ISSN 2278-8808 SJIF 2014 = 4.889
An International Peer Reviewed & Referred
SCHOLARLY RESEARCH JOURNAL
FOR INTERDISCIPLINARY STUDIES

DEVLOPMENT OF ECOFRIENDLY SYNTHETIC MTHOD FOR SYNTHESIS OF BIOLOGICALLY IMPORTANT IMIDAZOLE ANALOGUES

Ashok H. Dhamane

Abstract

Ultrasound assisted ecofriendly fast, solvent free and highly efficient method for the synthesis of substituted imidazole analogues has been reported. The method is principal and establishes oxalic acid as a catalyst, giving excellent yields in shooter reaction times these newly synthesized compounds were characterized using spectral techniques like IR and ^{1}H NMR. All the synthesized compounds, imidazole, antimicrobial activity, oxalic acid.

Keyword:- *Ultrasound, imidazole, antimicrobial activity, oxalic acid.*

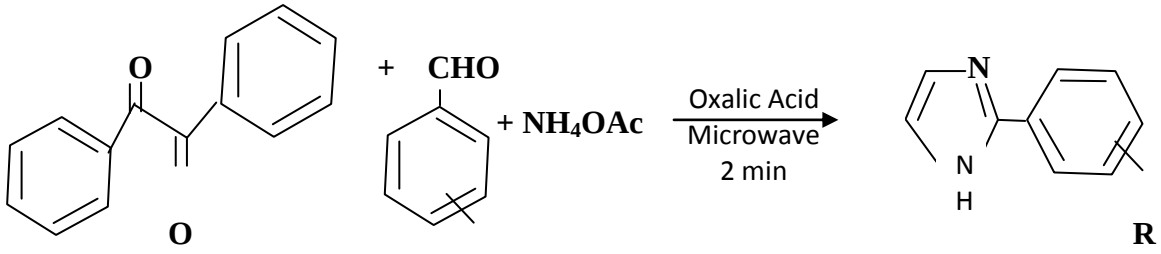
Introduction

Imidazole has received significant attention as a result of their diverse medical use. Imidazole derivatives are industrially important as they are associated with several biological and pharmacological properties. Imidazole moiety exhibit strong antifungal activity and is the core of drugs such as miconazole, econazole and oxiconazole. Compounds with an imidazoles moiety have biological activity it reduces the platelet in animal and human species. Triaryl imidazoles are use in photography as photosensitive compounds. They are of added interest because of their herbicidal, analgesic, antifungal and antithrombotic activity. Imidazole is an important heterocyclic molecule which is also studied for activities like anticancer, antibacterial, antioxidant. The synthesis of imidazoles were catalyst like AcOH, acidic Al_2O_3 HY/ silicagel, $ZrCl_4$, $NiCl_2$. $6H_2O$, iodine, Yb $(OTf)_3$, and iconic liquids. Hence we decided to devlop ultrasound assisted efficient and convenint method for synthesis of imidazoles analogues. We herein report the synthesis of imidazoles analogues catalyzed by oxalic acid as a nontoxic catalyst.

Result and discussion

The main aim of our research was focused on developing and establishing oxalic acid as a novel catalyst by employing it as a catalyst in ultrasound assisted multi component synthesis of imidazoles. Hence we attempted to improve the existing methods and developing mild, environment friendly protocol for the synthesis of highly substituted imidazoles scheme 1.

Scheme 1. Synthesis of the imidazole analogues (4a-h)



1 **2** **3** **4 a-h**

Initially, our investigation bagan for ultrasound assisted mild and facile synthesis of trisubstited imidazoles by employing the reaction of benzyl (1 mmol), benzaldehyde (1 mmol), ammonium acetate (4 mmol) with different seate of solvent in ultrasound. Solvent like ethnol gave (75% yield) methanol gave (65% yield), tetrahydrofuran gave (55% yield) while dichloromethane gave (62% yield). But surprisingly in solvent free condition we got 85% yield. Hence we carried out the synthesis of trisubbstituted imidazoles analogues under solvent free condition

Table 1. Ultrasound assiset and Oxalic acid catalyzed synthesis of trisubbstituted imidazole (4a-h).

Sr.no	Aldehyde	Time (sec)	Yield(%)	Melting Point (^{0}C)	
				Observed	Reported
4a	Benzaldehyde	100	85	271-273	270-272
4b	4-methoxy benzaldehyde	120	75	230-232	231-233
4c	2-naphthaldehyde	150	82	240-242	242-243
4d	4-choloro benzaldehyde	180	75	260-262	261-263
4e	4-methyl	180	75	232-234	233-236

	benzaldehyde				
4f	Furan-2-carbaldehyde	120	80	198-200	242-243
4g	Thiophene-2-carbaldehyde	150	80	261-263	260-262
4h	4-Nitro benzaldehyde	150	75	241-243	242-243

Antibacterial activity

Antibacterial activity of compounds was determined by using test solution and streptomycin having conc. 40mg/ ml and which were prepared in DMF. The paper disc (6mm) was immersed in seeded agar containing petri dish. The solution was dropped into the filter paper disc. The inhibition zone for each test solution was measured in mm. the synthesized compounds were tested for antibacterial activity as mentioned in (table2) against S. aureus, S. typhi and S. mutans, E. coli using streptomycin as a standard drug. Many of the synthesized compounds were found to show good antibacterial activity. From the antibacterial activity data (table2), it was observed that compounds 4f and 4g are the most active among the tested compounds against all the tested organisms.

