الجامعة العراقية/ كلية التربية/ قسم الكيمياء
Elafchemist16.3@gmail.com

الجامعة العراقية/ كلية التربية/ قسم الكيمياء
mustfa.j.mohammed@aliraqia.edu.iq

الجامعة التكنلوجيا/ قسم العلوم التطبيقية/ فرع الكيمياء
Sallal.a.abdullha@uotechnology.edu.iq

Azo imidazole derivatives and some of its applications: A literature review

Sallal A.H. Abdullah
صلال عبد الهادي عبدالله

Elaf M.M. Raoof
إيلاف مؤيد محمد رؤوف

Mustafa J. Mohammed
مصطفى جاسم محمد

Abstract

Imidazoles have held a distinct place in the field of heterocyclic chemistry, and having two non-adjacent nitrogen atoms significantly improved both synthetic and natural compounds. In recent years, derivatives have garnered significant attention due to their versatile properties in both chemistry and pharmacology. Imidazole is a heterocyclic ring that contains nitrogen and has biological and pharmacological significance. Hence, Imidazole compounds have continued to captivate researchers' interest for more than a century. As a polar aromatic compound that can be ionized, it improves pharmacokinetic characteristics. One important synthetic approach in drug development is the consolidation of the imidazole unit. imidazole derivatives are utilized for wide spectrum of biological activities such as antibacterial, anticancer, antitubercular, antifungal, analgesic, and anti-HIV activities. This paper aims to review the biological activity, industrial, and agricultural of imidazole azo compound during the past years

Azo – Compounds

Azo – Compounds are one of the most crucial colored organic compounds, characterized by the presence of a group (-N=N-) in its chemical structure [1, 2]. They are distinguished by a lone pair of orbitals containing two electrons on a nitrogen atom [3]. A wide range of colours, including yellow, red, orange, blue, and even green, can be found in azo compounds [4].

Azo compounds acquire color due to the presence of chromophore and auxochrome groups, making them easily preparable. Chemically stable and offering a wide variety of colors, azo compounds surpass natural dyes in color diversity. Therefore, they have played a significant role for many years in the dye and pigment industries[5]. The color appearance is attributed to the presence of a double bond between the two nitrogen atoms, allowing for light absorption in the visible region between (400 - 750) nm[6]. Indeed, approximately half of the dyes currently utilized in industry are azo dyes, primarily synthesized from diazonium salts [7, 8]. The synthesis of azo dyes involves two steps: diazotization followed by coupling[9]. Traditional acid/base catalyzed reactions demonstrate efficacy in the synthesis of azo dyes. Diazotization involves protonating the compound under acidic conditions at a low temperature, and the subsequent coupling of the diazo compound with the nucleophile is carried out under basic conditions[10].

Azo imidazole derivatives

Azo imidazole derivatives (AID) exhibit enhanced stability in their structures when aryl rings serve as the (R) groups and tend to possess a crystalline nature, as seen in compounds like azo benzene, in contrast to when The (R) groups consist of alkyl groups due to the formation of the (-N=N-) group become integrated into an extended delocalized system that involves the aryl groups[11].AID exhibits an extended π electron conjugation system, leading to increased chemical and thermal stability, The characteristics of aromatic azo compounds are directly influenced by the substituents on the aromatic ring which encouraged the development of functional photoresponsive materials with molecular-level [12]. AID are generated through a coupling reaction that involves a diazonium salt and a coupling agent[13]. There are two types of AID are acknowledged: homo and heterocyclic azo compounds [11].

