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Review

Exploring the Chemistry, Reactions, Applications, and Biomedical Potentials of 2-Nitrobenzaldehyde and 2-Chlorobenzaldehyde

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Abstract: This article investigates the diverse chemical reactions and applications of 2-nitrobenzaldehyde, exploring its versatility in synthetic organic chemistry. The focus is on key reactions such as reduction to yield 2-aminobenzaldehyde, Schiff base synthesis with primary amines, Michael addition reactions, Sandmeyer reaction for the formation of 2-nitrobenzoic acid, selenium dioxide oxidation to 2-nitrobenzoic acid, and condensation reactions leading to benzanthrone derivatives. Each reaction pathway is discussed along with its potential applications in various fields. The second part of the review shifts the spotlight to 2-chlorobenzaldehyde, emphasizing its physical and chemical properties. Further exploration of 2-chlorobenzaldehyde's chemical reactivity reveals its engagement in nucleophilic addition reactions, alcoholysis reactions, acetylation reactions, reductive amination reactions, Witting reactions, and halogenation reactions. These reactions showcase the compound's adaptability and utility in diverse synthetic pathways. This article also discusses the biomedical application of 2-chlorobenzaldehyde and 2-nitrobezaldehyde.

***Keywords*:** Michael addition, reductive amination, nucleophilic addition, selenium dioxide oxidation, carbonyl group

1. Introduction

The 2-nitrobenzaldehyde is an organic compound with the chemical formula $C_7H_5NO_3$. It is a solid that appears pale golden and emits a strong fragrance. This molecule serves as one of the most crucial building blocks in organic synthesis. The melting and boiling points of 2-nitrobenzaldehyde are 43 °C and 156 °C, respectively.[1] Water barely dissolves it, while organic solvents like ethanol, ether, and benzene can dissolve it completely. Depending on the purity, its color can range from yellow to orange. The chemical properties of 2-nitrobenzaldehyde are crucial for the creation of Schiff bases, as they are formed when an aldehyde (such as 2-nitrobenzaldehyde) or a ketone reacts with primary amines. These compounds have a variety of uses in organic chemistry such as chelating agents in metal analysis, catalysts in organic reactions, pigments and dyes, antimicrobial agents and ligands in coordination chemistry.[2-3] The carbonyl group of the aldehyde is attacked by the main amine in a nucleophilic manner, forming an imine intermediate. The addition of a reducing agent like sodium borohydride causes the imine intermediate to be reduced to the Schiff base.[4] In the literature review, various methods for the synthesis of Schiff bases using 2-nitrobenzaldehyde have been reported. One of the most commonly used methods involves the reaction of 2-nitrobenzaldehyde with primary amines in the presence of a reducing agent. For instance, a study by Nada et al. reported the synthesis of a series of Schiff bases derived from 2-nitrobenzaldehyde and various primary amines, which exhibited significant antifungal activity against

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Candida albicans.[5] According to the findings of different studies by Agata et al., 2-nitrobenzaldehyde is employed as a precursor in the synthesis of hydrazones, which are widely used as antitubercular and antifungal medicines. In the catalyst-free method, 2-nitrobenzaldehyde and hydrazine hydrate were condensed during the reaction. The resultant hydrazone compounds demonstrated strong antifungal and antitubercular properties.[6-7] The literature review has emphasized various methods for the synthesis of Schiff bases using 2-nitrobenzaldehyde and their potential applications. The Schiff bases derived from 2-nitrobenzaldehyde have been widely used in various fields, such as drug discovery, polymer chemistry, and analytical chemistry.

2-chlorobenzaldehyde, a chlorinated benzaldehyde derivative is a colorless, pale yellow liquid known for its pungent odor and chemical versatility. It has a boiling point of approximately 214 °C, a melting point of 9 °C, and a density of 1.228 g/cm^3, making it slightly soluble in water but more so in organic solvents like ethanol, ether, and chloroform. Its reactivity, enhanced by the electron-withdrawing chlorine atom, makes it integral to various synthetic processes in pharmaceuticals, agrochemicals, dyes, pigments, perfumes, and flavorings. In comparison, 2-nitrobenzaldehyde, characterized by a nitro group ($-NO_2$) on the benzene ring, shows different reactivity due to the stronger electron-withdrawing effect of the nitro group. With a boiling point of 156 °C, a melting point of 43 °C, and a density of 1.286 g/cm^3, it is more electrophilic, making it more reactive towards nucleophilic attacks than 2-chlorobenzaldehyde.[1] Exploring the chemistry of these compounds is crucial for advancing drug discovery, polymer chemistry, and analytical chemistry, as it enables the development of new pharmaceutical agents, novel polymers, and advanced analytical methods, thereby contributing to significant progress in these fields.