Table2. Antibacterial activity of trisubstituted imidazole analogues (4a-h).

Zone of inhibition in mm					
		Gram + ve		**Gram – ve**	
Entry	**Concentration (mg/ml)**	**S. mutans**	**S. typhi**	**S. aureus**	**E. coli**
4a	20	17	15	12	14
	40	15	17	13	18
4b	20	11	13	12	11
	40	13	14	13	15
4c	20	15	13	11	14
	40	15	12	17	13
4d	20	11	14	12	15
	40	19	18	17	12
4e	20	13	15	12	14

	40	12	10	13	17
4f	20	12	15	14	13
	40	14	16	15	17
4g	20	13	13	11	12
	40	14	15	14	14
4h	20	12	11	12	16
	40	14	12	10	11
streptomycin	20	21	17	18	18
	40	23	22	21	21

Experimental section

All regents were purchased from sigma Aldrich. All synthesized compounds 4a-h were characterized with ^{1} NMR and mass. Ultrasonication was performed in an Ultrasonication was performed in an Ultrasonic bath sonicator of PCI analytics, having ultrasound cleaner with a frequency of 35 kHz and an nominal power of 200 w. whereas the melting point recorded were compared with the corresponding literature melting points and found to be matching with those in literature data. Progress of reaction was checked on TLC and melting points were determined in open capillary tubes and are uncorrected and were found to be in accordance with literature data. ^{1} NMR spectra were recorded on a 400 MHz bruker spectrometer as parts per million (ppm) downfield from a tetramethylsilane internal standard. The following abbreviations are used, singlet (s), doublet (d), triplet (t), quartet (q), multiplate (m) and broad (br). Mass spectra were taken with Micromass – QUATTRO-II of WATER mass spectrometer

General procedure for synthesis of 2, 4, 5- triary imidazole (4a-h).

In a 50 ml round bottom flask, benzyl (10mmol) ammonium acetate (40mmol) substituted aldehydes (10mmol) and oxalic acid (1mmol) were added and irradiated in ultrasound for mentioned time in table1. The progress of reaction was monitoried by TLC (20% Ethyl acetate: L n-hexane). After completion of the progress of the reaction, the reaction mixture with excess of water to get crude product the crude product was then recrystallized from ethanol to afford pure product in good yield (table 1).

Spectroscopic data of the synthesized compounds (4a-h)

2, 4, 5- triphenyl-1h-imidazole (4a) :

White Solid, Melting point: 271-273^{0}C

ES-MS m/z (%): 297 (M+6H).

[1] NMR (400 MHz, $CDCL_3$): PPM 7.15-8.17 (m, 15H), 12.17(s, 1H).

Reference

Lednicher, D. Drugs Based On Five-Membered Heterocycles. In Strategies For Organic Drug Synthesis And Design; Wily: New York, NY, 1998; Chapter 8, Pp 185-241.

Admas, J. L.; Boehm, J. C: Gallagher, T.F.; Kassis, S.; Webb, E.F.; Hall, R.; Sorenson, M.; Garigipati, R.; Griswold, D.E.; Lee, J.C. Bioorg. Med. Chem. Lett. 2001, 11, 28672870.

Wang, J. ; Mason, R.; Derveer, D. V.; Feng, K.; Bu, X.R.J. Org. Chem.. 2003, 68, 5415

Wolkenberg, S.E.; Wisnoski, D.D.; Leister, W.H.; Wang, Y.; Zhao, Z.; Lindsley, C.W. Org. Let. 2004, 6, 1453

Sparks, R.B.; Combs, A.P. Org. Let.2004, 6, 2473.

H.Zang, Q. Su, Y. Mo, B.Cheng, S. Jun, Ultrasound. Sonochem. 17 (2010) 749.

Shaabani, A,; Rahmati, A. J. Mol. Catal. A: Chem. 2006, 249, 246

Heravi, M.M.; Bakhtiari, K.: Oskooie, H.A.; Teheri, S.J. Mol. Catal. A: Chem. 2007, 263,279.

S. Demirayak, U. A. Mohsen, A.C. Karaburun, Eur.Jour. Med. Chem.37 (202) 255-260.

A.R. Martin, In Wilson And Gisvlod's Textbook Of Organic Medicinal And Pharmaceutical Chemistry, 10th Edition, 173 (1998).

M.J.Pelzar, "Microbiology", 5th Ed, Tata Mcgraw Hill Publication, 74, 75, 346.

V.V. Kale, P. K. Bhusari, Applied Microbiology", Ed 1st, Himalaya Publishing House, 58 (2001).

W.B. Hugo, A.D. Russell, Pharmaceutical Microbiology, 6th Edition, Blackwell Sci, Ltd, UK, 25, 130 (1998).