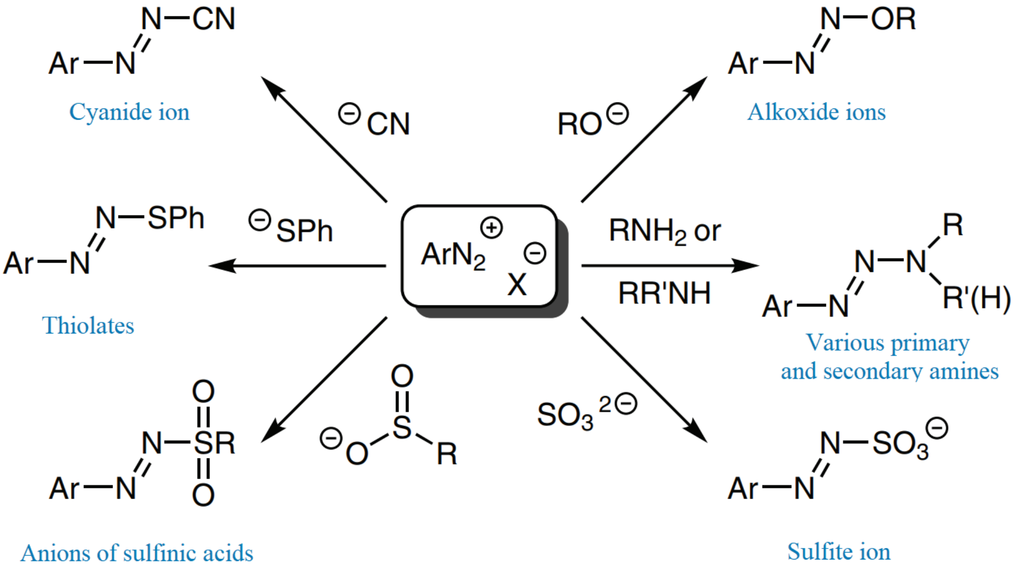
To enhance the color of azo dyes, it is crucial for them to incorporate Heterocyclic compounds incorporating nitrogen, oxygen, or sulfur, this incorporation results in the generation of distinct shades with varying intensities. Currently, azo dyes that integrate heterocyclic moieties demonstrate improved coloring characteristics, tinctorial strength, thermal stability, and more favorable solvatochromic behaviour compared to dyes derived from straightforward aromatic amines [14-16]. Until now, various synthetic methodologies have been established and documented for the synthesis of azo dyes incorporating heterocycles and compounds derivatives.

During the diazotization process, the initial step involves the conversion of the aromatic or heterocyclic amine into a diazonium salt[17]. The diazotization reaction typically takes place at a reduced temperature in the existence of salts and acids. Subsequently, the resultant diazonium complex engages in interactions with diverse nucleophilic components for diazo-coupling, like phenol, naphthol, or amine[18]. Even though azo dye derivatives incorporating heterocycles play a significant role in pharmaceuticals and drug development, the available reports on this topic are still inadequate [19, 20].In recent times, the creation of azo dyes incorporating heterocycles and their derivatives has garnered significant attention. This is attributed to their potent bioactivities[21, 22]. Numerous techniques have been elucidated for the production of aromatic azo compounds, and these methods have gained significant popularity due to the diverse range of applications they offer[23].

Diazonium salts

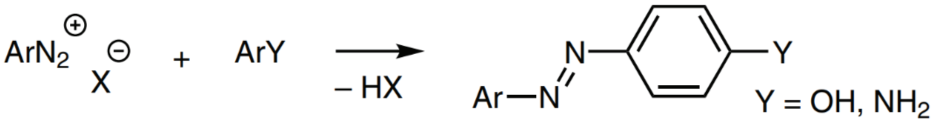
Diazonium salts belong to a class of organic substances that have the following general formula $[R\text{-}N{\equiv}N]^+[X]^-$In this formula, R can represent either an alkyl or aryl group[24]. Alkyl diazonium salts are highly unstable and tend to decompose, releasing colorless and unreactive nitrogen gas along with other products. aliphatic and aromatic primary amines can generate diazonium salts through their reaction with HNO_2 at a temperature range of 0 to 5 °C. The acid employed to produce the diazonium salt is utilized due to the instability of the acid, and it is typically produced in a reaction, often initiated by the action of dilute H_2SO_4 or HCl on $NaNO_2$[25]. Aryl-diazonium salts play a significant role in organic chemistry, commonly employed as reactants for diverse synthetic processes. For example, the elimination of nitrogen from diazonium cations is a crucial step in the Meerwein [26] and Sandmeyer [27] reactions. In both of these reactions, enhancing the yield depends on the use of diazonium salts that efficiently undergo dinitrogen (N2) loss. The increasing popularity of aryl-diazonium salts is further attributed to their efficacy in surface functionalization, using diazonium salts has emerged as a highly potent technique for coatings, particularly in situations where covalently attached coatings on (semi)-conducting materials incorporate a diverse array of functional groups.[28] by linking (bio)molecules [29], polymers [30], or nanoparticles [31].

Additionally, to the elimination of the N_2 group, diazonium salts have the capability to undergo reactions with nucleophiles, which results in the addition of the terminal nitrogen, as illustrated in Scheme 1[1]. These reactions, established over several decades, lead to the creation of (di) azo compounds. One example is the formation of arenediazoethers from alkoxide ions [32]. Tetrazene compounds can be synthesized from primary and secondary aliphatic as well as aromatic (or heterocyclic) amines, accompanied by the release of H+. Arenediazosulfonates are generated from sulfite ions [1]. Diazonium salts, when combined with anions of sulfinic acids ([RSO(O)]–) in a mildly watery acidic medium result in the formation of arenediazosulfones [33]. Unstable arenediazothioethers are generated through the addition of thiolates, and these compounds tend to decompose (explosively) yielding N2 and the corresponding sulfide [34]. Finally, the reaction with cyanide ions results in the formation of arenediazocyanides[35].



