WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 9, Issue 4, 791-799. Research Article ISSN 2277– 7105

SYNTHESIS AND EVALUATION OF SOME NOVEL OXADIAZOLE DERIVATIVES

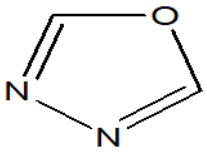
Teja Kumar Reddy Konatham* and K. Ashok Babu

Department of Harmaceutical Chemistry, Osmania University, Hyderabad, Telangana.

Article Received on
28 Jan. 2020,
Revised on 18 Feb. 2020,
Accepted on 10 March 2020
DOI: 10.20959/wjpr20204-17019

***Corresponding Author**
Teja Kumar Reddy Konatham
Department of Harmaceutical Chemistry, Osmania University, Hyderabad, Telangana.

OXADIAZOLES

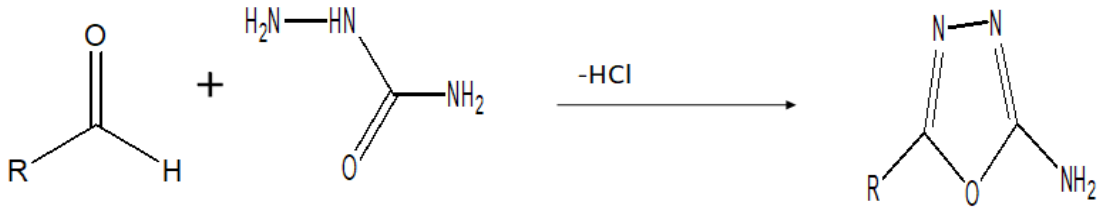


1,3,4-oxadiazole

IUPAC NAME	:	1, 3, 4-oxadiazole
MOLECULAR FORMULA	:	$C_2H_2N_2O$
MOLECULAR MASS	:	70.051 gm. Mol^{-1}
MELTING POINT	:	$34\text{-}35^0$
SOLUBILITY	:	Soluble in water

PREPARATION OF OXADIAZOLES

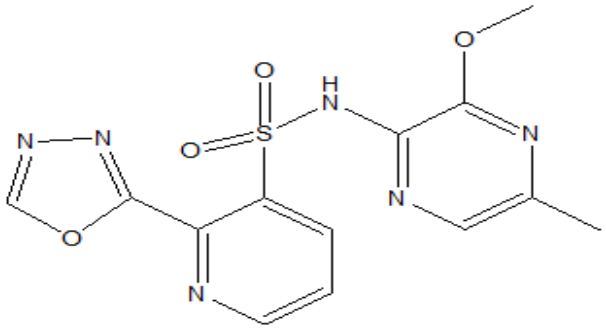
A transition-metal-free condensation of Semicarbamazide /thiosemicarbamazide with aldehydes followed by I_2-meditred oxidative C-O/C-S bond formation provides 2-amino-substituted 1,3,4-oxadiazoles in an efficient and scalable fashion.



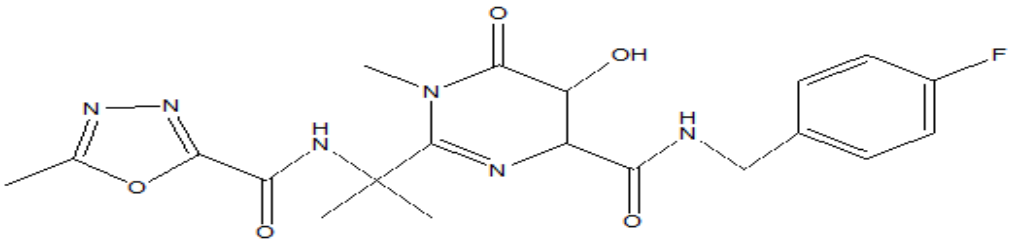
Some Marketed Preparations Having Oxadiazole Nucleus

In drug discovery and development, a number of compounds containing an oxadiazole moiety are in late stage clinical trials including Zibotentan (162) as an anticancer agent and Ataluren(163) for the treatment of cystic fibrosis. Raltegravi (164)r, one oxadiazole

