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Synthesis of Imidazole by Using Different Schiff's Base

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Abstract: *The new Schiff bases are synthesis from various and aldehyde and amine under magnetic stirrer method .Andthe Schiff base are yellow colour solid and having sharp melting point and insoluble in organic solvents. The naturally occurring five-member imidazole derivatives have shown interesting biological as well as physiochemical properties and consequently they have found several chemicals, optical, pharmaceutical, and other useful biological applications. The interesting biological properties and wide applications of polyfunctionalized imidazole molecules attract researchers to develop novel strategies for the synthesis of polyfunctionalized imidazole moieties. As a result, several research articles have been published in the literature. In this review article, we have disclosed various applications as well as the traditional and modern green approaches for the synthesis of imidazole derivatives including conventional synthesis, microwave- assisted synthesis, ultrasound promoted synthesis, and synthesis under green catalyst or a without catalyst. The most of the traditional methods of imidazole synthesis, there is no requirement of high pressure, energy, temperature, or toxic chemicals. However, the modern methods are accomplished through catalyst- and solvent-free conditions with high purity and excellent yields of the products.*

Keywords: New Schiff bases, sharp melting point, yellow solid colour. One-pot multicomponent reaction.

I. INTRODUCTION

Inorganic elements play crucial role in biological and biological medical processes, and it is evident that many organic compounds used in medicine do not have a purely organic mode of action, some are activated or bio transformed by metal ions metabolism . Many drugs possess modified toxicological and pharmacological properties in the form of metal complex and probably Schiff bases are versatile C=N (Imine) containing compounds possessing broad spectrum of biological activity and incorporation of metals in form of complexes showed some degree of antibacterial, antifungal , antitumor and anti-inflammatory activity.[1]

Schiff base are the compound containing azomethine group (-HC=N-). They are condensation products of ketones (or) aldehydes (aldehyde and ketones) with primary amines and were first reported by Hugo Schiff in 1864.[2] Formation of Schiff base generally takes place under acids or base catalysis or with heat. The common Schiff base are crystalline solids, which are feebly basic but at least some form insoluble salts with strong acids. Schiff base are used as intermediates for the synthesis of amino acids or as ligands for Preparation of metal complexes having a series of different structures.

Imidazole (1,3-diaza-2,4-cyclopentadiene) is an N-heterocyclic aromatic organic molecule that was first discovered in 1840. The chemical formula of the imidazole molecule is C3H4N2 which is a five-member Nheterocyclic compound having two nitrogen atoms in the aromatic ring. Imidazole moiety constitutes a very basic structural and fundamental building block of the various type of medical scaffolds [1–3]. This molecule is highly polar and amphoteric for nature. It is a colorless organic molecule and its boiling point and melting point lied 256 C and 89–91 C respectively [4–6] with high polarity having a dipole moment around

The core imidazole motif is aromatic in nature due to the presence of six π-electrons. It plays a vital role in various physiological actions for important biological functions. The core unit of imidazole is also present in the structural framework of vitamin B12, histamine

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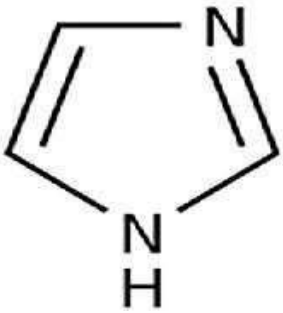
II. IMPORTANCE OF IMIDAZOLE DERIVATIVES



Imidazole is fundamental building blocks of the variety of pharmaceutical medical scaffolds. It also acts as acorrosion inhibitor for iron moiety. These molecules have also found applications in the field of catalysis [10],industry [11], natural product synthesis [12], and material science [13]. The 2-substituted imidazole derivativesare also used as catalysts [14–16], chiral auxiliaries [17], and ligand [18,19]. The Imidazole ring can also be able to interact with enzymes through different kinds of interactions such as hydrogen bond, iondipole interaction, van der Waals force, and π- π stacking [10,11]. The imidazole scaffold is also applied in the fieldof agrochemical ingredients [32], synthetic pharmaceuticals [13], and synthetic organic chemistry [14]. The imidazole salt i.e. imidazolium acts as a fascinating precursor for the carbene ligand in the wide range of metalcomplexes [15].