Scheme 1 Summary of the reactions involving nucleophiles as Lewis bases with diazonium salts[36].

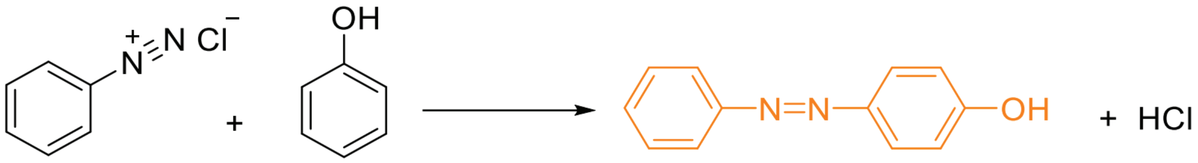
A commonly observed and familiar reaction involves a nucleophile adding to the terminal nitrogen, typically via electrophilic aromatic substitution as described in Scheme 1. In this situation, the para-position of the phenyl group in aniline or phenol, featuring highly Substitutions that activate, undergoes addition to the N_2 portion of the diazonium salt [1].



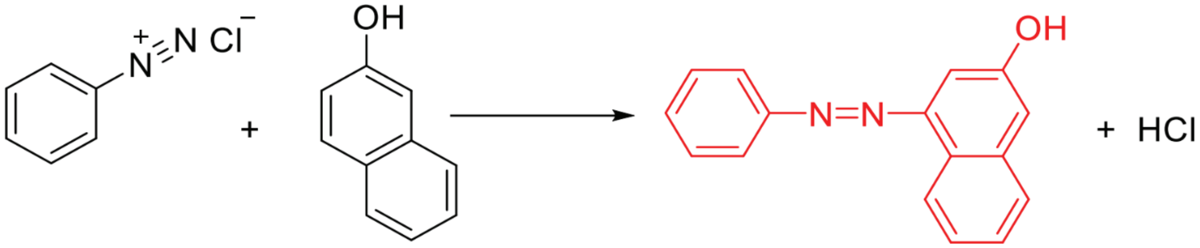
Scheme 2 A diazonium salt undergoes electrophilic aromatic substitution with an amine or phenol[36].

Diazo Coupling Reactions

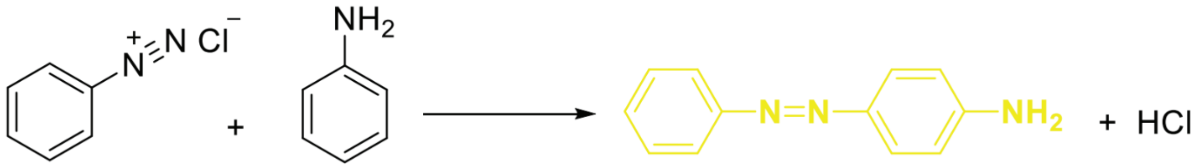
It is the organic reaction of an unstable diazonium compound in a cold aqueous solution with another aromatic compound (the coupling agent), like the benzene ring, ultimately yielding a colored precipitate of an azo compound. Within this electrophilic aromatic substitution reaction, the aryldiazonium cation acts as the electrophile, while the activated arene acts as the nucleophile. Azo dyes are synthesized through a two-step process. In the initial step, the diazonium salt is generated. Subsequently, in the second step, it undergoes a reaction with highly reactive aromatic compounds, such as phenol. Various pathways are pursued to achieve the desired color properties of dyes.The coupling agent consistently participates in a reaction at either the two or four positions of the benzene ring (one of these positions featuring the functional group). The color of the resulting compound is determined by the coupling agent used in the reaction with the diazonium salt [37]. The reaction of a diazonium salt with phenol derivatives results in the formation of a yellow/orange azo compound:



An alkaline napthalein-2-ol solution forms a red azo compound:



Scheme 6. Synthesis of crimson azo compound[38]