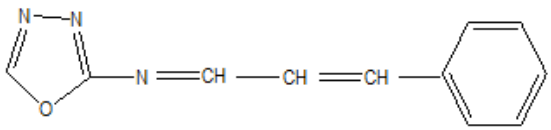
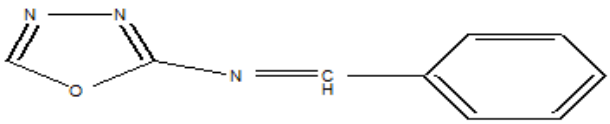
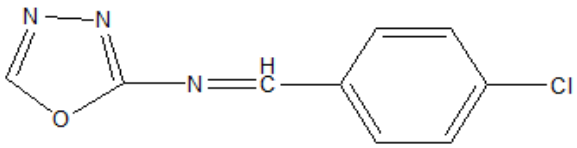
containing compound is an antiretroviral drug for the treatment of HIV infection, has been launched onto the market place



Zibotentan (anticancer drug)



Raltegravir(antiviral drug)

COMPOUND NAME	STRUCTURE AND IUPAC NAME
S1	 3-Phenyl allylidiene 1,3,4 oxadiazole
S2	 *N-Benzylidene-1,3,4-oxadiazole*
S3	 4-Chloro benzylidine 1,3,4 oxadiazle

EXPERIMENTAL WORKS

Materials and Methods

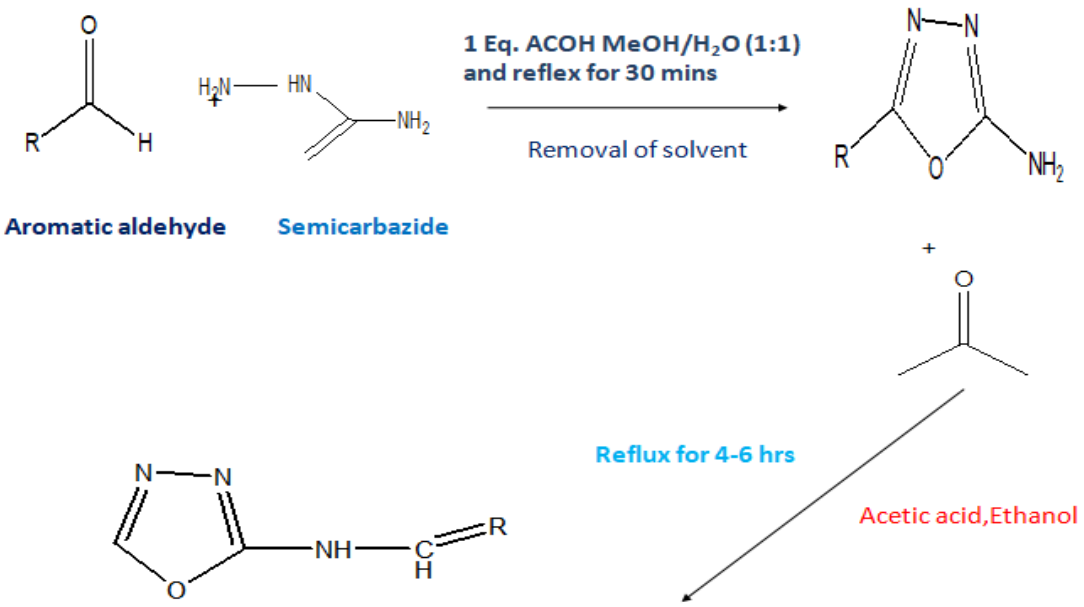
The melting range of the substituted compounds were performed by LAB-INDIA MS-VISUAL melting point apparatus and is uncorrected. The IR spectrum studies of the

synthesized compounds were recorded and Pressed pellet technique.IR spectra was recorded in KBR press (shimadzu).

CHEMICALS AND REAGENTS

Benzaldehyde, Semicarbazide Hydrochloride, Acetone, Methanol, Benzene, Silica gel, Distilled water.

