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Short Communication

Evaluation of New 2-N-tert-butyl-5-aryl-1, 3, 4-Oxadiazol-2-Amines for Antimicrobial Activity

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Abstract

A series of five membered heterocyclic oxadiazole derivatives synthesized by intramolecular cyclisation of N-tert-butyl-2-aroyl hydrazine carbothioamides (IIa-g) with iodine-pot.iodide in basic medium were tested for their biological activities against selected microorganisms. The newly synthesized compounds were investigated for their antimicrobial activities by Agar diffusion method. For antibacterial study, the bacterial strain used included both gram-positive strains like Ecoli and gram negative strain S.aureus. Antifungal activity was performed against the fungus A. niger. Among the synthesized compounds (IIIa-g), few compounds showed weak antimicrobial activities in comparison with standard drugs.

Keywords: 1,3,4-oxadiazoles, Antimicrobial activities, Gentamycin, Amphotericin.

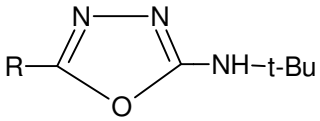
Introduction

Since the past few decades extensive work had been done on the synthesis and pharmacological activities of various heterocyclic compounds specially substituted azole derivatives. Among the five membered heterocyclic rings, oxadiazole is one of the important compounds for designing potential bioactive agents. The oxadiazole derivatives are known to have wide biological activities such as antimicrobial[1-4], anticonvulsant[5-6], analgesic activity[7], antitubercular[8]. The 1,3,4-oxadiazoles is one of the popular bio-active molecule in pharmaceutical and medicinal chemistry. Most of the antimicrobial agents are known with different structures which are generally used in the treatment of fungal infections, activity of these drugs is based on structure antimicrobial relationship. Various different methods have been proposed to synthesize substituted oxadiazoles. The oxidative cyclization of carbothioamides[9-16] is one of the important methods for oxadiazole synthesis. In the present study, we have discussed about evaluation of some 2,5-substituted 1,3,4-oxadiazoles for antimicrobial studies. The synthesized compounds were tested against some selected microorganisms for their antibacterial and antifungal activities.

Materials and Methods

Chemistry: A new series of 2-N-tert-butyl-5-aryl-1,3,4-oxadiazol-2-amines (IIIa-g) were generated by oxidative cyclization of different N-tert-butyl-2-aroylhydrazine carbothioamide (IIa-g) according to the known procedure. The structure and purity of the compounds synthesized was confirmed by C,H,N analysis,: IR, ^{1}H NMR spectral methods and TLC.

Biological Activities: A new series of different 2,5--substituted oxadiazoles were subjected to antimicrobial screening have the following general formula.



Scheme-1
2-**N-tert-butyl-5-aryl-1,3,4-oxadiazol-2-amines (IIIa-g)**

Where: R, a = p-$NO_2C_6H_4$_, b = -$CH_2C_6H_5$, c = -C_6H_5, d = O-OHC_6H_4-, e = O-ClC_6H_4-, f = P-ClC_6H_4-, g = -C_4H_5N

The microbiological assay was done by comparing the inhibition growth of microorganisms with measured concentrations of test compounds with the known concentration of a standard drug. The antimicrobial activity of a compound is generally expressed as its inhibiting effect toward the growth of the bacterium in nutrient broth or nutrient agar. The present antimicrobial study used the agar diffusion method[17-19] to deals with the study of synthesized compounds for antifungal and antibacterial activity.

Biological Activity: Using agar diffusion method the antibacterial activities of the compounds were tested. The bacterial strain used included both *Staphylococcus aureus* and *Escherichia coli.*

The medium used for the study of antibacterial activity of newly synthesized compounds having the following composition.

Media Used (Nutrient broth): NaCl-10g, Peptone-10 g and Yeast extract 5g, Agar 20g in 1000 ml of distilled water. The two bacterial organism were used for testing the antibacterial activities of the compounds namely *Staphylococcus aureus* and E. *coli* bacteria using concentration 20 mg/mL by agar diffusion method. The antibiotic Gentamycin was used to compare the activities of compounds. All the compounds were diluted in Dimethyl sulfoxide with the concentration of 20 mg/ml. Nutrient broth of above composition was used as a growth media. The stock solution was serially diluted to give concentrations of 0.0625, 0.125, 0.25, 0.5, 1.0 and 2.0 mg in nutrient broth. The incubation periods for all the plates were 24 h at 37^0C for and inhibition zones diameter were noted.

The antifungal activity was performed using the similar method. The fungus used was - *Aspergillus niger.* The medium used for the study of antifungal activity of these newly synthesized compounds having following composition, was of fungistatic grade. It was found to be suitable for the growth of fungus, *Aspergillus niger* used in the present study.

Czapek-Dox agar medium was made ready with 56.01 g of ingredients and 1 liter of distilled water. Initially, the inoculum in broth media of stock cultures was done and grown at 27^0C for 48 hrs.

Dimethyl sulfoxide was used to dissolve the test compounds and to give 10 mg/ml of concentration. The agar plates were made ready with agar and developed the wells. Each plate was inoculated of plates was done for 48 h old cultures (100 µl 10^4 CFU). The different dilution 0.0625, 0.125, 0.25, 0.5, 1.0 and 2.0 mg of samples was done to prepare the well. The antibiotic was used to fill the control wells. The standard drug Amphotericin was used. The incubation of plates was done at 27^0C for 72 h and the observations were made for the diameters of inhibition zone.

Results and Discussion

The growth of various bacterial and fungal organisms on test compounds for testing their antimicrobial activities is summarized in Table-1. The screening results of the newly synthesized compounds (IIIa-g) revealed that the compounds (IIIc), (IIId) and (IIIg) showed moderate bactericidal activity while other was totally inactive. Compound (IIIe) and (IIIf) were found to be weakly fungicidal against the organism *A. niger* while the other compounds were not active.

Conclusion

In conclusion, in present we investigated the antimicrobial activities of some newly synthesized oxadiazole derivatives says 2-N-tert-butyl-5-aryl-1,3,4-oxadiazol-2-amine (IIIa-g). The bacterial strain *S. aureus* and *E. coli* were used to test the antimicrobial activities of the compounds. For comparison Gentamycin was used. The antifungal activity was performed against *Aspergillus niger*. Amphotericin used as standard. Compounds were least active against tested microorganism. However, it was found that the tested compounds are much less reactive when compared with the standard drugs used.

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Table-1
Antimicrobial activity of 2-N-tert-butylamino-5-aryl-1,3,4-oxadiazole(IIIa-g)

Organism	Conc.	IIIa	IIIb	IIIc	IIId	IIIe	IIIf	IIIg
E. Coli	1.0 mg	0	0	6	7	4	4	5
	2.0 mg	3	5	12	13	7	6	8
	MIC mg	2	2	0.5	0.5	1	1	0.5
S.aureus	1.0 mg	2	2	7	10	0	0	0
	2.0 mg	7	6	12	13	2	2	0
	MIC mg	1	1	0.5	0.5	2	2	NF
A. niger	1.0 mg	5	0	0	3	9	7	0
	2.0 mg	9	6	3	6	13	12	2
	MIC mg	1	1	2	1	0.5	0.5	2

Note: NF- MIC not found among the concentrations screened.

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