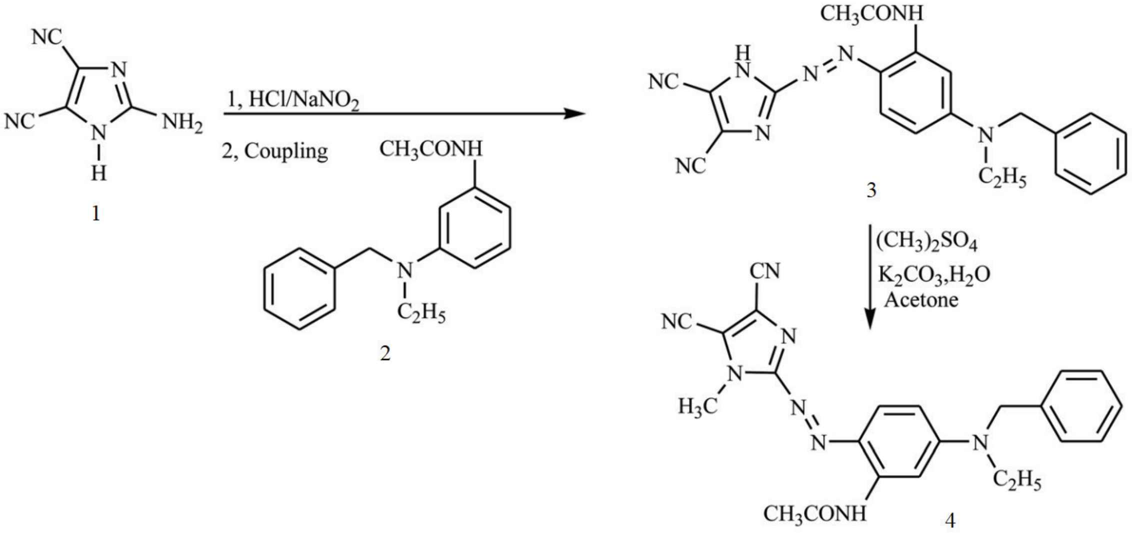


Scheme 7. Synthesis of an azo compound[38]

Imidazol azo compounds

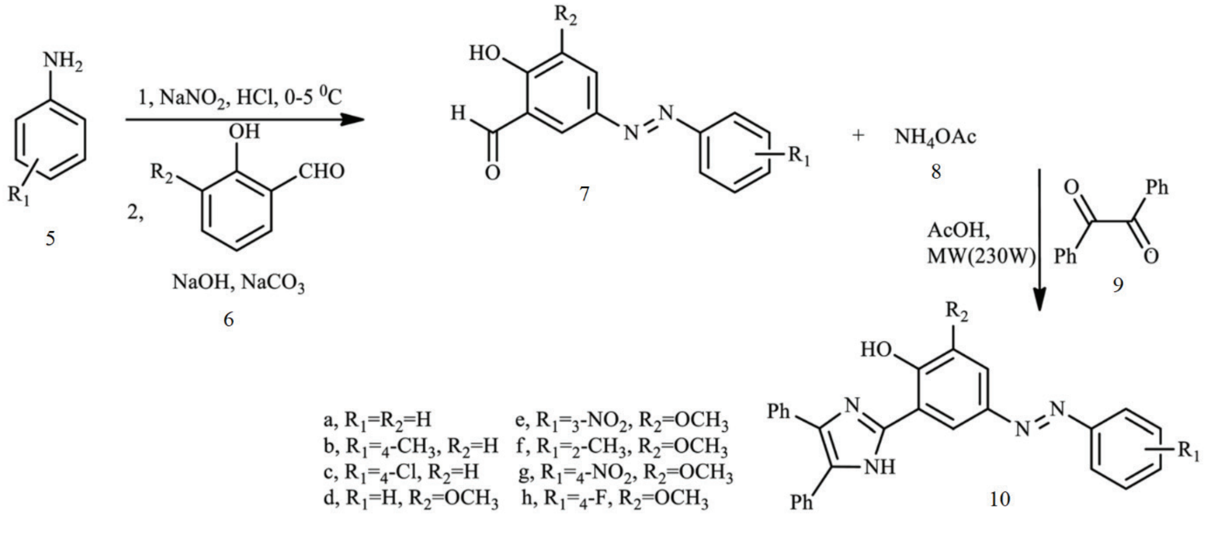
Imidazoles are recognized heterocyclic compounds that possess a prevalent π-acidimine (-C=N-) group, constituting a key characteristic in numerous medicinal agents. The classification of the compound as aromatic is attributed to the existence of a sextet of π-electrons , this sextet comprises a pair of electrons originating from the protonated nitrogen atom and one electron from each of the remaining four atoms in the ring. Imidazole exhibits amphoteric behavior, functioning as both an acid and a base. Additionally, imidazoles are characterized by their ability to form salts [39]. Imidazole derivatives exhibit important pharmacological properties, contributing significantly to various biochemical processes as inhibitors, fungicides, and therapeutic agents[40, 41].

