www.sphinxsai.com

ChemTech

International Journal of ChemTech Research
CODEN(USA): IJCRGG ISSN : 0974-4290
Vol.2, No.2, pp 1094-1096, April-June 2010

Synthesis and Biological Evaluation of 2, 5-Disubstituted-1, 3, 4 - Oxadiazoles

B.C.Revanasiddappa*, E.V.S.Subrahmanyam[1]

***Department of Pharmaceutical Chemistry, NGSM Institute of Pharmaceutical Sciences, Paneer, Deralakatee-574160, Mangalore, Karnataka, India**

[1]Department of Pharmaceutical Chemistry, Srinivasa College of Pharmacy, Valachill-574 143, Mangalore, Karnataka, India

Corres. author: evergreen_revan@rediffmail.com
Tel. No. : +91-0824-2203991-93
Fax No. : +91- 0824-2203992

ABSTRACT: A new series of 2, 5-disubstituted-1, 3, 4-oxadiazoles were prepared by reaction of nicotinic acid hydrazide with various substituted aromatic acids in presence of $POCl_3$, as potential biological active agents. The newly synthesized compounds were confirmed from IR, MASS and ^1H NMR spectral data. Some of the synthesized compounds showed very good antifungal activity when compared to antibacterial activity.
Key words: 1, 3, 4-oxadiazoles, 2, 5-disubstituted-1, 3, 4-oxadiazoles, Anti bacterial and Anti fungal activity.

INTRODUCTION

1, 3, 4-oxadiazoles are biologically active, synthetically useful and important heterocyclic compounds. Various biological activities are reported to be associated with 1, 3, 4-oxadiazoles like antibacterial[1], antifungal[2], herbicidal[3], anti-inflammatory[4] etc., Similarly 2,5-Disubstituted-1,3,4-oxadiazole derivatives possess broad spectrum of activities like antifungal[5], anticonvulsant[6] anticancer[7] etc., Encouraged by these reports the present study has been undertaken.

The starting material, Pyridine-3-carboxylic acid ethyl ester was prepared by the esterification of Pyridine-3-carboxylic acid with absolute ethanol in presence of conc. H_2SO_4. Pyridine-3-carboxylic acid hydrazide was prepared by the condensation of hydrazine hydrate with the ester in presence of alcohol. This hydrazide was condensed with various substituted aromatic acids in presence of $POCl_3$ to yield the title compounds. The sequence of reactions is as shown in **Scheme-1.**

EXPERIMENTAL

Melting points were determined using open capillary tube method and are uncorrected. Thin layer chromatography [silica gel G (E.Merck) plates] was used to monitor the reactions and purity of the newly synthesized compounds. IR spectra were recorded using KBr disk on a Shimadzu Perkin-Elmer 8201 FT-IR. The PMR spectra were recorded on BRUKER AVANCE II 400 NMR SPECTROMETER in $CDCl_3$ and DMSO-d_6 using TMS as internal reference. The FAB mass spectra were recorded on JEOL SX-102/DA-6000 Mass spectrometer operating at 70ev.

Synthesis of pyridyl-3-carbohydrazide[8]

A mixture of Pyridine-3-carboxylic acid ethyl ester[8] (0.1 mol), and hydrazine hydrate (99%) (0.1 mol), in absolute alcohol (50ml) was refluxed for about 4hrs. The excess of solvent was removed and the residue was poured into ice cold water (125ml). The solid which is obtained was recrystallized from ethanol to get white crystalline product. Yield-82%, Mp 162

^{O}C, IR (KBr): 1612 (C=N), 1670(C=O), 3048 (-CH of pyridyl).

General procedure for the synthesis of 2-aryl-5-pyridyl-1, 3, 4-oxadiazoles

A mixture of nicotinic hydrazide [0.01mol] and various aromatic acids [0.01mol] in presence of $POCl_3$ [8ml] were refluxed for 8-14hrs in an oil bath. The contents were cooled and poured into crushed ice. It was neutralized with $NaHCO_3$ solution and the resulting solid was filtered, dried and recrystallized from ethanol.

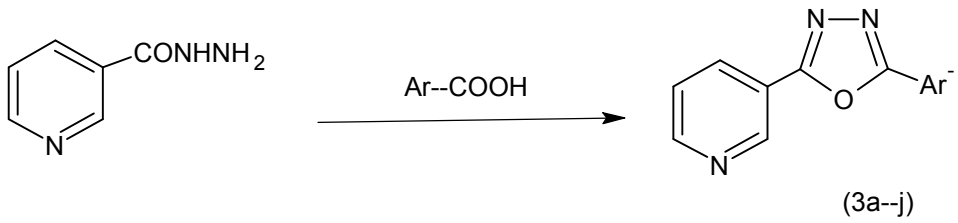
3a: IR (KBr): 3058 (C-H), 1575 (C=C), 1670 (C=N), 1069 (C-O-C) **^{1}H NMR (DMSO-d_6)**: 7.6-9.3 (m, Ar-H, 9H) **Mass:** M/Z= 223[M^+].
3d: IR (KBr): 1621(C=N), 1534 & 1312 NO_2, 1555 (C=C), 3087(C-H), 1073 (C-O-C). **^{1}H NMR (DMSO-d_6)**: 7.2-9.2 (m, Ar-H, 6H), 9.15 (s, 1H, OH). **Mass:** M/Z= 329[M^+].
3e: IR (KBr):1642 (C=N), 1553 & 1343 NO_2, 1083 (C-O-C) **^{1}H NMR (DMSO-d_6)**: 7.6-8.6 (m, Ar-H, 4H) of pyridyl ring, 8.2-8.8 (d, Ar-H, 4H) of phenyl ring. **Mass:** M/Z= 268[M^+].