III. METHADOLOGY/ PROCEDURE

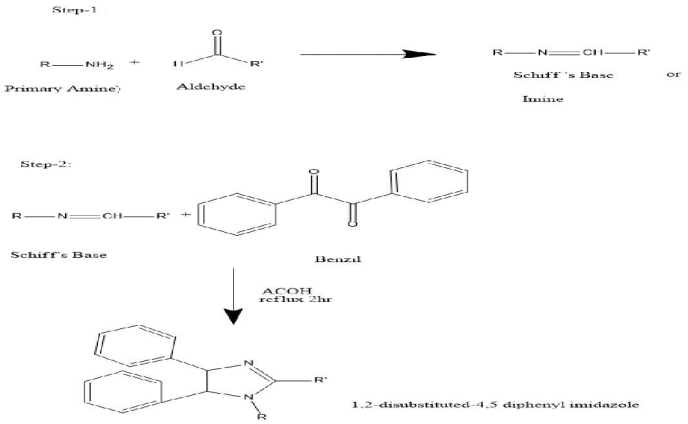
Synthesis of schiff's Base

- Disslove 1gm of aniline in 25ML of ethanol or isopropanol in round bottom flask equipped with acondenser and heating gently.
- Add 1.2 gm of benzaldehyde to the flask and heat the mixture at reflux for 2-3 hours.
- Cool the reaction mixture on ice and filter the solide product using a Buchner funnel.
- Wash the solide product with cold water and dry it.
- Recrystallize the purified Schiff base from ethanol and dry it again.

Synthesis of Imidazole

- Dissolve 1gm of the purified Schiff base in 10ml of acitic acid in a round bottom flask. • Add 1 gm ofpurified benzyl to the flask and heat the mixture at reflux for 2-3 hr
- Cool the reaction mixture on ice and filter the solid product .
- Wash the Solid product with cold water .
- Recrystallize the purified Imidazole from ethanol and dry it again.

General Reaction:



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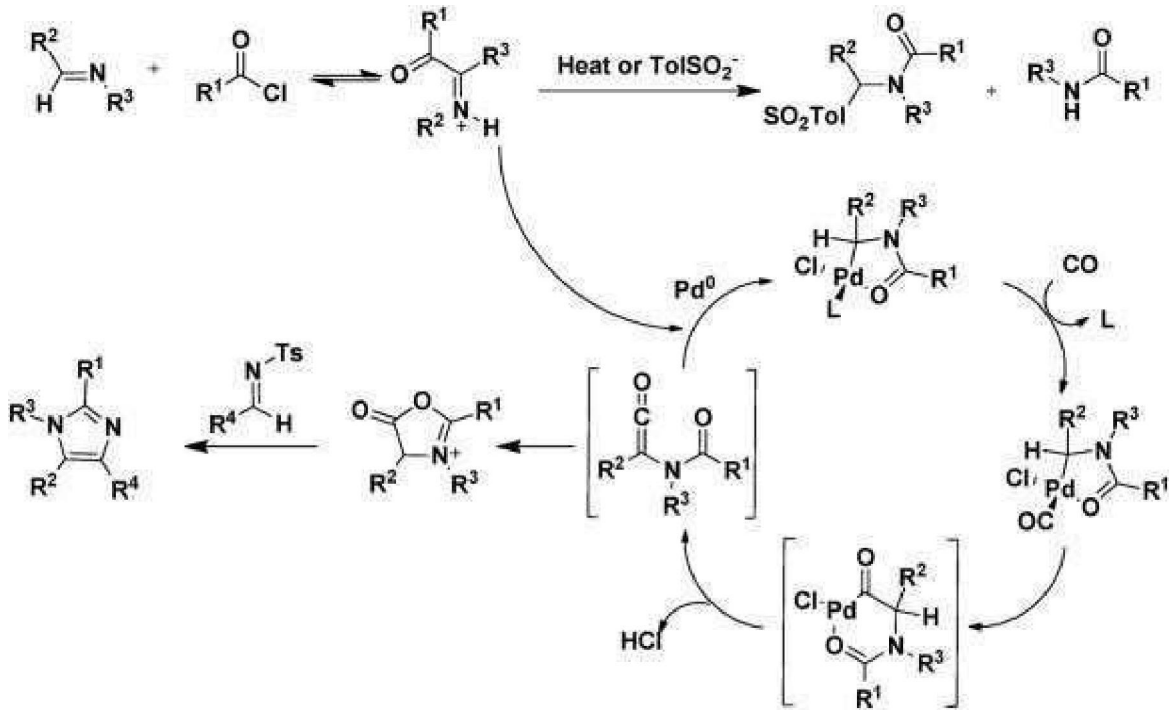
Schiff's Base;

