International Journal of Scientific Research in Chemistry (IJSRCH)
© 2022 IJSRCH | Volume 7 | Issue 6 | ISSN : 2456-8457

Green Approach in the Synthesis of Substituted Imidazole

Ajay M. Patil[1*], Kailash R.Borude[2], Archana Kachare[3], Mahananda Raut[4]

[1*] Department of Chemistry, Pratishthan College Paithan, Aurangabad, India.

[2]Department of Chemistry,Katruwar arts Kabra Science College Manwath,Parbhani ,India.

[3]Department of Chemistry, Sunderrao Solanke Mahavidyalaya Majalgaon, Dist.-Beed India.

[4]Department of Chemistry, Pratishthan College Paithan, Aurangabad, India.

Article Info
Volume 7, Issue 6
Page Number : 07-12

Publication Issue :
November-December-2022

Article History
Accepted : 01 Dec 2022
Published : 18 Dec 2022

ABSTRACT

A convenient and rapid method is described for the synthesis of nitrogen heterocyclic derivatives by one-pot three component reaction of substituted aromatic aldehydes, Benzil and Ammonium Acetate using commercially available chitosan in 2% acetic acid in aqueous media at 60–65°C. Chitosan, as a biocompatible and biodegradable pseudo-natural polysaccharide is one of the excellent choices for the preparation of suitable catalytic systems due to its unique properties. Chitosan was used as an efficient biodegradable and reusable green catalyst for this multicomponent reaction. The chitosan catalyst can be reused 10 times in fresh reaction. Imidazole is a five-membered heterocyclic moiety that possesses three carbon, two nitrogen, four hydrogen atoms, and two double bonds. It is also known as 1, 3-diazoleAmong the different heterocyclic compounds, imidazole is better known due to its broad range of chemical and biological properties. Imidazole has become an important synthon in the development of new drugs.

Keywords: Imidazole, Chitosan, Green Catalyst, Polysaccharide

I. INTRODUCTION

Chitosan (CS) is an example of a polysaccharide that is widely distributed in living organisms [1]. Being hydrophilic and possessing basic moieties,1,2 chitosan is a particularly attractive polysaccharide for application in catalysis[2]. Chitosan (CS), as a *pseudo*-natural polysaccharide, is an excellent material for developing new types of green catalytic systems due to its fascinating and innately properties such as biodegradability, biocompatibility, renewability, non-toxicity, affordability, recyclability, stability to air and moisture, remarkable thermal and chemical stability, physiologically inertness, high surface area, the existence of numerous and accessible basic sites, insolubility in most of the organic solvents as well as aqueous reaction mediums (except in acidic aqueous solutions), and so on[3-5].

Catalytic applications of unmodified and modified chitosan have thoroughly and meticulously been investigated in the one-pot multi-component synthesis of diverse heterocyclic compounds, which were published approximately by the first quarter of 2020.

Notably, in this survey, only those researches in which the heterocyclization process has taken place in the reaction pot are covered. In other words, the mere presence of a heterocyclic framework in the final product structure has not been considered in this paper. Therefore, the one-pot synthesis of 4,4′ -(arylmethylene)bis(3-methyl-1-phenyl-1*H*-pyrazol-5-ol) derivatives [6] bis(indolyl)methanes (*viz.* 3,3′ -(phenylmethylene)bis(1*H*-indole) skeletons) [7], 3-hydroxy-3-indolyl-2-oxindoles[8] and many others, which were catalyzed by chitosan-based or chitosan-containing systems is prepared. A simple strategy for the green one-pot two-component synthesis of diverse oxygen- and nitrogen-containing heterocyclic frameworks using a catalytic amount of chitosan in water or ethanol at reflux conditions has described by Al-Matar and co-workers[9]. In 2013, Siddiqui and Khan developed an efficient one-pot two-component Friedl¨ander synthesis of some benzopyranopyridine derivatives through the solvent-free condensation of 4-amino-3-formylcoumarin and various active methylene compounds under conventional thermal heating at 80 ◦C in the presence of chitosan as a basic green heterogeneous catalyst in good-to-excellent yields[10].