2-chlorobenzaldehyde is characterized by a benzene ring substituted with a chlorine atom and an aldehyde group at the ortho position. The presence of the chlorine atom, an electron-withdrawing group, increases the reactivity of the benzaldehyde, making it a valuable intermediate in numerous synthetic processes. 2-chlorobenzaldehyde's enhanced reactivity due to the chlorine atom allows it to participate in a variety of organic reactions, including nucleophilic aromatic substitution, condensation reactions, and Grignard reactions. This reactivity makes it an essential building block in several industrial applications. In pharmaceuticals, it is used to synthesize active pharmaceutical ingredients and intermediates. In agrochemicals, it plays a role in producing pesticides and herbicides. Furthermore, it is used in the production of dyes and pigments and as an intermediate in the manufacture of aromatic compounds for perfumes and flavorings. These applications underline the compound's versatility and importance in various sectors.[8]

Comparatively, 2-nitrobenzaldehyde, another derivative of benzaldehyde, features a nitro group ($-NO_2$) instead of chlorine. This substitution significantly impacts its chemical behavior and physical properties. 2-nitrobenzaldehyde like 2-chlorobenzaldehyde, it is more soluble in organic solvents than in water. However, the nitro group's strong electron-withdrawing effect makes 2-nitrobenzaldehyde more electrophilic, increasing its reactivity toward nucleophiles compared to 2-chlorobenzaldehyde.[9] The nitro group's influence on 2-nitrobenzaldehyde's reactivity is profound. It not only makes the compound more susceptible to nucleophilic attack but also affects its participation in electrophilic aromatic substitution reactions. The enhanced electrophilicity due to the nitro group enables 2-nitrobenzaldehyde to engage in a broader range of chemical reactions, making it a valuable compound for different synthetic applications. This increased reactivity can be particularly advantageous in synthesizing complex organic molecules, including those used in pharmaceuticals and advanced materials. Exploring the chemistry of both 2-chlorobenzaldehyde and 2-nitrobenzaldehyde is crucial for advancing multiple scientific and industrial fields. In drug discovery, understanding these compounds' reactivity and properties can lead to the development of new pharmaceutical agents with improved efficacy and safety profiles. The unique chemical properties of these benzaldehyde derivatives can be leveraged to create novel drugs targeting various diseases, contributing to the advancement of medical science.[10]

In polymer chemistry, these compounds can be used to synthesize novel polymers with specific properties tailored for various applications, such as high-performance materials, biodegradable plastics, and smart materials with responsive characteristics. The reactivity of 2-chlorobenzaldehyde and 2-nitrobenzaldehyde enables the incorporation of functional groups into polymer chains, enhancing the materials' performance and expanding their potential uses.[11] Analytical chemistry also benefits from studying these compounds, as their distinct chemical signatures can be utilized in developing advanced analytical methods for detecting and quantifying various substances. The reactivity of these benzaldehyde derivatives can be harnessed in designing sensitive and selective assays, improving the accuracy and reliability of analytical techniques used in research and industry.

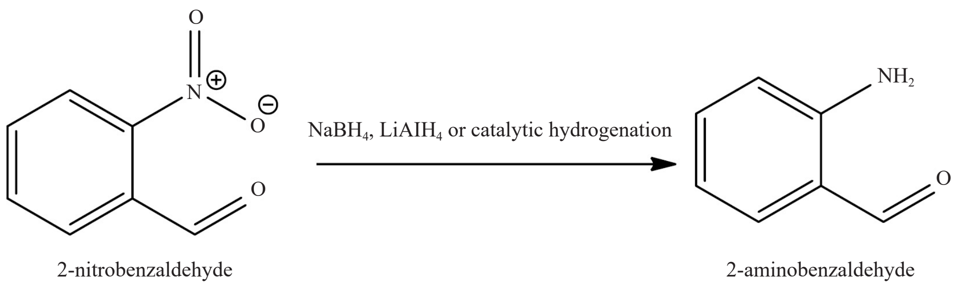
2. Methodology section

This review article was organized from already available literature present in the form of research articles, books, thesis, and some actual works. The data were firstly collected, then analyzed and the information was explored to the best of our knowledge and was organized in the form of review articles. Some important chemical reaction and their mechanism were also analyzed and included in this review article.

3. Different chemical reactions of 2-nitrobenzaldehyde

3.1 *Reduction reaction*

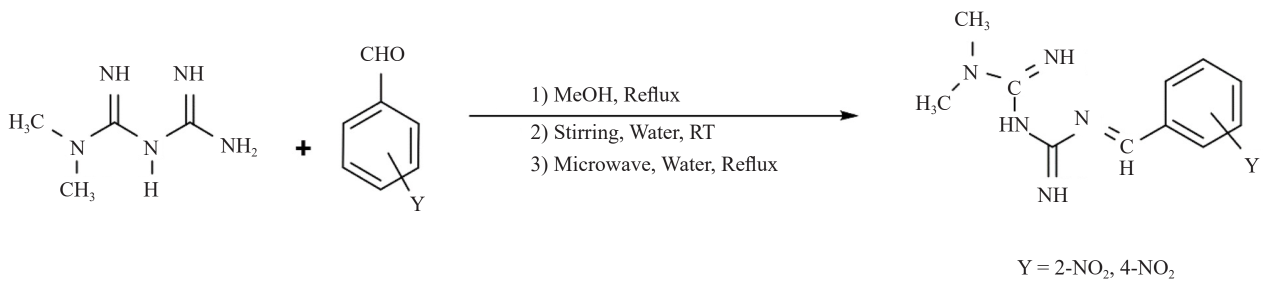
2-nitrobenzaldehyde undergoes a reduction reaction to form 2-aminobenzaldehyde. This reaction can be carried out using various reducing agents such as $NaBH_4$, $LiAlH_4$ or catalytic hydrogenation (Scheme 1).[12-13]