Previously published research described the creation of new red azo dyes incorporating imidazole derivative 4 via the diazo-coupling reaction. The synthesis of compound 4 involved the conversion of imidazole derivative 1, achieved through a diazotization process conducted when HCl is present and NaNO2, leading to the formation of its corresponding diazonium salt. Compound 3 successfully obtained a substantial yield by subjecting the salt to coupling with N-benzyl N-ethyl-m-acetamide aniline 2. [42]. Methylation of the imidazole ring in compound 3 is achieved through a reaction with an alkylating agent, yielding ring-methylated product 4 as illustrated in Scheme 2.



Scheme 2: Pathway for the general synthesis of azo dye derivatives including imidazole4 [43].

Similarly, Mahmoodi and colleagues documented the synthesis of new azo-imidazole derivatives 10 (a–h), compound 10 was synthesized with satisfactory to high yields using microwave irradiation, where the appropriate azo dyes 7, ammonium acetate 8, and benzyl 9 participated. This reaction occurred in the presence of glacial acetic acid (AcOH) serving as both the solvent and organocatalyst, with abbreviated reaction periods. The principal role of AcOH is to enhance and facilitate the carbonyl group's nucleophilic attack by ammonia, ultimately yielding compound 10. A process involving the diazotization of aniline derivatives 5 when both HCl and $NaNO_2$ are present at 0–5°C, followed by coupling utilizing derivatives of aldehyde 6, resulted in the formation of precursor azo dyes 7. Azo dyes 7 resulting from the previous steps underwent a subsequent condensation reaction with ammonium acetate 8. This was followed by a condensation with benzyl 9, leading to the rearrangement of benzyl 9 and the formation of azoimidazole 10, as illustrated in Scheme 3[44].



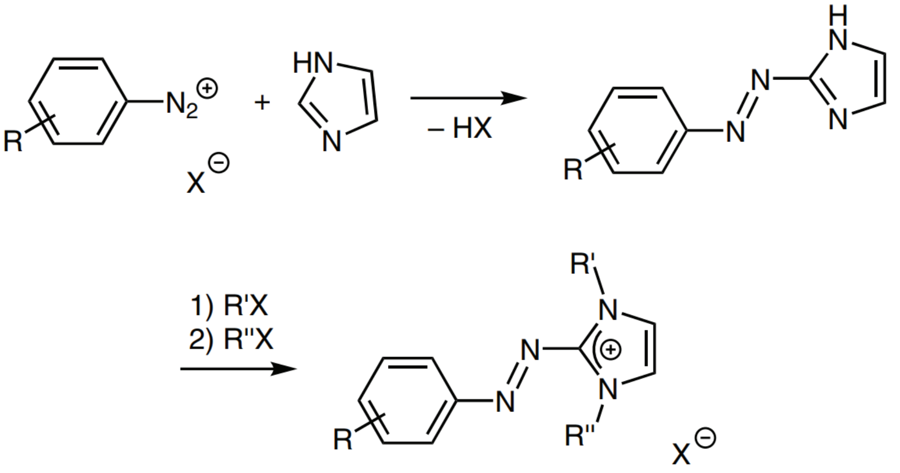
Scheme 3 Pathway for general synthesis of azo-imidazole derivatives [43].

The coupling of imidazoles with diazonium salts.

The diazonium salt, functioning as an electrophile, can thermodynamically be perceived as an N-based Lewis acid, enabling its reactivity with Lewis bases. The reactivity demonstrated by the compounds in Scheme 1 is atypical, particularly for nitrogen-based molecules with a single pair, which are conventionally recognized as Lewis bases[36].

Gandelman and Stephan's recent research has illustrated that nitrogen-based compounds can be manipulated and optimized to serve as effective Lewis's acids.

In general, the synthesis of cationic azo dyes featuring imidazolium groups involves the combination of an aromatic diazonium compound with imidazole through coupling, functioning as a nucleophile, and then alkylation, as depicted in Scheme 4[45].



Scheme 4:A schematic depicting the reaction between an imidazole and an aromatic diazonium molecule, followed by the alkylation; R′ and R″ can be comparable (R′ and R″ = alkyl). X-counter-ion [36].