SCHEME OF WORK



SYNTHETIC METHODS

General Procedure for Synthesis of Oxadiazoles

Step 1: Synthesis of 2-Amino Substituted 1,3,4 Oxadiazole

Take 0.1 mol of aromatic aldehydes and add Semicarbazide of 0.1 mol was taken in a 250ml round bottomed flask and add MeOH / H2O in 1:1 ratio to the reaction mixture and reflex it for 30 minutes. Then the solvent was removed and add K_2CO_3 and Dioxane then reflux it for 3 hours and the resultant mixture is cooled rapidly with ice cold water and precipitate formed is filtered and recrystallized using Ethanol.

Step 2: Synthesis of 3-Phenylallylidiene 1,3,4 Oxadiazole 2-Amine

Take 0.1 mol of Cinnamaldehyde and add 2-amino substituted 1,3,4 oxadiazole of 0.1 mol was taken in a 250ml round bottomed flask and add Acetic acid and Ethanol to the reaction mixture and reflex it for 30 minutes then the solution was cooled rapidly with crushed ice cold water and precipitate formed is filtered and recrystallized using Ethanol.

MELTING POINT- 180^0C.

Synthesis of Benzylidine 1,3,4 Ozadiazole

Take 0.1 mol of Benzaldehyde and add 2 –amino substituted 1,3,4 oxadiazole 0.1 mol was taken in a 250ml round bottomed flask and add Acetic acid and Ethanol to the reaction mixture and reflex it for 30 minutes then the solution was cooled rapidly with crushed ice cold water and precipitate formed is filtered and recrystallized using Ethanol. MELTING POINT-170^{0}C

Synthesis of 4-Chloro Benzylidine 1,3,4 Oxadiazole

Take 0.1 mol of 4-Chloro Benzaldehyde and add 2 –amino substituted 1,3,4 oxadiazole of 0.1 mol was taken in a 250ml round bottomed flask and add Acetic acid and Ethanol to the reaction mixture and reflex it for 30 minutes then the solution was cooled rapidly with crushed ice cold water and precipitate formed is filtered and recrystallized using Ethanol. MELTING POINT-220^{0}C

Thin Layer Chromatography

Thin layer chromatography is a solid-liquid form of chromatography here the stationary phase is a polar adsorbent and the mobile phase can be single solvent or combination of solvents.

4.4.1.1 MATERIAS AND METHODS

Preparation of plates

Silica gel G was mixed in a glass motor to smooth consistence with requisite amount of water and slurry was quickly transferred to a spreader. The mixtures have been spread over the plates in thickness of 0.2mm allow setting into a suitable holder and after minutes, plates were dried at120^0 for further activation of the adsorbent.

Sample application

About 2mm of adsorbent from the edge of the plate was removed to give sharply defined edges.2-5µ l volumes of synthesized compounds were spotted with the help of capillary tubes, just above 1cm from the bottom of coated plates.

SPECTRAL STUDY OF SYNTHESIZED COMPOUNDS

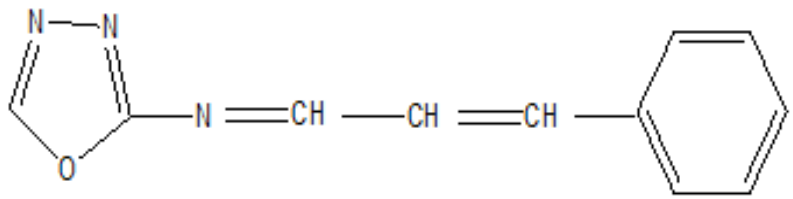
Ir Study

The IR spectral studies of synthesized compounds were obtained by pressed-pellet technique. IR spectrums were recorded in KBR disc n FTIR 8300(shimadzu) spectrometer.

Physico-Chemical data of synthesized compounds

All the 3 compounds (S1 to S3) were synthesized by followed above the procedure and their Physico-chemical and spectral data has given as follows