Scheme 1. Reduction of 2-nitrobenzaldehyde

3.2 *Schiff base synthesis*

2-nitrobenzaldehyde is a key starting material for the synthesis of Schiff bases. The reaction involves the condensation of 2-nitrobenzaldehyde with primary amines to form Schiff bases (Scheme 2), which have applications in various fields such as drug discovery, polymer chemistry, and analytical chemistry.[14]



Scheme 2. Synthesis of Schiff base from 2-nitrobenzaldehyde

3.3 *Michael addition reaction*

2-nitrobenzaldehyde can undergo a Michael addition reaction with various nucleophiles such as active methylene compounds, β-keto esters, and various enolate ions. The reaction forms 1,4-addition products, which have applications in synthetic organic chemistry.[15]

3.4 *Sandmeyer reaction*

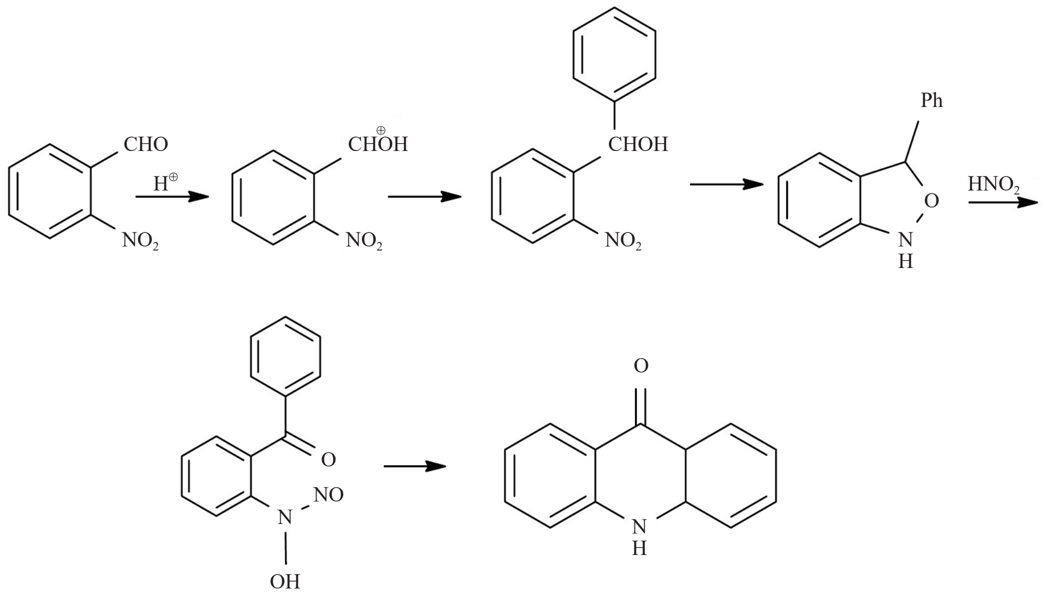
2-nitrobenzaldehyde can undergo a Sandmeyer reaction to form 2-nitrobenzoic acid. The reaction involves the conversion of the nitro group ($-NO_2$), to a diazonium ion ($-N_2$ + X-) which is then converted to the corresponding carboxylic acid by hydrolysis.[16]

3.5 *Selenium dioxide oxidation*

2-nitrobenzaldehyde can undergo an oxidation reaction using selenium dioxide to form 2-nitrobenzoic acid. The reaction is carried out in the presence of an acidic solvent and under reflux conditions.[17]

3.6 *Condensation reaction*

2-nitrobenzaldehyde can undergo a condensation reaction with aromatic hydrocarbons to form various classes of organic compounds like acridones. Acridones are formed in the presence of H_2SO_4 followed by treatment with nitrous acid at room temperature (Scheme 3).[18]



Scheme 3. Synthetic route of acridones from 2-nitrobenzadehyde[18]

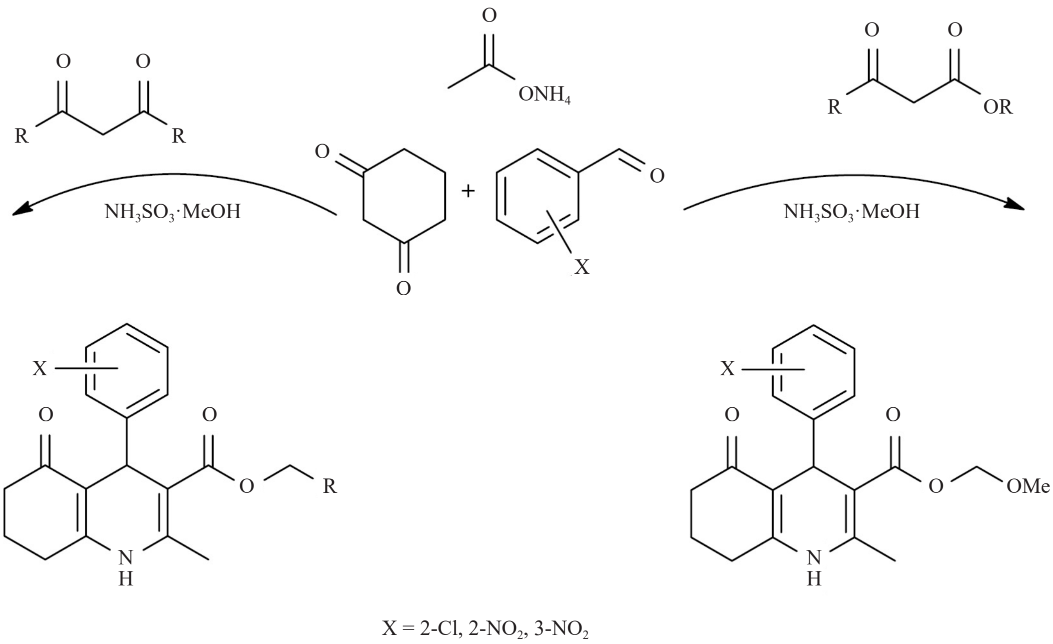
4. Versatility and applications of 2-nitrobenzaldehyde

