds, *Mini Review of Medicinal Chemistry*, 2018; 18(18): 1548-1558. 10.2174/1389557518666180524113111.
- Kibrom Mezgebe and Endale Mulugeta, Synthesis and Pharmacological activities of azo dye derivatives incorporating heterocyclic scaffolds: a review, *RSC Advances*, 2022; 12: 25932-25946. DOI: 10.1039/d2ra04934a.
- Nurul Asma Razali and Zuhair Jamain, Synthesis, Chemical identification and biological application of

- azo-based molecules containing different terminal group: A review, *Journal of Molecular structure*, 2023; 1284: 135329. doi.org/10.1016/j.molstruc.2023.135329.
21. Su Ran, Lu Lei, S. Zeng., Y. Jin., S. An, Synthesis and characterization of novel azo-containing or azoxy-containing Schiff bases and their antiproliferative and cytotoxic activities, *Chemical Research in Chinese Universities*, 2015; 31(1): 60-64, DOI: 10.1007/s40242-015-4355-4.
 22. T.A. Farghaly, Z. A. Abdallah, Synthesis, azo-hydrazone tautomerism and antitumor screening of N-(3-ethoxycarbonyl-4, 5, 6, 7-tetrahydro-benzo [b] thien-2-yl)-2-arylhydrazono-3-oxobutanamide derivatives, *Arkivoc*, 2008; 17: 295-305.
 23. S. C. Patil, S. M. Koshti and S. S. Rajput, Synthesis, Antimicrobial, Anti-inflammatory activity and Molecular docking study of some substituted heterocycles containing 2,6- dichloro-4-trifluoromethyl moiety, *Rasayan Journal of Chemistry*, 2023; 16(4): 2163-2170.
 24. S. M. Koshti, S. K. Girase and J. B. More, Design, Synthesis and In-Vitro degradation study of azo compounds as prodrugs of 4-amino pyridine, *Heterocyclic letters*, 2024; 14(4): 859-872.