Reactant A	Reactant B	Product	Time (hr)	Colour	Melting point
Salicylaldehyde	P-chloro-aniline	Salicylaldimine	1.15 - 1.30	Yellow	214 °C
Acetalaldehyde	P-chloro- aniline	Acetaldimine	1.5	pal Yellow	210 °C
Formalaldehyde	P-chloro-aniline	Formaldimine	2.0	Yellow	188 °C
Benzaldehyde	P-chloro-aniline	Benzilimine	1.45	Pal Yellow	164 °C
3,4 dimethoxy benezaldehyde	P-chloro-aniline	3,4 dimethoxy benzilimine	1.30	Yellow	182 °C



Mechanism of Imidazole

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Imidazole:

Reactant A	Reactant B	Product	Time	Colour
Salicylaldimine	Benzil	2-(1-(4-chlorophenyl)-4,5-diphenyl-4,5-dihydro-1H-imidazol-2-yl)phenol	2.30 hrs	White
Acetaldimine	Benzil	1-(4-chlorophenyl)-2-methyl-4,5-diphenyl-4,5-dihydro-1H-imidazole	2.15 hrs	White
Formaldimine	Benzil	1-(4-chlorophenyl)-4,5-diphenyl-4,5-dihydro-1H-imidazole	1.45 hrs	White
Benzilimine	Benzil	1-(4-chlorophenyl)-2,4,5-triphenyl-4,5-dihydro-1H-imidazole	2.30 hrs	White
3,4 dimethoxy benzilimine	Benzil	1-(4-chlorophenyl)-2-(3,4-dimethoxyphenyl)-4,5-diphenyl-4,5-dihydro-1H-imidazole	2.45hrs	White

IV. RESULTS AND DISCUSSTION

The ligands are yellow colour solid and they are insoluble in organic solvents and the ligands having sharp melting point. The most common substrates for all of these methods are benzil, benzoin, α-diketone, aldehydes, ammonium acetate, imines, and various amines. the one-pot multicomponent reactions and other green methods for the synthesis of imidazole derivatives

Reaction Conditions and percentage yield for product:

Starting material	Reagent	Product	Melting Point	% Prc. Yield
Salicylaldimine	ACOH	2-(1-(4-chlorophenyl)-4,5-diphenyl-4,5-dihydro-1H-imidazol-2-yl)phenol	280 °C	75.45%
Acetaldimine	ACOH	1-(4-chlorophenyl)-2-methyl-4,5-diphenyl-4,5-dihydro-1H-imidazole	242°C	80.78%
Formaldimine	ACOH	1-(4-chlorophenyl)-4,5-diphenyl-4,5-dihydro-1H-imidazole	264 °C	85.66%
Benzilimine	ACOH	1-(4-chlorophenyl)-2,4,5-triphenyl-4,5-dihydro-1H-imidazole	168 °C	65.55%
3,4 dimethoxy benzilimine	ACOH	1-(4-chlorophenyl)-2-(3,4-dimethoxyphenyl)-4,5-diphenyl-4,5-dihydro-1H-imidazole	162 °C	60.67%