2-nitrobenzaldehyde is a key starting material in organic synthesis. The compound has a variety of applications in synthetic organic chemistry, mainly due to its strong electron-withdrawing properties of the nitro group ($-NO_2$) on the aromatic ring. Condensation and reduction reactions explored the chemical reactivity of 2-nitrobenzaldehyde as well as its derivatives, including Schiff bases, hydrazones, acridones and N-oxides.[18-19] In one study, Kumar et al. described the process of development of a brand-new class of fluorescent molecular sensors based on derivatives of 2-nitrobenzaldehyde.[20] The study looked at the fluorescence characteristics of 2-nitrobenzaldehyde derivatives that had their benzene rings changed with various substituents. The findings demonstrated that the electron-donating or -withdrawing characteristics of the substituents had an impact on the fluorescence features of the derivatives.[21-22]

The synthesis and crystal structure of a novel Schiff base made from 2-nitrobenzaldehyde and 2-aminopyridine were described in a different research by Ebosei et al. In the study, 2-nitrobenzaldehyde was described as a starting substance for the production of Schiff bases, which may be used as antibacterial and anticancer medicines.[23] According to a study by Randrspancher et al., a novel hydrazone molecule was synthesised using 2-nitrobenzaldehyde and 2-ethoxyethanol. The study looked into the possibility of using hydrazone to prevent mild steel from corroding in acidic environments. The findings demonstrated that the hydrazone compound efficiently prevented mild steel from corroding and suggested that it would be a good candidate for use as a corrosion inhibitor.[24] Lund et al. reported the synthesis of a novel N-oxide derived from 2-nitrobenzaldehyde and 4-chloroaniline. The N-oxide was found to exhibit significant antimicrobial activity against various bacterial and fungal strains. The study reported the importance of the nitro group in the benzaldehyde moiety for the antimicrobial activity of the N-oxide.[25] Finally, it should be noted that 2-nitrobenzaldehyde and its derivatives have been shown to be flexible building blocks for the synthesis of a variety of chemical molecules.

Nitro derivatives of benzaldehyde, especially 2-nitrobenzaldehyde, act as an intermediate in many organic syntheses, such as in the synthesis of drugs and antimicrobial compounds. Drugs used for treating cardiovascular and cerebrovascular diseases are often synthesized by utilizing 2-nitrobenzaldehyde as an intermediate species.[26-27] For example, the synthesis of quinazoline and 3-arylquinoline both require 2-nitrobenzaldehyde as an intermediate. These products exhibit a wide range of biological activities, including anti-endotoxin, antitumor, analgesic, and antifungal properties.[28-29] In the same way, Schiff bases synthesized from 2-nitrobenzaldehyde with multiple types of amines show excellent antibacterial, anticancer, antitumor, and anti-inflammatory properties, highlighting another benefit of 2-nitrobezaldehyde.[30-31] In chemical synthesis, 2-nitrobenzaldehyde also plays a key role in achieving good yields. For example, their Schiff bases complex with cobalt(II) can be used for the selective oxidation of primary alcohols, secondary alcohols, furans, and benzoin derivatives into their corresponding aldehydes and ketones.[32] The production yield of Schiff base using 2-nitrobenzaldehyde with the amine of interest is relatively high. Yu-Rou Jiang et al synthesized Schiff bases from the reaction of 2-nitrobenzaldehyde with L-valine, L-glycine, L-leucine, L-aspartic acid, and L-glutamic acid, achieving efficient yields of 92%, 87%, 96%, 88%, and 90%, respectively.[33] Other nitro derivatives of benzaldehyde also help in the formulation of pesticides, dyes, optical materials and pharmaceutical drugs.[34] Nifedipine, nisoldipine, nitrendipine, and micardipine belong to the dihydropyridine cardiovascular drugs group, which are very important pharmaceutical products. For such compounds, the nitro, chloro, and hydroxy derivatives are used as raw material. These group provide extra stability through electron withdrawing effects, thus enhancing biological activity.[35-36] Nitroaromatic compounds also show mutagenic properties.[37] The synthesis of mononitro derivatives of benzaldehyde is difficult to achieve in high purity and good yield.[38]

