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ADVANCES IN THE SYNTHESIS AND BIOLOGICAL EVALVATION OF SOME NOVEL DERIVATIVES OF PYRIDINE

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ABSTRACT

We have chosen molecule having moieties possessing antimicrobial activity of pyridine has been derived from benzene and its structure might be obtained by replacing a -CH moiety with a nitrogen atom. Which is reported to have antibacterial and anti-tubercular activity and other pyridine ring attached to fourth position of the benzene ring which possesses the antibacterial activity Present work deals with the preparation of pyridine 3-carboxylic acid in ethanol and thionyl chloride refluxed gives 2- {-5 pyridine-3-yl)-1, 3, 4- oxadiazole-2-yl) sulfonyl} acetohydrazide) with various substituted aromatic aldehyde and heterocyclic compound to form pyridine derivatives. Hydrazides were synthesized so as to increase intracellular concentration and so as to try and decrease the resistant developed due to decrease intracellular concentration of the drug these synthesized compounds were subjected to preliminary biological evaluation. The characterization of synthesized compounds was identified on the basis of IR,[1] HNMR, Mass spectroscopy. The compounds have been evaluated for antimicrobial activity.

KEYWORDS: Pyridine, Antibacterial activity, Intracellular concentration.

INTRODUCTION

Pyridine was a basic heterocyclic organic compound with the chemical formula C_5H_5N. It was structurally related to benzene, with one methyl group (=CH−) replaced by a nitrogen atom.[3] Pyridine was the parent ring system of a large number of naturally occurring products and important pharmaceuticals. Pyridine derivatives exhibit diverse pharmacological activities such as antimicrobial, anti-mycobacterium, anti-malarial, anti-tumor, cytotoxic, anti-diabetic, anti-arrhythmic, and anti-depressant.[4] Pyridines were class of both synthetically and naturally occurring heterocyclic compounds with a wide range of biological applications. Moreover, the current interest in the development of new antimicrobial agents can be partially recognized to both the increasing emerging resistance among new pathogens, appearance of multidrug resistance and adverse side effects were serious risk to public health. Therefore, the development of new and effective drugs was very significant goal, and most of the research effort in this field was directed towards the design of new agents.[5]

Scheme

All the compounds were synthesized by using a synthetic route given in scheme as follows:

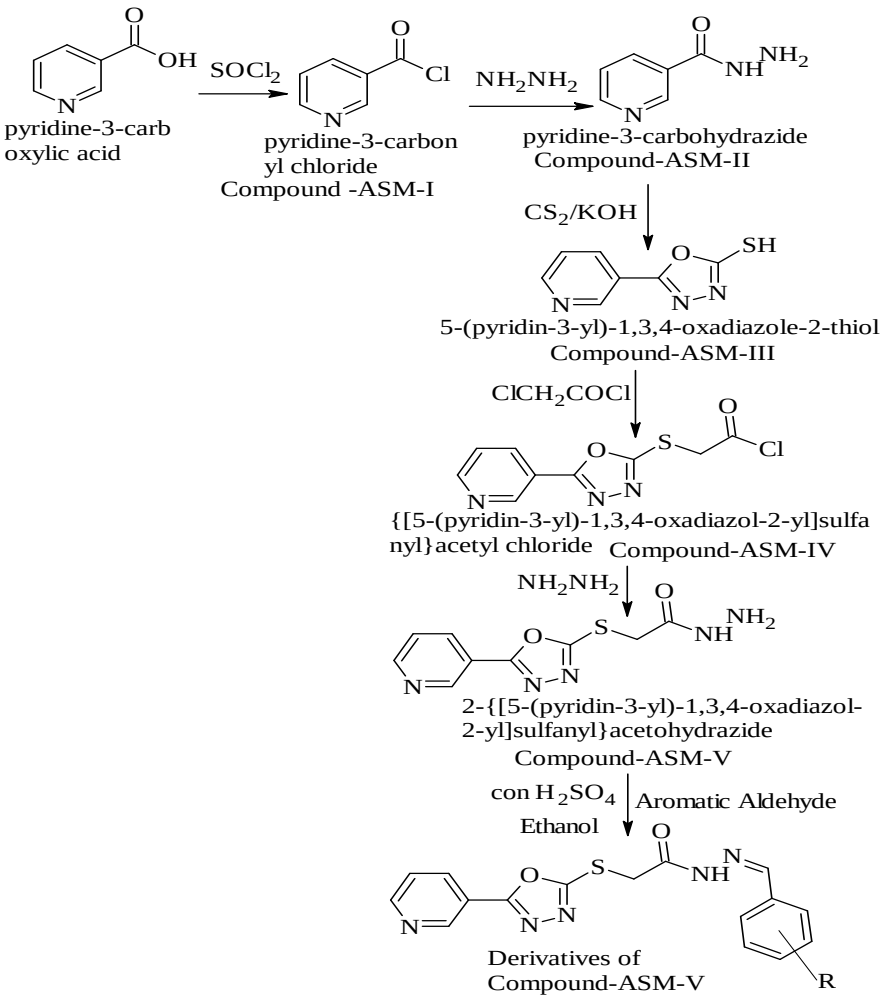

Fig. 1: Scheme of synthesis for pyridine derivatives.[6-11]

MATERIALS AND METHODS

Synthesis of pyridine -3-carbonyl chloride (ASM-I)

1mol Pyridine-3-carboxylic acid (nicotinic acid) In 25 ml ethanol and 3.3 ml of 0.5 mol thionyl chloride was refluxed filtered residue so collected and recrystallised from ethanol M.P 84-86°C Yield 114% Rf value 0.81.

