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Synthesis, Spectroscopic Characterization and Antimicrobial Activity of Imidazole Derivatives

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ABSTRACT

In this study, Substituted Imidazole is prepared from substituted aromatic aldehydes, Benzil and Ammonium Acetate using commercially available chitosan in 2% acetic acid in aqueous media at 65–70°C.Chitosan presence of Chitosan Catalyst. Imidazole ring is an important scaffold in many biologically important molecules. Green synthetic catalyst is used for the synthesis of imidazole. The structures of all synthesized compounds were chracterized by spectroscopic methods such as FT-IR, ^{1}H NMR, ^{13}C NMR and mass. Several methods of generating imidazole rings were reported and reviewed. In the recent past, synthesis of imidazole using metal-free conditions has become an important synthetic strategy. Compound showed an excellent antibacterial activity for all the tested bacterial and Fungal Strains

Keywords: Imidazole, Antimicrobial, Catalyst, Chitosan

I. INTRODUCTION

Natural polymers have recently been the subject of many studies for their application in catalysis. For example, chitosan has recently been used as a support for catalysis.[1-2] Chitosan is an abundant, biodegradable, and renewable green material with diverse functionalities. It is a valuable substance used prolifically in numerous applications, such as catalysis, adsorption, delivery of therapeutic agents, and remediation.[3] Datta, Reddy, and Zboril have assessed the application of polysaccharides for noble metal nanoparticles including a few examples about chitosan-based catalysts[4]. chitosan is a heteropolymer, structurally identical to cellulose, contains both glucosamine and acetylglucosamine units, and produced in huge quantities mainly from the shells of crustaceans. Because of its structural features together with its biocompatibility and biodegradability, it has a wide range of utilization possibilities [5]. Among many applications, its biomedical use (drug delivery, tissue engineering, regenerative medicine) is particularly abundant. A particular advantage is its easy transformation into varied physical forms (beads, fibers, mats, films, disks,

spheres, membranes, etc.), which enables a great flexibility in their conditioning. Its use in catalysis, in its own right and as support, is also prolific [6] There are a number of reviews with respect to the application of catalyst materials based on chitosan. In an early publication, Macquarrie and coworkers summarized results achieved with chitosan-based heterogeneous catalysts [7] characteristically, inorganic solid supports are coated with chitosan (also called a core– shell or yolk–shell structure) followed by modification with metal species. Alternatively, metal-loaded chitosan is mixed with the support material. Furthermore, in a number of cases, instrumental methods indicate the formation of a surface chitosan layer. Note, however, that for the sake of simplicity, such modified catalyst structures will be represented without a layer of chitosan. In fact, a rough surface is generated with a complicated morphology [8-9] The incorporation of imidazole nucleus, a biologically accepted pharmacophore in medicinal compounds, has made it versatile heterocyclic nucleus possessing wide spectrum of biological activities. Moreover, imidazole derivatives are structural isosters of naturally occurring nucleotides, which allows them to interact easily with the biopolymers of the living system which is responsible for their numerous biological activities and functions. In this study, we have made an attempt to collect biological properties of imidazole nucleus reported in the new millennium[10]

The incorporation of the imidazole nucleus is an important synthetic strategy in drug discovery. The high therapeutic properties of the imidazole related drugs have encouraged the medicinal chemists to synthesize a large number of novel chemotherapeutic agents. Imidazole drugs have broadened scope in remedying various dispositions in clinical medicines. Medicinal properties include anticancer and Antimicrobial activity [11] antidiabetic and antimalarial [12], all are unique characteristics known for imidazole derivatives.Kucukbay and other synthesized New benzimidazole, benzothiazole and imidazole derivatives were synthesized by reacting electron-rich olefins with appropriate reagents The compounds were found very effective to inhibit the growth of Enterococcus faecalis (ATCC 29212) and Staphylococcus aureus (ATCC 29213) at minimum inhibitory concentrations (MICs)[13]

