UGC MINOR RESEARCH PROJECT

Synthesis and characterization of potentially active compounds using green protocol

EXECUTIVE SUMMARY AND PAPER PUBLICATIONS

The present minor research project entitled **"synthesis and characterization of potentially active compounds using green protocol"** deals with synthesis of new N- benzoyl derivatives of amino acids, 1,3,4 oxadiazole and thiadiazole heterocyclic compounds using green protocols and evaluation of their biological activity. It is summarized as follows.

Objectives of project

The objectives of proposed work were

a) To synthesis new amino acid based heterocyclic compounds.
b) To design synthesis by using non conventional methods (green protocol).
c) Characterization of the new compounds.
d) To evaluate the biological activity of new compounds.

The progress of work has been according to original plan of work and towards achieving the objectives. We have synthesized the different N benzoyl derivatives from amino acids by using environmentally benign synthetic method resulting in high yield, less time . The new 1,3,4 oxadiazole derivatives were synthesised from N- benzoyl amino acids and hydrazides by using new methods . The 2,5 disubstituted 1,3,4 thiadiazoles containing Schiff's bases were synthesized from hydrazides and substituted aldehydes. The synthesized compounds were characterized with the help of sophisticated instruments like FTIR, H1NMR, LCMS spectrophotometers **.**Biological screening of the synthesized compounds were carried out. Most of compounds have shown wide range of antibacterial and antifungal activities.

Findings of project

In the search of novel heterocyclic molecules as well as novel environmentally benign synthetic methods, techniques or procedures following findings were observed.

In chapter I, we have concluded that the majority of *N*-benzoyl derivatives of amino acids can be possible to synthesis directly from the different amino acid and benzoyl chloride /p-methoxy benzoyl chlorides in one-pot syntheses. The procedure is simple addition. There is no need to acidify the reaction mixture in most of cases. This method has many advantages over the traditional methods. There is no need of protection, deprotection, or activation of group. The use of sodium bi carbonate and PEG 400 make it easy, inexpensive and simple. It avoids the formation of side product like substituted benzoic acid and ultimately increase yield.

In chapter II, it is found that CAN is a cheapest and readily available catalyst and highly efficient for the synthesis of new 2,5- disubstituted 1,3,4-oxadiazole derivatives. Moreover, PEG offers a convenient, inexpensive, non-ionic liquid, non-toxic, and recyclable reaction.

In chapter III, We have reported the novel synthesis of (1S)-2-(benzyloxy)-N-phenylmethylidene-1-[5-(pyridin-2-yl)-[1,3,4]-thiadiazol-2-yl] ethanamine derivatives containing [1,3,4]-thiadiazole ring. These were characterized by IR, Mass, ^{1}H NMR and ^{13}C NMR spectroscopic methods. The synthesized compounds **AP-1**to**AP-10** were evaluated for their biological activities against gram-positive, gram-negative bacteria's and different fungi *in-vitro*. The result reflected that most of synthesized compounds exhibit significant anti-microbial activities. Carbon diimidazole used as coupling reagent because of the byproduct imidazole is soluble in water to avoid the purification of compound –III.

Difficulties experienced while implementing project:

The date of sanction letter is considered as an effective date of starting project. date mentioned on sanction letter was 22 December 2016 but actual letter was received at college on 25 june 2017. Then chemicals were ordered towards suppliers. It took six months to receive chemicals. Actual work was started after june 2017 onward. The synthesis of compounds always requires more time than stipulated period framed in MRP due to different

experimental conditions, new methodology or new molecules. Further the total sanction grant amount of chemicals and glassware's should be released as a first installment because it is not possible to work even in absence of single chemical. That's why it will have to adjust number of times and inevitable for late submission.