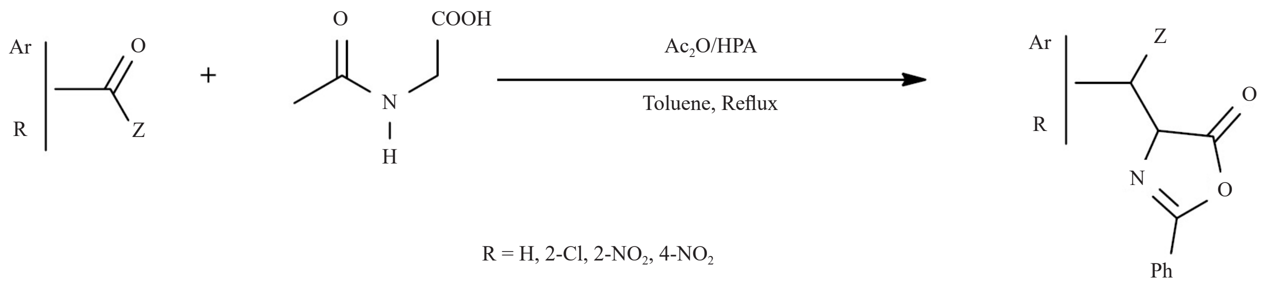
The condensation of carbonyl compounds (aldehydes and ketones) with primary amines was first discovered by Schiff who named them Schiff bases (ACD/Labs, 2005).[39] Organic compounds formed by the condensation reaction of aliphatic or aromatic amines with carbonyl compounds (aldehydes or ketones) in the nucleophilic addition reaction were termed Schiff bases by the German chemist Hugo Schiff.[40] It was found that aromatic Schiff bases are more stable than alkyl Schiff bases and can be easily synthesized.[41] The -C = N- bond present in Schiff bases is similar to the C = O bond, which can be easily reduced by metal ions, making them versatile ligands.[42] Generally di-, tri-, tetra- and so on dentate ligands form stable complexes with metal ions.[43] Schiff bases can also be used directly or indirectly in catalysis.[44] For example, in the catalytic oxidation of linear aliphatic olefins, styrene, cyclohexene and so forth we mostly prefer Mn-Schiff base complexes.[45] K. Girish Kumar et al. reported that a 2-nitroamino base Schiff base ligand is efficient for the removal of heavy metals from solutions. They found 90% removal of metals from a 30 ppm solution at the usage of 0.01 grams of the ligand, without the need of pH control.[46] Schiff bases form stable complexes with transition metal ions.[47-48] The Schiff base formed by the condensation of isoniazid and 2-nitrobenzaldehyde is used as a pharmaceutical drug in antituberculosis and antimycobacterial activity.[49-51] The activities of these Schiff bases can be tuned via complexation, which directly depends on the stability of the obtained complexes. For example, Z. T. Omar et al. synthesized isoniazid and 2-nitrobenzaldehyde Schiff base complexes with M(II) ions, where M = Mn, Co, Ni, Cu, and Zn. They found that the order of stability and activity was Zn(II) > Ni(II) > Cu(II) > Mn(II) > Co(II).[47] Furthermore, complexes in which Schiff bases were used as ligands carry special importance in inorganic chemistry because of their physiochemical and pharmacological activities.[52] The Co(II) and Pd(II) complexes with Schiff bases act as anticancer and antitumor agents.[53] Besides Schiff base synthesis, 2-nitrobenzaldehyde and 2-chlorbenzaldehyde also play an important role in macromolecule synthesis. For example, Brinkerhoff et al. used 2-nitrobenzaldehyde and 2-chlorbenzaldehyde for the synthesis of different 2-or-3 substituted Polyhydroquinolines (PHQ) derivatives from fatty acids and fatty alcohol at good yields via a four-component reaction (4CR). He synthesized eighteen different 2- or 3-substituted Polyhydroquinolines (PHQ) derivatives (Scheme 4), where the chlorophenyl or nitrophenyl group was transferred from 2-chlorbenzaldehyde or 2-nitrobenzaldehyde, and found all of them to have efficient antioxidant activities. These activities were determined using 2,2-diphenyl-1-picrylhydrazyl (DPPH), 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) and ferric ion reducing antioxidant power (FRAP) assays.[54]



Scheme 4. 2-nitrobenzaldehyde and 2-chlorbenzaldehyde for the synthesis of different 2-or-3 substituted Polyhydroquinolines

The 2-nitrobezaldehyde shows unique properties as compared to their 3-nitro and 4-nitro isomer, because they have internal hydrogen bonding of 8.06 KJ/mol.[55] Mahmoud Sunjuk et al.[56] observed that Schiff bases of N-heteroaromatic bases like 2-amino-6-methoxybenzothiazole with 2-substituted-benzaldehyde (2-chlorobenzaldehyde, 2-nitrobenzaldehyde and 2-hydroxybenzaldehyde) make stable complexes with Metal(II) salts like Cu(II), Ni(II), Co(II), Cd(II), Cr(II) and Fe(II). These complexes are insoluble in water but soluble in ethanol, Dimethylformamide (DMF), and Dimethyl sulfoxide (DMSO). Therefore, it was concluded that complexes of 2-substituted-benzaldehyde Schiff bases can be indirectly used as water-resistant materials.[56]