COMPOUND ID S1



3-Phenyl allylidiene 1,3,4 oxadiazole

Molecular formula : $C_{11}H_{10}N_3O$

Molecular weight : 200 gms

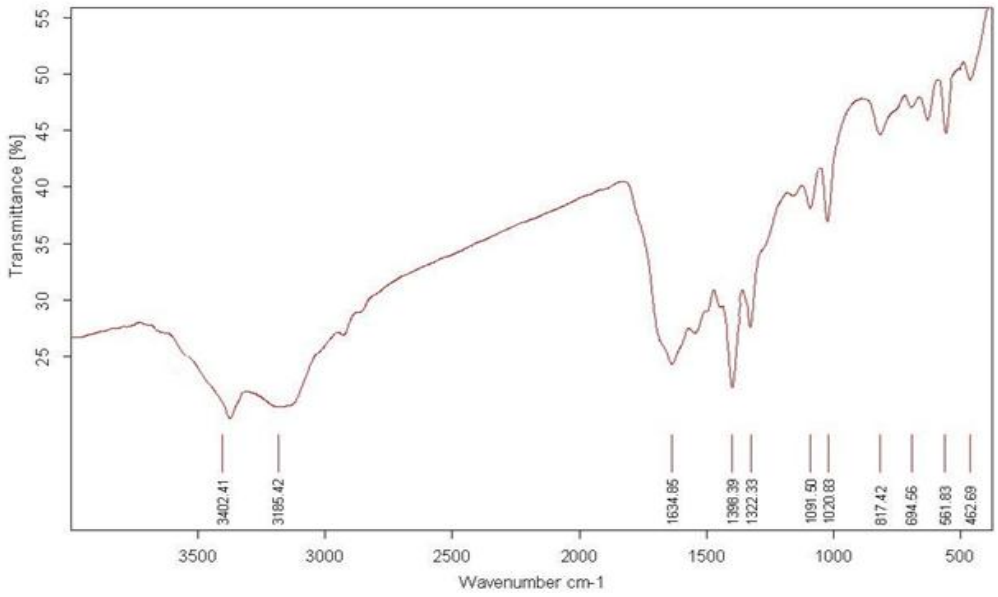
Melting point : 180^0C

Percentage of yield : 55.75%

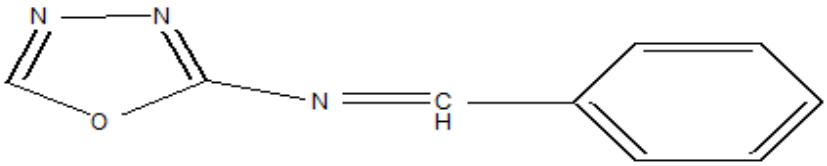
T.L.C RF (solvent) : Methanol: Benzene (6:4)