Synthesis of pyridine -3-carbohydrazide (ASM-II)

Pyridin-3-carbonyl chloride in 15 ml of methanol 99% of 1.94 ml hydrazine hydrate refluxed precipitate was filtered recrystallized from 50% aqueous ethanol. M.P 241°C, Yield 90.117% Rf value 0.70.

Synthesis of 5(pyridine-3-yl) 1, 3, 4-oxadiazole)-2-thiol (ASM-III)

Pyridine-3-carbohydrazide 10 ml and carondisulphide 0.6 ml potassium hydroxide 0.56 g in 50ml H_2O 50 ml ethanol was refluxed and filtered was recrystallized from 50% aqueous ethanol. M.P 255-256 ^{0}C Yield 62.144% Rf value 0.41.

Synthesis of 5(pyridine-3-yl) 1, 3,4-oxadiazole- 2-yl-Sulfonyl acetyl chloride (ASM-IV)

5(pyridine-3-yl) 1, 3, 4oxadiazole)-2- thiol in glacial acetic acid 30 ml and chloroacetyl chloride was drop wise, refluxed and filtered was recrystallized from 50% aqueous ethanol. M.P 160 ^{0}C Yield 121% Rf value 0.70

Synthesis of 5(pyridine-3-yl)1,3,4-oxadiazole- 2-yl-Sulfonyl acetohydrazide (ASM-V)

5(pyridine-3-yl) 1,3,4-oxodiazole-2-yl Sulfonyl acetyl Chloride in 15 ml of methanol 99% 1.94 ml hydrazine hydrate was refluxed the precipitate was filtered and recrystallized from 50% aqueous ethanol M.P 160^{o}C Yield 88% Rf value 0.9

Derivatives of 2-{-5(pyridine-3-yl)-1, 3, 4oxadiazole -2-yl}-sulfonyl acetohydrazide. (ASM-VA-VH)

2-{-5(pyridine-3-yl)-1,3,4-oxadiazole-2-yl}sulfonyl Acetohydrazide 0.1 mol and aromatic aldehyde and few drops of glacial acetic acid in ethanol refluxed the final crude product was filtered and was recrystallized from aqueous ethanol. (ASM-VA-VH) M.P 84-186^{o}C Yield 81-95% Rf value 0.60-90 IR Spectrum of compound ASM-VC 3150 N-H Stretch of 2^o amine 3050

Aromatic C-H Stretch 2945 Aliphatic C-H Stretch 1618 C=O Stretch 1571 C=N Stretch 1488, 1443

1H-NMR Spectrum 1.55-1.61 δ –NH 7.15-9.932 δ -Ar-H (9H) Mass Spectrum Peak at m / Z 416 (Molecular weight of compound is 416)

Biological Evalvation

Antibacterial Activity

The minimum inhibitory concentration (MIC) was determined by the cup plate method. Chloramphenicol was employed during the test procedures as reference.

Table 1: Antibacterial activity of Compounds ASM-VA to ASM-VH.

Sr. No.	Compound Code	Escherichia coli (gram -ve)			Staphylococcus aureus (gram +ve)		
		Concentration of derivatives (µg /ml)			Concentration of derivatives (µg /ml)		
		250	500	750	250	500	750
		Mean zone of Inhibition (mm)					
1	ASM-V-A	12	18	19	11	12	13
2	ASM-V-B	10	11	11	11	12	14
3	ASM-V-C	11	12	13	12	14	16
4	ASM-V-D	12	14	17	10	13	14
5	ASM-V-E	13	12	14	15	13	11
6	ASM-V-F	12	17	14	11	16	13
7	ASM-V-G	10	16	11	14	18	17
8	ASM-V-H	11	12	13	15	12	14
Std	Chloramphenicol (100mcg/ml)	25			15		

RESULTS AND DISCUSSION

All synthesized compounds were analyzed by FT-IR, ^{1}H-NMR, and Mass spectral studies. The new compounds ASM-VC, ASM-VD, ASM-VF, ASM-VH, are having good Bacterial activity.

CONCLUSION

The novel derivatives of 2-{-5(pyridine-3-yl)-1, 3, 4oxadiazole -2-yl}-sulfonyl acetohydrazide. (ASM-VA-VH) can be used for further scope of antibacterial agents

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Conflict of Interest

All the authors have no conflicts of interests.

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