In the same way, Panchsheela et al.[57] synthesized Cu(II) complexes with Schiff bases derived from the condensation reaction of 2-nitro, 2-chloro, and 4-bromo substituted benzaldehydes with the N-heteroaromatic base 2-amino-6-methoxybenzothiazole. They found that these complexes exhibit efficient anticancer activities in comparison to the standard drug Adriamycin. Further, these complexes were also found to be efficient against both gram-positive and gram-negative bacteria, along with free radical scavenging ability.[57] It was also observed that the nature of catalysts remains unchanged and cannot be denatured when used during Erlenmeyer-type reactions of 2-chlorbenzaldeyde, 2-nitrobenzaldehyde, and other related compounds. This reaction essentially involves the condensation of aldehydes with hippuric acid in the presence of acetic anhydride (Scheme 5).[58]



Scheme 5. Erlenmeyer-type reaction

5. Physical properties of 2-chlorobenzaldehyde

2-chlorobenzaldehyde is an organic compound with the molecular formula C_7H_5ClO. The compound is a colorless to yellow solid that has a strong pungent odor. 2-chlorobenzaldehyde has many applications in organic synthesis because of its chemical properties and functionality.[59] In this article, we will discuss the physical and chemical properties of 2-chlorobenzaldehyde and its role in Schiff base synthesis. The conditions under which 2-chlorobenzaldehyde can go through numerous chemical transformations depend greatly on its physical characteristics. This substance has a flash point of 97 °C and a melting point of 9-11 °C. It has a density of 1.248 g/cm^3, and while it is mostly soluble in organic solvents like ethanol, benzene, and ether, it is only weakly soluble in water. The yellow hue of the compound gets stronger the purer it is. The molecule is an appropriate starting material for a variety of organic synthesis reactions due to its melting, boiling temperature, and solubility in different solvents.[59]

6. Chemical properties of 2-chlorobenzaldehyde

The chemical characteristics of 2-chlorobenzaldehyde make it an excellent starting point for the synthesis of many organic molecules. It has a carbonyl group (C = O) that enables it to go through a variety of processes, including Schiff bases formation and nucleophilic addition. It also has a chlorine atom, which increases its reactivity to a variety of organometallic reagents.

6.1 *Schiff base synthesis with 2-chlorobenzaldehyde*

The reaction of a primary amine with an aldehyde or ketone to produce a Schiff base is a significant procedure in organic synthetic chemistry. In the production of Schiff bases, 2-chlorobenzaldehyde reacts with primary amines to form Schiff bases. An amine attacks the 2-chlorobenzaldehyde carbonyl group in a nucleophilic way, forming an imine intermediate as a result. After the initial formation of the imine (Schiff base), the product can be isolated directly. In some cases, if further reduction of the imine is desired, reducing agents such as sodium borohydride or lithium aluminum hydride can be used to reduce the imine to an amine. The 2-chlorobenzaldehyde Schiff bases have shown potential for antibacterial, antifungal, and anticancer effects.[60-61] The production of Schiff bases using different primary amines and 2-chlorobenzaldehyde has been extensively studied. This research highlights the significance of the 2-chlorobenzaldehyde moiety as an antibacterial and antifungal agent. The produced Schiff bases were tested for their antifungal and antibacterial activity. The outcomes demonstrated that 2-chlorobenzaldehyde Schiff bases exhibit effective antibacterial and antifungal action against a variety of bacterial and fungal species.[62] In another work, Singh et al. described the synthesis of 2-chlorobenzaldehyde Schiff bases and their assessment as effective inhibitors of maize alpha-amylase. The enzyme maize alpha-amylase is responsible for breaking down soluble starch in maize. The study discovered that maize alpha-amylase was strongly inhibited by the Schiff bases of 2-chlorobenzaldehyde. Consequently, 2-chlorobenzaldehyde Schiff bases could be utilized as potential antidiabetic drugs.[63] Additionally, 2-chlorobenzaldehyde is valuable in the production of heterocyclic compounds including pyrimidines, pyrazoles, and pyridazines. When combined with amino acids, it facilitates the creation of pyrimidines. To produce isoxazoline intermediates, 2-chlorobenzaldehyde and hydrazides undergo a reaction in the presence of acetic acid. Subsequent cyclization of these intermediates leads to the formation of pyrimidines. As a result, 2-chlorobenzaldehyde is a useful precursor in chemical synthesis. It is an appropriate reagent for many transformations, including Schiff bases' synthesis, due to its distinct chemical and physical characteristics.[63] The pharmaceutical sector uses 2-chlorobenzaldehyde Schiff bases extensively because of their antibacterial and anticancer properties. As powerful maize alpha-amylase inhibitors, 2-chlorobenzaldehyde Schiff bases have also been employed. Moreover, in pharmaceutical research and drug development, heterocyclic molecules synthesized from 2-chlorobenzaldehyde play a pivotal role as crucial building blocks. Consequently, 2-chlorobenzaldehyde holds significant promise and may play a critical role in the development of novel medicinal drugs.[64]