The resistance of common pathogens to standard antibiotic therapies is rapidly becoming a major public health problem throughout the world. The incidence of multidrug-resistant gram-positive and gram-negative bacteria is increasing, and infections caused by Staphylococcus aureus and Salmonella typhi are particularly problematic[14] There is real perceived need for the discovery of new compounds endowed with antibacterial activity, possibly acting through mechanisms of action, which are distinct from those of well-known classes of antibacterial agents to which may clinically relevant pathogens are now resistant. Through the various molecules designed and synthesized for this aim, it was demonstrated that N-alkyl imidazoles could be considered as future antibacterial candidate.[15-17] Recently, we have reported that N-alkylimidazole with the most simple structure possess inhibitory effects on several pathogenic bacteria.15[18] new antibacterial compounds, we have synthesized some chloroaryloxyalkyl benzimidazole and imidazole derivatives. In view of realizing potential antibacterial activities of synthesized compounds, screening experiments were performed for two significant pathogenic bacteria, that is, S. typhi O-901 and S. aureus A 15091. [19]In continuation with our research program concerning the synthesis and antimicrobial evaluation of medicinally important compounds.

II. METHODS AND MATERIAL

An All the chemical of analytical grade. Benzil, 3-Chloro-4-methoxybenzaldehyde, Ammonium Acetate(Sigma-Aldrich) were purchased from Sigma-Aldrich and used without further purification. IR Spectra recorded on Perkin Elmer Spectrometer in range 4000-400 cm-1 KBr pellets. Room Temperature magnetic moments by Guoy's method in B.M.Electronic Spectra using DMSO on Varian Carry 5000 Spectrometer. Molar Conductance measurements in dry DMSO having 1×10-3 concentration on Systronics conductivity bridge at room temperature. Elemental analysis (C, H, N) were carried out by using perkin Elmer 2400 elemental analyzer.

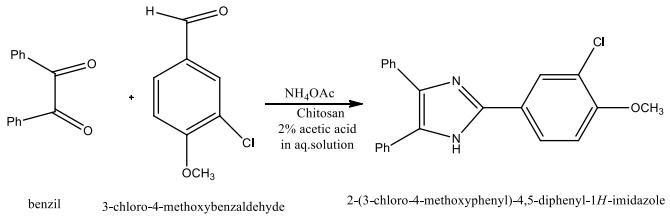
Antimicrobial Activity

2-(3-chloro-4-methoxyphenyl)-4,5-diphenyl-1H-imidazole was evaluated in vitro their antibacterial activity against two Gram-Positive bacteria,viz, *B. Subtilis*; *S. aureus,* Two fungal strains *A. niger* and *F. oxysporum* by Kirby-Bauer disc diffusion method [20].The experimental value compare with standard drug value Miconazole for the Antifungal activity and Ciprofloxacin for the antibacterial activity.

Synthesis of 2-(3-chloro-4-methoxyphenyl)-4,5-diphenyl-1H-imidazole

3-Chloro-4-methoxybenzaldehyde (0.30g, 2 mmol), benzil (0.42 g, 2 mmol) and ammonium acetate (0.32 g, 4.2 mmol) were added in a round-bottom flask with 0.09g of chitosan in 2% aq.acetic acid solution[21]. The reaction mixture was stirred a room temperature for 5 min.Then reaction mixture was heated at 65-70°C for 4 hr . The reaction was allowed to cool to room temperature. The resulting precipitate was collected by filtration and washed with cold ethanol to afford the product. The crude product was purified by recrystallization from ethanol (Scheme.1).

Scheme 1. Synthesis of Substitute imidazole

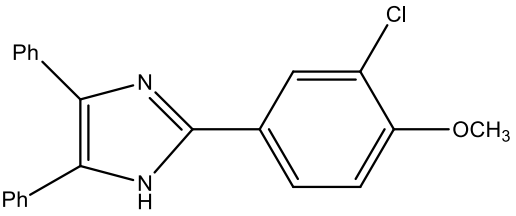


benzil 3-chloro-4-methoxybenzaldehyde 2-(3-chloro-4-methoxyphenyl)-4,5-diphenyl-1*H*-imidazole

III.RESULTS AND DISCUSSION

2-(3-chloro-4-methoxyphenyl)-4,5-diphenyl-1H-imidazole is prepared (Table.1).Imidazole is stable at room temperature in solid state. The Imidazole is soluble in organic solvent DMSO, DMF, The solid imidazole products, which separated out, were filtered, washed with water and dried. The crude products, thus isolated, were pure (single spot on TLC). After completion of the reactions, solid mass was filtered and the filtrate having chitosan catalyst was reused in the next run as such without any further treatment. Recycled chitosan catalyst was reused for 15 times. Acetic acid was used in this reaction only for homogenizing the chitosan catalyst and itself did not work as catalyst which has already been studied in experiment.