Khan and Siddiqui have developed an eco-compatible and highly efficient procedure for the microwave-assisted one-pot multi-component synthesis of tri- and tetra-substituted imidazole derivatives from benzils using Chitosan-SO3H as a biodegradable solid acid catalyst in EtOH[11]. In 2015, Maleki and Paydar introduced Graphene oxide-Chitosan (GO-CS) nanocomposite as a biocompatible and biodegradable heterogeneous nanocatalyst for the green and efficient synthesis of 2,4,5- trisubstituted-1*H*-imidazoles using a simple solvent-free one-pot three-component reaction of benzoin or benzil, aromatic aldehydes, and ammonium acetate at 120 ◦C[12] the catalytic activity of the prepared Fe3O4@Chitosan NPs investigated in the convenient three-component synthesis of 2,4,5-trisubstituted imidazoles by a one-pot condensation of benzil derivatives, aryl aldehydes, and an excess amount of ammonium acetate (5 mmol) in EtOH at reflux in excellent yields[13].In recent years, diverse and efficient catalytic applications of chitosan in organic synthesis have been reported[14-17].pyridine and imidazole derivatives are bioactive compounds and have a large spectrum in biological, agricultural, and other activities synthesizing these molecules in an advanced yield, at mild conditions, and environmental benign approach is an utmost interest [18].

The present work reports the synthesis of 2-(4-methoxyphenyl)-4,5-diphenyl-1H-imidazole using chitosan as a biodegradable green catalyst in water as a green solvent.

II. METHODS AND MATERIAL

All the chemical of analytical grade. Benzil, 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

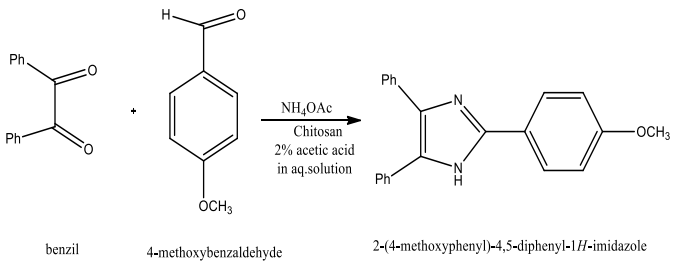
Antimicrobial Activity

2-(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[19].The experimental value compare with standard drug value Miconazole for the Antifungal activity and Ciprofloxacin for the antibacterial activity.

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

4-methoxybenzaldehyde (0.27 g, 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 0.08g of chitosan in 2% aq.acetic acid solution[20]. The reaction mixture was stirred a room temperature for 5 min.Then reaction mixture was heated at 60-65°C for 3 h. 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

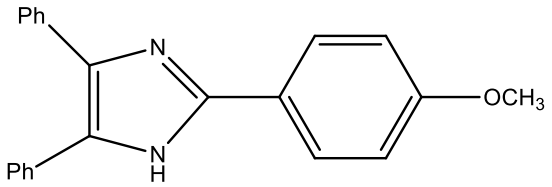


benzil 4-methoxybenzaldehyde 2-(4-methoxyphenyl)-4,5-diphenyl-1*H*-imidazole

III. RESULTS AND DISCUSSION

2-(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 10 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: Table 1: Proposed Structures of Subtituted Imidazole



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

1 Chacterization of 2-(4-methoxyphenyl)-4,5-diphenyl-1H-imidazole White Solid; $C_{22}H_{18}N_2O$,M.P.:96°C;Yield:96%; IR(KBr Cm^{-1}): 1218,1640,2475,2882,3432; ^1H NMR (400 MHZ.DMSO d_6) δ ppm: δ1H NMR ($CDCl_3$/DMSO-d_6, 200 MHz) δ 3.82(s,3H), 6.90–6.98(d, J=8.8 Hz,2H), 7.28–7.62(m,10H),8.04–8.08 (d, J= 8.8 Hz, 2H), 12.54 (brs, 1H); ^{13}C NMR($CDCl_3$/DMSO-d_6, 400 MHz) δ 54.8, 112.3, 121.9, 125.4,127.6, 127.5, 127.9, 133.7, 146.6, 158.2; $C_{22}H_{18}N_2O$:calcd C, 80.96, H, 5.56, N, 8.58; found C, 80.88, H, 5.42, N,8.42.