6.2 *Different chemical reactions of 2-chlorobenzaldehyde*

The important reactions of 2-Chlorobebzaldehyde are nucleophilic addition reaction, alcoholysis, acetylation. Reductive amination, witting reaction, halogenation etc, 2-chlorobenzaldehyde can undergo nucleophilic addition reaction with various nucleophiles like active methylene compounds and β-keto esters.[65] In the alcoholysis reaction in the presence of alcohols and P_2O_5 to yield 2-(alkoxy)benzaldehydes.[66] The acetylation reactions in the presence of acetic anhydride form 2-chloro-1-acetylbenzene with 2-chlorobenzaldehyde.[65] 2-chlorobenzaldehyde can undergo reductive amination reactions with primary amines in the presence of ammonia and hydrogen to form secondary amines.[67] Witting reaction in the presence of triphenyl phosphine and sodium methoxide yield 2-(diphenylphosphinomethyl)-benzaldehyde[68] while in halogenation reactions such as Friedel-Crafts reactions with various halide containing carbonyls,[69] respective alky halides. 2-chlorobenzaldehyde is a versatile organic molecule widely employed in synthetic organic chemistry. Its unique chemical properties make it invaluable for the synthesis of various organic compounds. In this review, we will explore the diverse applications of 2-chlorobenzaldehyde in industries such as nanotechnology,[70-71] pharmaceuticals, and materials science, as documented in the literature.[72-73] One study by Elemike et al. demonstrated the synthesis of a novel Schiff base derived from 2-chlorobenzaldehyde and Isatin. The study reported the use of the compound in the antibacterial and antifungal applications. The Schiff base showed potent antibacterial and antifungal activities against several bacterial and fungal strains. Therefore, the Schiff base of 2-chlorobenzaldehyde possesses significant potential in the development of novel antimicrobial agents.[74] Another study by Salihovic et al. reported the synthesis of a new class of Schiff bases from 2-chlorobenzaldehyde and different amino acids. The Schiff bases were evaluated for their antimicrobial activities, which ranged from moderate to good. The study highlighted the functional role of 2-chlorobenzaldehyde in Schiff base synthesis for pharmaceutical applications.[75] Furthermore, a study by Li et al. reported the use of chlorobenzaldehydes in the synthesis of graphene quantum dots (GQDs). The study utilized chlorobenzaldehydes as one of the starting materials in the synthesis of GQDs. The resulting GQDs possessed excellent fluorescence properties and potential applications in the field of nanotechnology.[76-77]

7. Biomedical applications of 2-nitrobenzaldehyde

Biomedical research constantly seeks innovative compounds with diverse applications in the diagnosis, treatment, and understanding of diseases. Among such compounds are 2-nitrobenzaldehyde and 2-chlorobenzaldehyde, organic molecules that exhibit versatile properties useful in various biomedical contexts.[78-80]

7.1 *Amino acid detection*

A notable application of 2-nitrobenzaldehyde lies in its role in detecting and quantifying amino acids. Through its reaction with primary amines, it forms Schiff bases, enabling the development of spectrophotometric assays for amino acid analysis. This method provides a sensitive and selective means of identifying and measuring amino acids in biological samples, aiding in diagnostics and research. For example, Nayyab Hussain designed a novel pathway as shown in Figure 1, for the detection of creatinine in human urine samples via an electrochemical process. The content of creatinine was detected from their reaction with 2-nitrobenzaldehyde.[81]

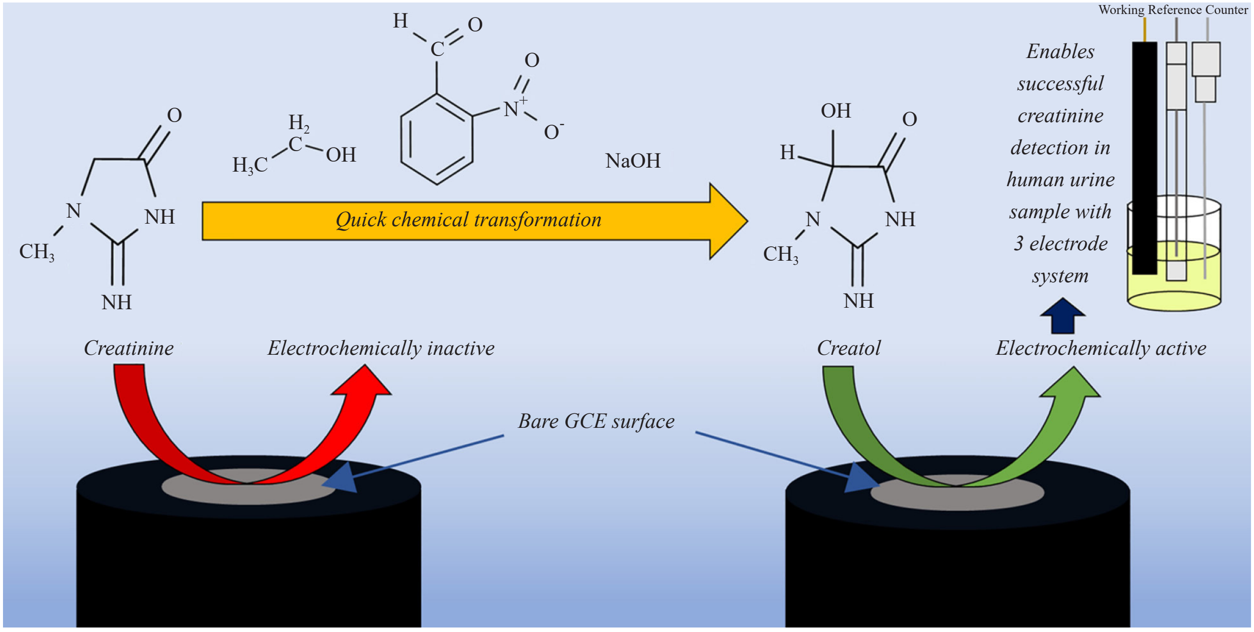


Figure 1. Detection of creatinine in human urine samples using electrochemical process by their specific reaction with 2-nitrobenzaldehyde[81]