Table 1 : Proposed Structures of Subtituted Imidazole



2-(3-chloro-4-methoxyphenyl)-4,5-diphenyl-1H-imidazole

Chacterization of 2-(3-chloro-4-methoxyphenyl)-4,5-diphenyl-1H-imidazole

Yellow white Solid; $C_{22}H_{17}ClN_2O$,M.P.:126°C;Yield:95%; IR(KBr Cm^{-1}): 680 (C-Cl)1220,1642,2474,2884,3434; ^1H NMR (400

MHZ.DMSO d_6) δ ppm: δ1H NMR ($CDCl_3$/DMSO-d_6, 200 MHz) δ3.86(s,3H), 7.92 (s,1H), 7.36–7.56(m,10H), 7.84 (d,1H), 6.96 (d,1H),12.58 (s,1H); ^{13}C NMR($CDCl_3$/DMSO-d_6, 400 MHz) δ δ 56.2, ,124.5-132.6(Benzene),114.2-156.3,122.4 176.8(Imidazole) ; $C_{22}H_{17}ClN_2O$: calcd C, 73.23; H, 4.75;; N, 7.76; ,; found C, 72.36; H, 4.72; N, 7.68;

IR Spectra of 2-(3-chloro-4-methoxyphenyl)-4,5-diphenyl-1H-imidazole show peak at 3434 Cm^{-1} for imidazole ring nitrogen atom confirms the formation of Imidazole, peak at 680 Cm^{-1} due to C-Cl stretching in imidazole ring. Also different peak at 1220,1642,2474,2884 Cm^{-1} also suggest substituted imidazole compound is formed[22].^1H NMR Peak at δ 3.82 for s for 3H of methoxy group attached to aromatic ring, Aromatic ring peak observed in between range of δ 6.90–6.98(d, J=8.8 Hz,2H). δ 7.36–7.56 is m,for 10H of two phenyl ring proton. δ 12.58 is for 1H attached to nitrogen atom confirms the formation of imidazole. ^{13}C-NMR spectra of imidazole show peak at δ 56.2 for methoxy carbon attached to benzene ring,Aromatic carbon in benzene show peak in range between δ124.5-132.6 and imidazole ring carbon show peak in between range δ 114.2-176.8[23].Mass Spectra of Substituted imidazole shows peak at m/z 360.12 [M+H,100%], which is M+H peak at 100% intensity this peak support to the structure of the Imidazole. [24].

Antimicrobial Activity

The antimicrobial activity in vitro on selected two gram positive bacteria *S. aureus and B.Subtlis* two fungi *A. niger* and *F.Oxysporum* was carried out shown in table.2. 2-(3-chloro-4-methoxyphenyl)-4,5-diphenyl-1H-imidazole show substantial antimicrobial activity against bacteria S. aureus ,B.Subtlis and fungal species A. niger and F.Oxysporum. The results indicated that synthesized compound show good antibacterial and antifungal activity against all tested bacteria and Fungi.hence there was a strong correlation between the lipophilicity and the antimicrobial activity of investigated compounds[25].

Table 2. Antimicrobial activity of Imidazole

Compounds	Antibacterial Activity		Antifungal Activity	
	S.aureus	*B.subtilis*	*A.niger*	*F.oxysporum*
	Diameter of inhibition Zone in mm	Diameter of inhibition Zone in mm	Diameter of inhibition Zone in mm	Diameter of inhibition Zone in mm
	500 ppm	500 ppm	500 ppm	500 ppm
S.Imidazole	23	27	26	21
Ciprofloxacin (Standard)	34	33	----	----
Miconazole (Standard)	----	----	31	27

IV.CONCLUSION

Herein we are reporting the efficient method using inexpensive, biodegradable and environmental benign green Catalyst for the synthesis of imidazole. This method provides a better performance and higher product yield for aromatic aldehydes. Imidazole derivatives is the significant class of heterocyclic compounds, showed promising results in most of the pharmacological activities, and also has fascinating results including antibacterial, antifungal activities. It will be interesting to observe that in the future many new pharmacological profiles will be added to it as it is still unrevealed and can be taken as a lead for future development to get safer and more effective compounds.

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