Contribution to Society

The novel synthesis of heterocyclic compounds containing oxadiazole, thiadiazole, pyridine, pyrazole, schiffs base, thiazolidone nucleus using green protocol have attracted great attentions of medicinal and synthetic chemists. This is because they are used as significant pharmacophore for the treatment of tuberculosis, urinary tract infection, HIV, anxiety, depression, diabetes, cancer and many others disease. The green methods and techniques are useful to minimize environmental pollutions and their consequences. In recent years, there is a great bifocal challenge before scientists to minimize environmental problems as well as to design and develop alternatives methods and techniques to synthesis biologically important novel molecules. There is a severe human health problem due to modern and fast life style of human beings. The environmental pollution, many natural disasters, epidemic and pandemic virus diseases has threaten future generation on earth. The Ebola, swine flu , Corona cannot be controlled by any existing drugs. These types of biological disasters have urged medicinal scientists to search more efficient drugs which could prevent or cure these diseases and have minimum side effects. The bacteria and viruses which are responsible for infections undergo mutation in such a way that the existing drugs become tolerant against them.

Keeping in view, the importance of these compounds and innovative green protocols, we have planned to synthesis of new bioactive molecules containing such heterocycles and screening of their antibacterial activity.

1,3,4-Oxadiazoles are a important class of heterocycle which have attracted by many research scholars due to the significant activities in medicinal, pesticide, and polymer chemistry. The

oxadiazoles are important class of bioactive molecules which exhibit anti-inflammatory, anticonvulsant, antitubercular, anti-HIV activity. Schiff's bases are important starting materials for synthesis of bioactive heterocycles and possess wide variety of biological activity. Compounds containing [1,3,4] thiadiazole scaffold shows *in-vitro* anti-bacterial and antifungal activity. The Schiff bases containing [1, 3, 4]-thiadiazole ring shows tyrosine inhibitory activities.

The aim of present work was to develop a series of novel substituted N-benzoyl derivatives of amino acids, substituted 1,3,4 oxadiazole and schiffs bases containing thiadiazole, compounds by using green protocol. When reactions carried out by conventional methods, long reaction time was observed. To overcome these problems, new green catalysts and green solvents were utilized to reduce reaction time, pollution, and difficulties in reaction. The catalyst like CAN, CDI,were used in the present investigation. The use of green catalysts has received considerable attention in different areas of organic synthesis. The green solvent like PEG400 is used to minimize the environmental pollution. The compounds are synthesized and characterized in the entire work. The representative series of compounds were tested for antimicrobial activity. The result reflected that most of the synthesized compounds exhibit significant anti-microbial and antifungal activities. The remaining novel compounds may be forwarded to evaluate anticancer and antitubercular activities. The synthesized molecules might be used as a starting material for further synthesis by various researchers or lead molecule as a drug.

Moreover, it was engaged to develop and design innovative methods and techniques to synthesis bioactive molecules. The new methods and techniques were known while synthesizing compounds. It might be helpful to chemists for synthesis in future. The green solvent like PEG400 is used in new method. The catalysts like CAN, CDI, were used in this investigation to increase the yield and lower the time of reaction. The contribution of this

work will be helpful for the benefit of society. The two papers have been published in different online international journals and one is communicated to other international journal. This work may be useful to others as a reference work for future study. It has created benchmark to work in this direction. One of research fellow is enrolled for Ph D at me to extend this work.

PUBLICATIONS

	Title of Paper	**Nameof Journal**	**Name of Author**	**Impact Factor /Peer Reviewed/UGC CARE listed**	**Year of publication**
	Green Synthesis of 2, 5 substituted 1, 3, 4Oxadiazoles from N-Benzoyl Amino Acids.	Our Heritage ISSN: 0474-9030Vol-68, Special Issue-38 **one day national conference on recent advances in sciences.**	Magare B K	UGC CARE listed/peer reviewed National	**2020**
	An efficient synthesis of n- benzoyl derivative of amino acidsUsing PEG-400 as a green and recyclable catalyst	International Journal of Innovative Research in Science, Engineering and Technology Vol. 9, Issue 3, ISSN 2319-8753(online)	B. K. Magare[1*], D W Shinde[1]and M. B. Ubale[2]	Peer Reviewed Journal/International	2020
	Synthesis of Novel 2,disubstituted 1, 3, 4-thiadiazolebasedimine derivatives,their*In Vitro* anti-microbial evaluation and Molecular Docking Study	Synthetic comm	Amit Pund[a], ShwetaS Saboo[b], Gajanan MSonawane[c], AmolCDukale[d]andBab		Communicated Manuscript ID:

			anK Magare[a]*		LSYC 2020-14313; 3July2020

OUR HERITAGE
ISSN: 0474-9030Vol-68, Special Issue-38
ONE DAY NATIONAL CONFERENCE ON RECENT ADVANCES IN SCIENCES
Held on: 13th February 2020.
Organized by: Department of PHYSICS, CHEMISTRY, MATHEMATICS, BOTANY & ZOOLOGY Shivaji Arts, Commerce and Science College Kannad. Dist: Aurangabad (MS)

Green Synthesis of 2, 5 substituted 1, 3, 4 Oxadiazoles from N-Benzoyl Amino Acids.

Magare B. K.*

**Shivaji Arts, Commerce and Science College Kannad, Dist. Aurangabad (M.S.) India*

**Corresponding email: magarebk75@gmail.com*

Abstract

A simple and highly efficient protocol for the synthesis of 2, 5-disubstituted 1,3,4-oxadiazoles derivatives from various n- benzoyl derivative of amino acids with isoniazid and benzhydrazide in the presence of ceric ammonium nitrate(CAN) as catalyst in polyethylene glycol(PEG400) as a sustainable, recyclable, and eco-friendly medium has been used. This protocol is effective for various compounds of different functionalities. The easy and eco-friendly reaction with high yield and mild reaction conditions have shown advantageous over conventional reactions.

Keywords: 1,3,4-oxadiazole;Ceric Ammonium Nitrate (CAN); Polyethylene Glycol (PEG); Amino acids; Isoniazid.

Introduction

1,3,4-Oxadiazole have paramount role in pharmaceutical and biological activities. The 1,3,4-Oxadiazole is a heterocyclic precursor present in many drugs which are used as anti-inflammatory (1),anticonvulsant (2), and antibacterial drugs (3), antimitotic (4), antifungal (5),and muscle relaxant drugs (6). In view of the significant medical important, a number of synthetic routes have been developed for synthesis of 1,3,4-oxadiazoles (7,9). Many of these methods have demerits of expensive reagents, strong acidic conditions, tedious work up procedures, long reaction times and harsh experimental conditions that increase cost and generate large amounts of toxic waste. Hence the development of eco-friendly, simple, efficient, and cost effective synthetic protocol is inevitable and is a big challenge for chemists. Recently, cerium (IV) ammonium nitrate (CAN) has emerged as an significant reagent to build up carbon carbon and carbon heteroatom bonds (10,11). It has excellent solubility in water, high reactivity, fast conversions and convenient work up procedures. It is less expensive, ecofriendly, easy to handle, makes it a potent catalyst in organic synthesis. The most important catalytic property of CAN is that it catalyse organic reactions which is involved electron transfers and Lewis acidic property (12,14). The use of water as a solvent is probably the most desirable approach but this is often not possible due to the hydrophobic nature of reactants. The use organic solvents as media to provide a homogeneous phase which allows molecular interaction is efficient for completion of reaction. Besides these, the demand of green organic solvent to avoid environmental pollution makes researchers to develop alternative methods which are environmentally benign.