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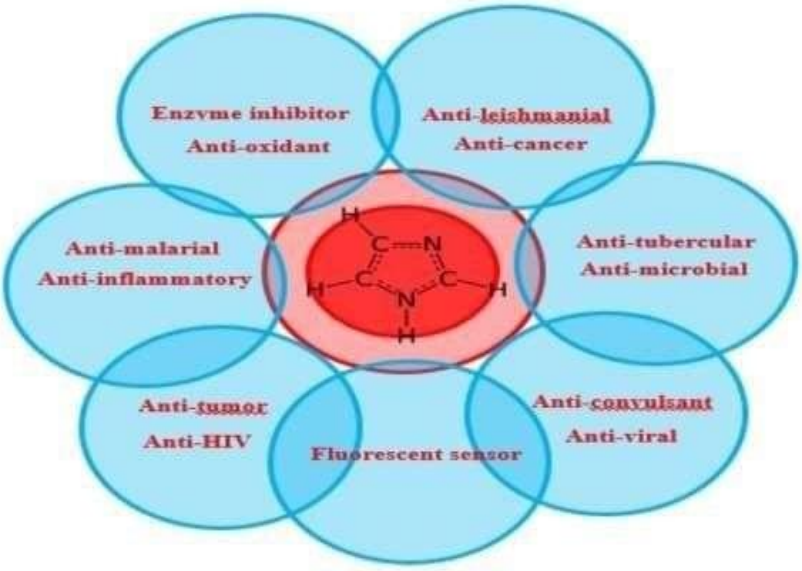
APPLICATIONS



The imidazoles derivatives are widely used in clinical drugs to treat different types of illness [36]. The imidazole moiety shows the various kind of biological activities such as anti-inflammatory (cimicoxib (a), triphenyl imidazoles (b), bis-imidazoles (c)) [37a,b-39], anti-bacterial (porphyrin-metronidazole adducts (d), porphyrin-metronidazole adducts of triphenyl imidazole derivatives (e, f)) [38,40,41], anti-fungal (clotrimazole (g), eberconazole (h), oxiconazole (i)) [38,42] anti-cancer,(dacar-bazine (j), zoledronicacid (k),azathioprine (l)) [38, 43,44] & anti-parasitic (5-(1-methyl-5-nitro-1H-imidazole-2-yl),-1,3, 4- thiadiazol2amine (m), 4-nitro-1-(4-(trifluoromethoxy)phenyl)-1H-imidazole (n), nimorazole (o) [38,45] Someof the structure of biologically active imidazole compounds is shown below in Table 1. Apart from these biological activities, imidazole derivatives can also be used as dyes, polymerizing agents, and antioxidants [46]. The imidazole derivatives have also been used for the preparation of buffer solution with a pH range of 6.2–7.8 at room temperature [47]. These molecules are also used as herbicides, fungicides in plant growth [48] and chelating agents for the binding of various divalent cations.

V. CONCLUSION

- The new Schiff bases are synthesis from various aldehyde and amine under magnetic stirrer method & the Schiff base are solid and having sharp melting point.
- we have discussed all the pharmacological and biological activity such as the anti-cancer, antiinflammatory, the antiparasitic, anti-bacterial, and anti-fungal activity of the imidazolederivatives.
- Further, we have discussed the importance of imidazole scaffolds in various fields such as material sciences, natural product chemistry, industries, catalysis, medicinal, and agriculture fields. Finally, the different synthetic protocols for the synthesis of tri-substituted and tetra-substituted imidazole derivatives by one pot multicomponent reactions which are available in the literature have been presented .
- we have summarizes all the one-pot multicomponent synthesis of imidazole scaffold via the variable methods including conventional method, microwave-assisted synthesis, catalytic synthesis,
- The most common substrates for all of these methods are benzil, benzoin, α-diketone, aldehydes, ammonium acetate, imines, and various amines. Overall in this review summarized all the one-pot multicomponent reactions and other green methods for the synthesis of imidazole derivatives.

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