Similarly other derivatives **(3a-3j)** were synthesized and their physical data is given in table-1

Antibacterial and Antifungal activity

Ten compounds from the series were screened for their antibacterial and antifungal activity. Antibacterial activity was carried out against *S.aureus, P.aeruginosa, E.coli* and *B.subtilis* by the cup plate method[9] at a conc. of 100 µg/ml (table-2). The standard drug used was Ampicillin and DMF was kept as solvent control. The antifungal studies were carried out against fungus *C.albicans* and *A.niger* using Griseofulvin as standard. When compared to antibacterial activity, most of the compounds showed very good antifungal activity.

Scheme-1



(3a--j)

Table-1: Physical data of 2-aryl-5-pyridyl-1, 3, 4-oxadiazoles (3a-j)

Comp	Ar-COOH	MP (^{O}C)	Yield (%)
3a	Benzoic acid	112	62
3b	Salicylic acid	176	54
3c	Phenyl acetic acid	160	48
3d	3,5-dinitrosalicyclic acid	180	70
3e	p-nitro Benzoic acid	105	68
3f	p-chloro Benzoic acid	148	61
3g	p-hydroxy Benzoic acid	190	70
3h	o-amino Benzoic acid	166	74
3i	p-amino Benzoic acid	122	69
3j	Gallic acid	198	55

Table-2: Antimicrobial activity of the synthesized compounds (3a-j)

Comp.	Diameter of zone of inhibition (mm)					
	S.aureus	***B.subtitis***	***E.coli***	***P.aeruginosa***	***C.albicans***	***A.niger***
3a	09	11	12	13	13	14
3b	11	09	11	15	14	15
3c	13	08	10	12	14	11
3d	11	12	14	12	15	14
3e	12	14	09	15	14	16
3f	08	14	08	15	15	12
3g	10	07	08	09	13	14
3h	12	12	13	14	15	15
3i	09	10	11	07	14	16
3j	15	14	13	14	15	13
Ampicillin	21	22	22	21	-	
Gresiofulvin	-	-	-	-	22	21

RESULTS AND DISCUSSION

Compounds 3d, 3e, 3h, 3j exhibited greater inhibition against both gram positive and gram negative organisms. Similarly compounds 3a, 3b, 3c showed moderate inhibition against ***E.coli*** and ***P.aeruginosa.***

The antifungal activity shows slighty greater inhibition (13-16) when compared to the antibacterial activity. All the ten compounds showed very good inhibition against both the fungal organisms. It is observed that compounds 3b, 3d, 3e, 3h, and 3i showed very good antifungal activity.

Acknowledgement

The authors are thankful to NITTE Education Trust for providing the necessary facilities. The authors are also grateful to the Directors, RSIC, Chandigarh and CDRI, Luck now for providing IR, NMR and Mass spectra respectively.

REFERENCES

1. Jain S, and Mishra P, *Indian J.Heterocyclic Chem.*, **13,** 307, (2004).
2. Googi PC and Kataky JCS, *Indian J.Chem,* **29B**, 1159, (1990).
3. Ram VJ, and Pandey HN, *Eur.J.Med.Chem,* **25,** 541, (1990).
4. Misra U, Hikari A, Saxena AK, Gurtu S and Shanker K *Eur.J.Med.Chem.,* **31,** 819, (1996).
5. Adams SS, Cliffe EE, Lessel B and Nicholoson JS, *J. Pharm. Sci*, **56**, 1986, (1967).
6. Omar A, Mohsen ME, and Aboul WOM, *J. Heterocycl. Chem,* **21**, 1415, (1984).
7. Bhat KS, Karthikeyan MS, Holla BS and Shetty NS, *Indian J.Chem.* **43B,** 1765, (1984).
8. Furniss BS, Hannford AJ, Smith PWG, Tatchell AR, *Vogel's text book of practical organic chemistry* **5th edn** Singapore Pearson education 2000, (2005).
9. Cruickshank R, Duguid JP, Marmoin BP and Swan HA, *The Practice of Medical Microbiology, Vol 2,* **12th edn,** Churchill Livingstone, London 190, (1975).

*****