7.2 *Antimicrobial properties*

The 2-nitrobenzaldehyde and its derivatives show promising properties against microbes like bacteria and fungi. These compounds exhibit activity against various microorganisms, including bacteria and fungi. Understanding and harnessing these antimicrobial effects could lead to the development of novel therapeutic agents to combat infectious diseases, addressing the growing concern of antimicrobial resistance.[82]

7.3 *Anti-cancer potential*

Investigations into the cytotoxic effects of certain nitrobenzaldehyde derivatives against cancer cells have been conducted. These compounds demonstrate the ability to induce cell death in cancerous tissues, suggesting potential applications in cancer therapy. Further exploration of their mechanisms of action and efficacy could lead to the development of new treatments for various types of cancer.[83]

7.4 *Photodynamic therapy (PDT)*

2-nitrobenzaldehyde derivatives have garnered interest in the field of photodynamic therapy (PDT), a treatment modality for cancer and other diseases. These compounds can serve as photosensitizers, generating reactive oxygen species upon light activation. This localized production of cytotoxic agents enables the targeted destruction of tumor cells while minimizing damage to surrounding healthy tissue, offering a promising approach for cancer treatment.[84]

8. Biomedical applications of 2-chlorobenzaldehyde

8.1 *Synthesis of benzaldehyde derivatives*

2-chlorobenzaldehyde serves as a key intermediate in the synthesis of various benzaldehyde derivatives.[85] These derivatives exhibit diverse biological activities, including antimicrobial, anti-inflammatory, and anticancer properties. The ability to modify the chemical structure of 2-chlorobenzaldehyde allows for the creation of compounds tailored to specific biomedical applications, facilitating drug discovery and development.[85]

8.2 *Fluorescent probes*

Chlorobenzaldehyde derivatives have been utilized in the design of fluorescent probes for biological imaging and sensing. These probes enable the visualization of specific cellular components or the monitoring of biochemical processes in living systems.[86] Their fluorescence properties make them valuable tools for studying cellular dynamics and elucidating disease mechanisms, contributing to advances in diagnostics and therapeutics.[87]

8.3 *Enzyme inhibition*

Studies have investigated the inhibitory effects of chlorobenzaldehyde derivatives on enzymes implicated in various disease processes. These compounds demonstrate the potential to modulate enzyme activity, offering opportunities for the development of therapeutic agents. By selectively targeting key enzymes involved in pathological pathways, chlorobenzaldehyde derivatives may provide new avenues for treating a range of diseases, including cancer, metabolic disorders, and infectious diseases.[88]

8.4 *Organic synthesis*

The versatility of 2-chlorobenzaldehyde makes it a valuable building block in organic synthesis, particularly in the preparation of pharmaceuticals and biologically active compounds.[89] Its reactivity allows for the creation of diverse molecular scaffolds with potential biomedical applications. Through strategic chemical modifications, researchers can optimize the pharmacological properties of chlorobenzaldehyde derivatives, enhancing their efficacy and safety for clinical use.[90] 2-nitrobenzaldehyde and 2-chlorobenzaldehyde represent promising compounds with a wide range of biomedical applications. From amino acid detection and antimicrobial activity to cancer therapy and enzyme inhibition, these molecules offer valuable tools and therapeutic opportunities in biomedical research and clinical practice.[91-92] Continued exploration of their properties and development of novel derivatives hold the potential to advance diagnostics, treatments, and our understanding of complex biological processes.

9. Conclusion

In conclusion, this review has provided a comprehensive overview of the chemical reactions and applications of 2-nitrobenzaldehyde and 2-chlorobenzaldehyde, shedding light on their versatility and importance in synthetic organic chemistry. The exploration of 2-nitrobenzaldehyde unveiled its involvement in reduction reactions leading to 2-aminobenzaldehyde, Schiff base synthesis, Michael addition reactions, Sandmeyer reactions, selenium dioxide oxidation, and condensation reactions. Each of these pathways contributes to the compounds' utility in various fields, ranging from drug discovery to polymer chemistry.[93-94] The examination of 2-chlorobenzaldehyde elucidated its physical and chemical properties, emphasizing its suitability as a starting material for organic synthesis reactions. The compound's reactivity in nucleophilic addition, alcoholysis, acetylation, reductive amination, Wittig, and halogenation reactions further underscores its versatility in synthetic pathways. The literature review on 2-chlorobenzaldehyde provided additional context, emphasizing its significance in organic synthesis and its role in Schiff base synthesis. The detailed discussion of its physical and chemical properties enhances our understanding of its behavior under different reaction conditions. Collectively, the insights presented in this review highlight the multifaceted nature of 2-nitrobenzaldehyde and 2-chlorobenzaldehyde, showcasing their potential applications and impact in the realm of organic chemistry. As researchers continue to explore new synthetic methodologies, these compounds stand as valuable building blocks, contributing to the ongoing advancement of chemical science. The diverse array of reactions and applications discussed in this review positions 2-nitrobenzaldehyde and 2-chlorobenzaldehyde as key players in the intricate landscape of organic synthesis, with promising avenues for future research and development.

Conflict of interest

The author declares no competing financial interest.

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