IR Spectra of 2-(4-methoxyphenyl)-4,5-diphenyl-1H-imidazole is show peak at 3432 Cm^{-1} for imidazole ring nitrogen atom confirms the formation of Imidazole also different peak also suggest at 1218,1640,2475,2882 Cm^{-1} imidazole compound is formed[21]. ^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 7.28–7.62 is m,for 10H of two phenyl ring proton. δ 12.54 is for 1H attached to nitrogen atom confirms the formation of imidazole. 13C-NMR spectra of imidazole show peak at δ 54.8 for methoxy carbon attached to benzene ring,Aromatic carbon attached to methoxy oxygen and imidazole ring carbon show peak in between range δ 112-147[22].Mass Spectra of imidazole shows peak at m/z 326.18 [M+H,100%], which is M+H peak at 100% intensity this peak support to the structure of the ligand.[23]

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.The substituted imidazole is having good antimicrobial activity [24].

Table 2. Antimicrobial activity of ligand and its Metal Complexes

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	24	26	28	22
Ciprofloxacin (Standard)	34	33	----	----
Miconazole (Standard)	----	----	31	27

IV. CONCLUSION

In conclusion, we have developed a mild, convenient and efficient protocol for the synthesis of biologically active Substituted imidazoles via the condensation of Benzil with aromatic aldehydes and ammonium acetate using a Chitosan as a recyclable medium as well as promoter. The process gives rise to excellent isolated yields of Substituted imidazoles in short reaction times this an environmentally benign methodology amenable for scale up.

V. ACKNOWLEDGEMENT

We are thankful to the Head of place of Research in C.I.F S.P.P.U Pune,S.A.I.F Panjab University, J.E.S College Jalna, Shivaji Arts, Commerce and Pratishthan Mahavidyalaya Paithan,Aurangabad India For their support.

VI. REFERENCES

[1] D.Elieh-Ali-Komi,&M. R. Hamblin,Chitin and chitosan: production and application of versatile biomedical nanomaterials,International journal of advanced research, 4,No.3,411,2016.

[2] M.Chtchigrovsky,A.Primo,P.Gonzalez,K.Molvinger,M.Robitzer,F.Quignard,&F.Taran,Functionalized chitosan as a green, recyclable, biopolymer-supported catalyst for the [3+ 2]Huisgen cycloaddition,Angewandte Chemie International Edition,48,No.32,5916-5920,2009.

[3] M. N. R.Kumar,A review of chitin and chitosan applications,Reactive and functional polymers,46,No.1, 1-27,2000.

[4] N.Anbu,S.Hariharan,&A.Dhakshinamoorthy,Knoevenagel-Doebner condensation promoted by chitosan as a reusable solid base catalyst,Molecular Catalysis, 484, 110744,2020.

[5] M. G.Dekamin, M.Azimoshan, & L. Ramezani,Chitosan: a highly efficient renewable and recoverable bio-polymer catalyst for the expeditious synthesis of α-amino nitriles and imines under mild conditions,Green Chemistry,15,No.3,811-820,2013.

[6] P. G.Patil, S.Sehlangia, & D. H.More,Chitosan-SO3H (CTSA) an efficient and biodegradable polymeric catalyst for the synthesis of 4, 4'-(arylmethylene) bis (1 H-pyrazol-5-ol) and α-amidoalkyl-β-naphthol's. Synthetic Communications,50,No.11, 1696-1711,2020.

[7] A.Kumar, C.Patel, P.Patil, S.Vyas, & A. Sharma,Chemoselective synthesis of bis (indolyl) methanes using sulfonic acid-functionalized chitosan. Chemical Papers,73, 3095-3104,2019.

[8] K.Rad-Moghadam, & N.Dehghan,Application of cellulose/chitosan grafted nano-magnetites as

efficient and recyclable catalysts for selective synthesis of 3-indolylindolin-2-ones,Journal of Molecular Catalysis A: Chemical, 392, 97-104,2014.

[9] H. M.Al-Matar, K. D.Khalil, H.Meier, H.Kolshorn, & M. H.Elnagdi,Chitosan as heterogeneous catalyst in Michael additions:The reaction of cinnamonitriles with active methylene moieties and phenols,Arkivoc,16,288-301,2008.