GROUP	RANGE (cm^{-1})
Ar-CH	3185.2
C=C	1634.85
N=C	1634.85
N-N	1398.39
C-O-C	1322.33

COMPOUND ID S1



COMPOUND ID S2



N-Benzylidene-1,3,4-oxadiazole

Molecular formula : $C_9H_8N_3O$

Molecular weight : 174gms

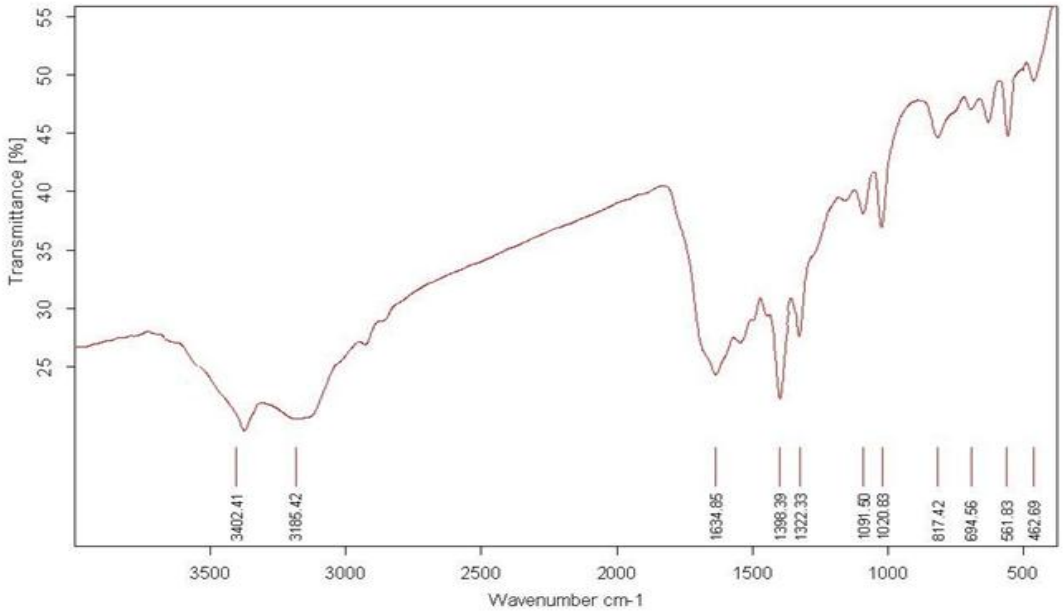
Melting point : 170^0C

Percentage of yield : 47.701%

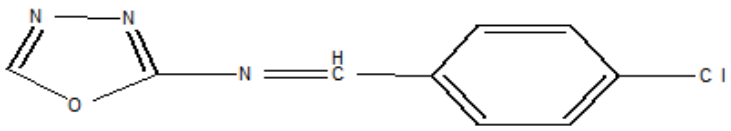
T.L.C Rf (solvent) : Methanol: Benzene (6:4)

GROUP	RANGE (cm^{-1})
Ar-CH	3151.42
N=C	1630.96
N-N	1251.90
C-O-C	1400.97

COMPOUND ID S2



COMPOUND ID 3



4-Chloro benzylidine 1,3,4 oxadiazle

Molecular formula : $C_9H_9N_3O_2Cl$

Molecular weight : 226

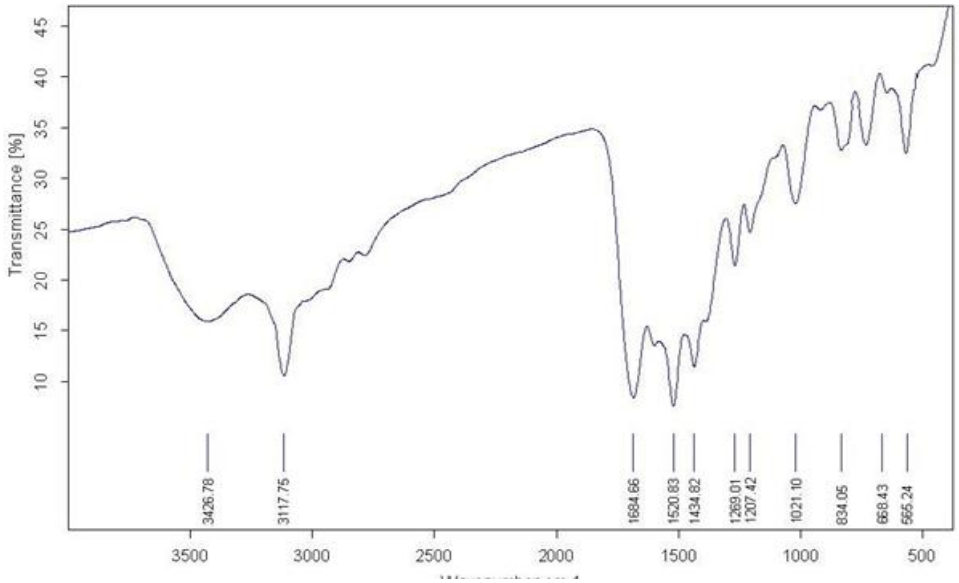
Melting point : 220^0C

Percentage of yield : 62.13%

T.L.C Rf (solvent: Methanol: Benzene (6:4)

GROUP	RANGE (cm^{-1})
Ar-CH	3117.75
N=C	1684.66
N-N	1269.01
C-O-C	1434.82
c-cl	834.05

COMPOUND ID 3



EVALUATION OF ANTI MICROBIAL ACTIVITY

5.1. Introduction

The microbial word comprises of microorganisms, which are microscopic in size but these microscopic organisms have several features that are common to high organisms bacteria (yeast and moulds) and microscopic algae are some of the microorganisms. These organisms can be distinguished in to two broad groups of prokaryotes and eukaryotes. The following conditions must be accomplished for the determination of proper antimicrobial activity.

1. There should be intimate contact between the test organism and substance.
2. Micro organisms should provided with the required conditions for growth.
3. Measurement of activity should be maintained.
4. Conditions should be maintained unchanged throughout the study.