International Journal of Innovative Research in Science, Engineering and Technology (IJIRSET)

| e-ISSN: 2319-8753, p-ISSN: 2320-6710| www.ijirset.com | Impact Factor: 7.089|

||Volume 9, Issue 4, April 2020||

An Efficient Synthesis of N- Benzoyl Derivative of Amino Acids Using PEG-400 as A Green and Recyclable Catalyst

B K. Magare[1*], D W Shinde[1] and M. B. Ubale[2]

Associate Professor, Dept of Chemistry, Shivaji Arts, Commerce and Science College Kannad, Dist. Aurangabad, (M.S.) India[1]

Professor, Dept of Chemistry, Vasantrao Naik Mahavidhyalaya, Aurangabad, (M. S.)India[2]

ABSTRACT : A simple, highly efficient synthesis of N-benzoyl derivatives of amino acids using polyethylene glycol (PEG-400) as a green and recyclable catalyst is described. Our aim is to reduce and control the exothermic nature of this reaction and enhance the yield. This green synthetic approach is highly convenient and safe. The product was isolated with maximum yield (80%). PEG-400, a strongly hydrophilic catalyst can be recyclable for further reactions.

KEYWORDS: Amino acids, PEG 400, substituted benzoyl chloride, N-benzoyl derivatives.

I. INTRODUCTION

The benzoylation of amine and amino acids is well known method to identify, characterize the amines as well as to protect the amino functionality in a multistep synthetic process presented in[1-3]. In addition, the author [4] proposed benzoylation of amino group is used for resolution of amino acids. The N benzoyl derivatives of amino acids can be used as a precursor for various syntheses of potentially active heterocyclic compounds studied in [5-7]. Thus, the development of an efficient and convenient methodology is an important area of research.

There are many methods for preparation of N acyl derivatives of amino acids described in[8-14].The Schotten-Baumann methods [15-20]of benzoylation using benzoyl chloride has wide application and been more preferentially used. During this chemical transformation a smaller addition of sodium hydroxide in benzoyl chloride creates heat and sometimes product is not recovered in [21]. Although a number of reagents, such as benzoyl chloride, benzoic anhydride, benzoyl tetrazole and 2-benzoylthio-1-methylpyridinium chloride were used to carry out this reaction in[22-23].The benzoylation of amino acid by using benzoyl chloride (fischers procedure3 moles benzoyl chlorides per mole of amino acids) in presence of excess sodium bicarbonates was preferably followed[24-25]. Because sodium bicarbonate is a weak alkali facilitate the formation of salts with liberation of carbon dioxide. Further, it was found that the aqueous sodium bicarbonate is non-carcinogenic and more advantageous. It has no hygroscopic characteristic, stability at a wide temperature range, non inflammable, non-volatile, economic, noncorrosive, eco-compatible and devoid of toxic effects. However, the net reaction time and yield of product had been compromised. The benzoyl derivatives so obtained frequently occlude unreacted benzoyl chloride which escapes hydrolysis and poses difficulty in isolating the product. Moreover, to obtain the benzoyl derivative of amino acids, the usual Schotten-Baumann method requires longer reaction time and tedious work-up. The amino acids forms zwitterion ion which make them quite insoluble in organic solvents which make it difficult to synthesis N-acyl derivatives of amino acids rather than the synthesis of simple aliphatic and aromatic amines. Though, there are many methods which are currently used for the preparation of *N*-acyl derivatives of amino acids and peptides, involve number of steps due to protection and deprotection of carboxylic group of the amino acid.
Considering the importance of benzoylation of amino acids and environmental hazards in the reaction, we have reported the green synthetic approach using PEG400 as a green solvent and catalyst.

II. EXPERIMENTAL METHODS

All reagents purchased were A.R. grade without further purification. The FTIR spectra were recorded as KBr pellets on Shimadzu Spectrophotometer. Thin layer chromatography (TLC) were performed on 0.2 mm silica gel 60 F254 with plastic support from Aldrich by using various proportion of ethyl acetate and n-hexane as the solvent. ^{1}HNMR were

MAGARE B. K (Principal Investigator)
Dept of chemistry