[10] Z. N.Siddiqui, & K.Khan,Friedlander synthesis of novel benzopyranopyridines in the presence of chitosan as heterogeneous, efficient and biodegradable catalyst under solvent-free conditions,New Journal of Chemistry,37,No.5,1595-1602,2013.

[11] K.,Khan, & Z. N.Siddiqui,An efficient synthesis of tri-and tetrasubstituted imidazoles from benzils using functionalized chitosan as biodegradable solid acid catalyst. Industrial & Engineering Chemistry Research,54,No.26,6611-6618,2015.

[12] A.Maleki, & R.Paydar,Graphene oxide–chitosan bionanocomposite:a highly efficient nanocatalyst for the one-pot three-component synthesis of trisubstituted imidazoles under solvent-free conditions. RSC advances,5,No.42,33177-33184,2015.

[13] M.Kalhor, Z.Zarnegar,Z.Seyedzade, &S. Banibairami,SO_3H-functionalized Zeolite-Y as an Efficient Nanocatalyst for the Synthesis of N-benzimidazole-2-aryl-4-thiazolidinones and tri-substituted Imidazoles,Current Organic Synthesis,17,No.2,117-130,2020.

[14] A.Molnar,The use of chitosan-based metal catalysts in organic transformations,Coordination Chemistry Reviews,388,126-171,2019.

[15] A.Dhakshinamoorthy,M.Jacob,N. S. Vignesh, &P. Varalakshmi,Pristine and modified chitosan as solid catalysts for catalysis and biodiesel production:A minireview,International Journal of Biological Macromolecules,167,807-833,2021.

[16] E. Guibal,Heterogeneous catalysis on chitosan-based materials: a review. Progress in polymer science,30,No.1,71-109,2005.

[17] A.ElKadib,Chitosan as a sustainable organocatalyst: a concise overview. ChemSusChem,8,No.2,217-244,2015.

[18] S. H.Gebre,Recent developments in the fabrication of magnetic nanoparticles for the synthesis of trisubstituted pyridines and imidazoles: A green approach. Synthetic Communications,51,No.11,1669-1699,2021.

[19] A.W.Bauer,D.M.Perry,and Kirby,"Single-Disk Antibiotic-Sensitivity Testing of Staphylococci: An Analysis of Technique and Results",AMA Arch Intern Med.,104,No.2,208–216,1959.

[20] P. K.Sahu, P. K. Sahu, S. K., Gupta, & D. D.Agarwal,Chitosan: An efficient, reusable, and biodegradable catalyst for green synthesis of heterocycles. Industrial & Engineering Chemistry Research,53,No.6,2085-2091,2014.

[21] J.,Simpson, S. K.Mohamed, A. A.Marzouk, A. H. Talybov, & A. A. Abdelhamid,2-(4-Methoxyphenyl)-1-pentyl-4, 5-diphenyl-1H-imidazole,Acta Crystallographica Section E: Structure Reports Online,69,No.1,o5-o6,2013.

[22] S. A.Siddiqui, U. C.Narkhede, S. S.Palimkar, T.Daniel, R. J.Lahoti, & K. V. Srinivasan, . Room temperature ionic liquid promoted improved and rapid synthesis of 2, 4, 5-triaryl imidazoles from aryl aldehydes and 1, 2-diketones or α-hydroxyketone. Tetrahedron,61,No.14,3539-3546,2005.

[23] M.Kidwai, P.Mothsra, V.Bansal, & R. Goyal,Efficient elemental iodine catalyzed one-pot synthesis of 2, 4, 5-triarylimidazoles. Monatshefte fur Chemie/Chemical Monthly,137,1189-1194,2006.

[24] C.Kucuk, S.Yurdakul, & B.Erdem, Experimental and theoretical Fourier transform infrared and

Raman spectroscopy, density functional theory, antibacterial activity and molecular docking studies on 1-(4-methoxyphenyl)-1H-imidazole. Chemical Papers,76,No.5,2833-2854,2022.

Suggested Citation :

Ajay M. Patil,Kailash R.Borude, Archana Kachare, Mahananda Raut, "Green Approach in the Synthesis of Substituted Imidazole", International Journal of Scientific Research in Chemistry (IJSRCH), ISSN : 2456-8457, Volume 7, Issue 6, pp.07-12, November-December.2022
URL : https://ijsrch.com/IJSRCH22763