The described coupling process shares similarities with the reaction between aniline or phenol and a diazonium salt (Scheme 2). The process of reaction and then alkylation had been granted an invention by the 1950s end, Klingsberg and Lewis documented this reactivity as the quaternization of N-alkylated imidazolium azo dyes. It is possible to carry out the alkylation step-by-step. Initially, An alkaline solution is used to dissolve the salt of azoimidazolium, and then an alkylating agent is added to perform the first alkylation. Due to its insolubility, the product precipitates from the reaction mixture, rendering it pure enough for direct utilization in the subsequent alkylation step. It is convenient to perform the second alkylation in an organic solvent with alkyl halide, sulfate, or arylsulfonate. This approach allows for the introduction of two different groups on the imidazolium nitrogen centers[46].

Applications of Imidazole Azo Compounds

Extensive research has been conducted on azo compounds because of their outstanding thermal and optical properties [47], they are recognized for their diverse applications and use across various domains of life [48, 49]. They also encompass numerous biomedical studies, such as the inhibition of RNA, DNA, and protein synthesis, In addition, It is part of the field of studies associated with carcinogenesis [50].

Moreover, they find advanced applications in organic synthesis and high-tech sectors such as lasers, liquid crystal displays, inkjet printers, and electro-optical devices [51].

Biological Activity of Imidazole Azo Compounds

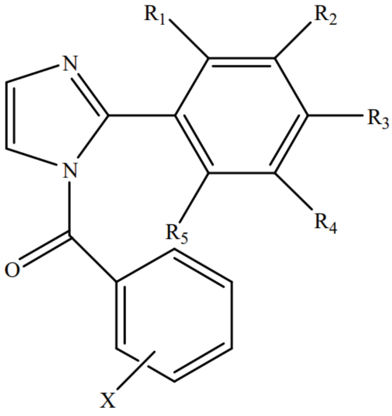
Imidazole derivatives constitute an important category of heterocycles acting as the fundamental framework in diverse natural products and biological systems. They occupy a unique position in the field of medicinal chemistry due to their powerful biological effects [52]. They are acknowledged for possessing numerous pharmacological properties and undertaking a vital role in diverse biochemical processes [53, 54].

These compounds demonstrate diverse biological activities, as they effectively inhibit viral actions and have been utilized for their anti-inflammatory and antibacterial properties [37]. They play a role in numerous biological reactions within the body, serving as inhibitors of nucleic acids

(RNA and DNA), participating in protein synthesis, and exhibiting properties such as anti-cancer, anti-diabetic, and disinfectant activities. Additionally, azo compounds find application as reagents in analytical chemistry [55, 56].

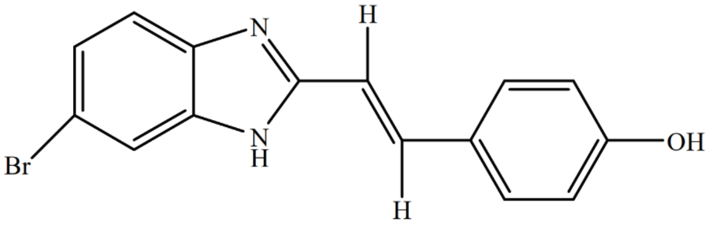
According to numerous literature surveys, imidazole derivatives exhibit diverse pharmacological activities. Siham Slassi, Adeline Fix-Tailler, et al detailed the synthesis, comprehensive analysis, and optical properties of four distinct Schiff base ligands(L1-L4) that incorporate an azo group, one imidazole group, and part of a Schiff base. Properties of the synthesized ligands were assessed, and the findings suggest that the inclusion of an azole group in these ligands significantly contributes to their biological activities, including antioxidant effects. These findings highlight the considerable potential of the recently developed azole ligands as valuable prospects for the creation of novel therapeutic agents [57].

Deepika Sharma and colleagues synthesized analogues of 2-(substituted phenyl)-1H-imidazole and (substituted phenyl)-[2-(substituted phenyl)-imidazol-1-yl]-methanone. The antimicrobial activity of these derivatives was assessed against bacteria, as well as fungal species. Norfloxacin served as the standard for comparison [58] and the following compound is the most potent.