MATERIALS AND METHODS

Various methods with their own advantages and limitations have been used from time to time to evaluate the anti-microbial activity of the drugs.

1. Agar diffusion method.

a. cup plate method

b. Cylinder method

c. Paper disc method

STANDARD DRUG

Amino Pencillin

AMINO PENICILLIN has activity against gram-positive and gram-negative aerobic and anaerobic bacteria. The bactericidal activity of amino penicillin results from the inhibition of cell wall synthesis and is mediated through amino penicillin to penicillin binding proteins (PBPs). Amino penicillin is a stable against hydrolysis by a variety of beta-lactamases, including penicillinases and cephalosporin and extended spectrum beta-lactamases.

Amoxicillin

AMOXICILLIN is considered a third generation or amino penicillin and is one of the most commonly prescribed antibiotics amoxicillin and other amino penicillin have been linked with idiosyncratic liver injury, but only rarely and in isolated case reports.

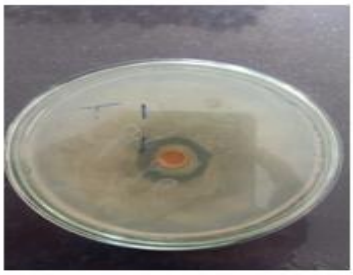
5.3. Preliminary Screening of Antimicrobial Activity

The sterilized medium (autoclaved at 121^0C for 20mins) was inoculated using 18hr slant cultures of the test organisms and transferred in to a sterile Petri dishes and allowed to solidify the media. Cups of 8mm diameters were made to solidify the media.

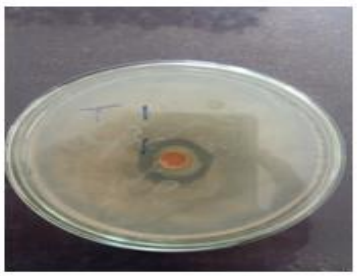
- Solutions of the synthesized compounds at a concentration of 1mg/ml were prepared in DMSO and 50µl of each solution was placed in the cups by means of sterile pipette.
- In each 1 cup was used as control with DMSO and other for standard. The plates thus prepared were left for 90mins in a refrigerator for diffusion.
- The plates were incubated at 37^0C for 24 and 48hrs for antibacterial activities, respectively and examined for inhibition zones.
- The experiment was performed in duplicate and the average diameter of the zones of inhibition was recorded in the table Amino penicillin (1µg/ml) is used as standard for antibacterial activity.

COMPOUNDS	ZONE OF INHIBITION (in mm)			
	BACTERIA			
	S.aureus	B.substalis	P.argenosa	E.coli
	Concentrations(Mg/ml^{-1})			
	50µg/ml	50µg/ml	50µg/ml	50µg/ml
S1	19	10	11	10
S2	18	12	14	10
S3	19	11	12	12
Aminopenicillin ($100µg/ml^{-1}$)	28	31	25	28
Control	--	--	--	--

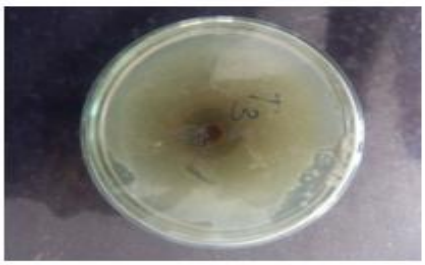
Anti microbial activity against E.coli



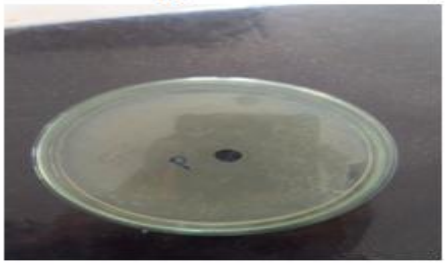
S1



S2



S3



Aminopencillin

RESULTS AND DISCUSSION

The synthesized compounds were screened for anti microbial activity by cup plate method. From the data shown in above table the observation were made as follows.

Most of the synthesized compounds exhibit moderate to good antimicrobial activity against the tested organisms.

When compared to standard drug (amino penicillin for anti bacterial) compounds S1 and S2 were found to exhibit moderate anti bacterial activity.