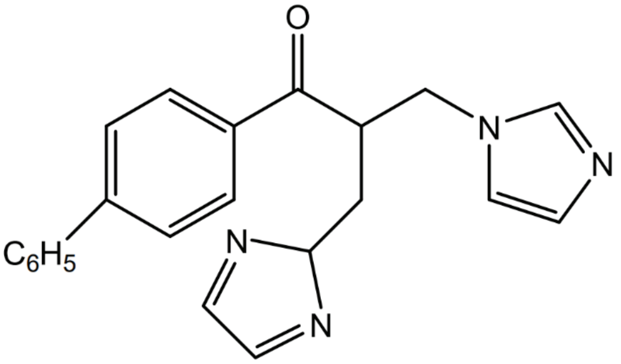
for compound 1 R_1=Cl, R_2=H,R_3=H,R_4=H,R_5=H,X=4-NO_2
2 R_1=COOH,R_2=H,R_3=H,R_4=H,R_5=H,X=4-NO_2
3 R_1=H,R_2=H,R_3=Cl,R_4=H,R_5=H,X=2-Br
4 R_1=H,R_2=H,R_3=NO_2,R_4=H,R_5=H,X=2-Br

Ramya V and collaborators synthesized Chains of innovative derivatives of azo compounds. Compounds underwent assessment for antibacterial activity against Staphylococcus aureus and Escherichia coli, Enterococcus faecalis, and Klebsiella pneumoniae, as well as antifungal activity against Candida albicans and Aspergillus fumigatus. The comparison was made with ciprofloxacin [39].

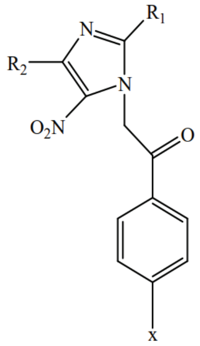


4-((*E*)-2-(6-bromo-1*H*-benzo[*d*]imidazol-2-yl)vinyl)phenol

Daniele Zampieri et al synthesized new diimidazole derivatives and their antibacterial and antifungal activity were determined. Almost all the compounds demonstrated acceptable activity against Candida glabrata. The in silico results indicated that the active compounds have the potential to interact at the protein's active site. Additionally, it was observed that the amount of free energy corresponded with the results of experimental activity [59].

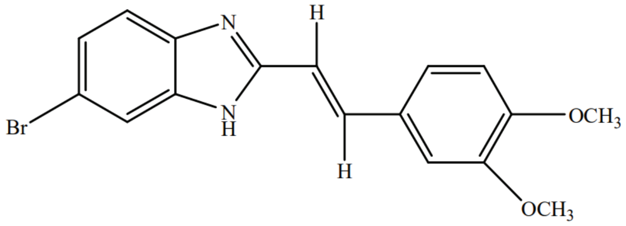


Dorota Olender et al synthesized nitroimidazole derivatives in alkylation reactions and the substances were assessed for their antifungal and antioxidant properties through the standard nutrient method against sclerophoma pityophila. The majority of them exhibited noteworthy antioxidant activity when compared to tocopherol, employed as a reference substance. This compound shows very strong potent fungistatic activity [60].



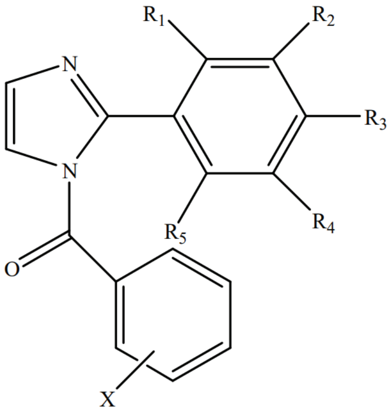
A R_1=H, R_2=Morpholine, X=H

B R_1=CH_3,R_2=Piperidine methyl, X=Cl



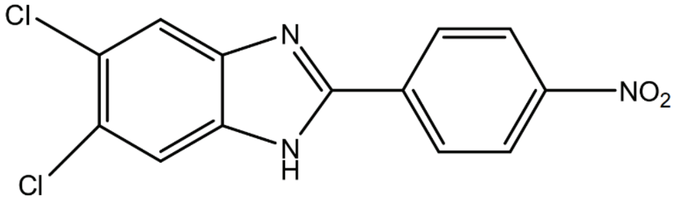
2-(3,4-dimethoxystyryl)-6-bromo-1*H*-benzo[*d*]imidazole

In their study, Deepika Sharma and others prepared compounds derived from imidazole and they found that it is important as antiviral, they revealed that components A, and B are of interest for the identification of new antiviral agent molecules as their antiviral agent activity the more effective. Ribavirin was employed as the standard drug in the study [58].



For compound A, R_1=H,R_2=H,R_3=Cl,R_4=H,R_5=H,X=4-NO_2
B, R_1=H,R_2=H,R_3=NO_2,R_4=H,R_5=H,X=4-NO_2

Michele Tonelli et al synthesized 76 derivatives of 2-phenylbenzimidazole, which were subsequently assessed for both antiviral activity and cytotoxicity against a range of DNA and RNA viruses. The compound ([5,6-dichloro-2-(4-nitrophenyl)benzimidazole]) demonstrated significant activity, surpassing the potency of reference drugs such as mycophenolic acid and 6-azauridine [61].



5,6-dichloro-2-(4-nitrophenyl)-1*H*-benzo[*d*]imidazole

Industrial of Imidazole Azo Compounds

Azo imidazole derivatives represent a very crucial category of chemical compounds that have garnered significant interest in scientific research [11].

These compounds have attracted considerable attention because of their diverse applications, including dyeing textile, biomedical studies, advanced organic synthesis, and applications in advanced technology areas such as printers, lasers, and electro-optical devices [62].

Azo compounds play a crucial role in the industrial sector, specifically in dyeing textiles like synthetic fibers, and wool (Polyamide, Polyesters), as well as in the dyeing of leather [25, 63-65], photography, foodstuffs, paper, cosmetics, and ink printers. Moreover, it finds application in cutting-edge technologies like lasers and is employed in the production of certain types of polymers equipped with electrical conductivity[66-69]

Imidazole is utilized in the industrial sector as a corrosion inhibitor for specific transition metals, including copper. The corrosion leads to a reduction in the conductivity of copper. Imidazole derivatives are present in many compounds of great importance in both industrial and technological contexts. The polybenzimidazole Associated with an imidazole, exhibits thermostability and functions as a flame retardant. It’s present in many chemical compounds employed in the fields of electronics and photography [70].

AshitoshB. Pawar, Sandeep P. More, et al produced three distinct azo compounds(modified dyes) through areca nut extract, a polyphenolic derived from plants to obtain dyes for textiles. These altered dyes were employed on polyester and nylon fabrics, and the dye exhaustion rate was assessed. The fabrics that underwent dyeing were subsequently subjected to assessments of their fastness properties. The outcomes from the fastness test reveal that the dyeability of polyester and nylon fabrics is satisfactory for all three modified dyes. The fabrics, post-dyeing, underwent testing for ultraviolet protection factor, demonstrating highly effective protection against ultraviolet radiation [71].

Agricultural of Imidazole Azo Compounds

Kasim Mohammed and Hello Nahla Ghaze Fahad synthesized a di-imidazolium chloride-silica has been prepared as a new type from the combustion of rice husks, and this led to a high yield of azo dyes. Di-imidazolium chloride-silica has been prepared as a new type of heterogeneous catalyst [72]. This catalyst can facilitate the on-site generation of nitrous acid and its formation as diazonium salt. This led to exceptionally high yields of azo dyes. Rice husks were used to synthesize the catalyst. Rice husk represents readily available biomass characterized by it has relatively high chemical resistance, and low quality [73, 74]. Various materials including catalysts can be extracted from the conversion of rice husks [75], zeolites, and activated carbon [76]. Under controlled conditions, when rice hulls are exposed to combustion, noncrystalline silica will be produced. The silica then undergoes conversion to sodium silicate through alkaline hydrolysis. In a one-pot method, alkyl silylation can be employed to functionalize sodium silicate. The primary vegetable dyes were obtainable in Asia and Europe were extracted from the madder roots. In India, the leaves of the indigo plant and red dye are used to create the blue dye that continues to be employed in the production of contemporary jeans [37].

Imidazole constitutes a component of the theophylline molecule, present in tea leaves and coffee beans, and it acts as a stimulant for the central nervous system in humans [70].

Cihan KANTAR, Zeliha ER, et al manufactured some azo compounds using catechins resulting from black tea processing waste with antioxidants and subsequently examined their properties to inhibit the urease enzyme and their antioxidant capabilities. They identified a correlation between the inhibition of urease and antioxidant capacity. The urease inhibitory effects of the recently synthesized azo compounds, which include catechins from black tea processing waste, were observed to surpass those of thiourea used as a standard reference substance [77].

Akaranta et al carried out the synthesis of azo dyes that incorporate phenolic compounds found in red onion peel and the dyeing characteristics of diverse textile items were examined the results have been observed and look good and promising, considering that red onion skin, a bioresource, was utilized in the study, It has the ability to act as a raw material for the formation of azo dyes and It was mentioned that agricultural residues with comparable compositions could be evaluated in a similar context [78].

M. Ahasanur Rabbi, Md, Mahasin Ali, and their colleagues synthesized azo compounds that incorporate polyphenols derived from a specific type of acacia tree, and the dyeing characteristics of these compounds were scrutinized for silk fabric, demonstrating stability when exposed to sun rays and diluted acid and It was underscored that semi-synthetic dyes of natural origin are environmentally sustainable and exhibit minimal toxic effects [79].

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