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SYNTHESIS AND EVALUATION OF SOME NEW THIADIAZOLES AS ANTIMICROBIAL AGENTS

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ABSTRACT

A new series of 2,5-disubstituted 1,3,4-thiadiazoles were synthesized by using different aromatic or aliphatic carboxylic acids (1) and thiosemicarbazide (2). The structures of the synthesized compounds were established by their spectral (IR, ^{1}H NMR and Mass) data. All the compounds were screened for their antimicrobial activity against *Staphylococcus aureus. Escherichia coli,* Compounds showed mild to moderate activity, but not comparable with the standard (Norflaxacin).

KEY WORDS: **1,3,4-thiadiazole, Synthesis, Antimicrobial activity, Cup plate method.**

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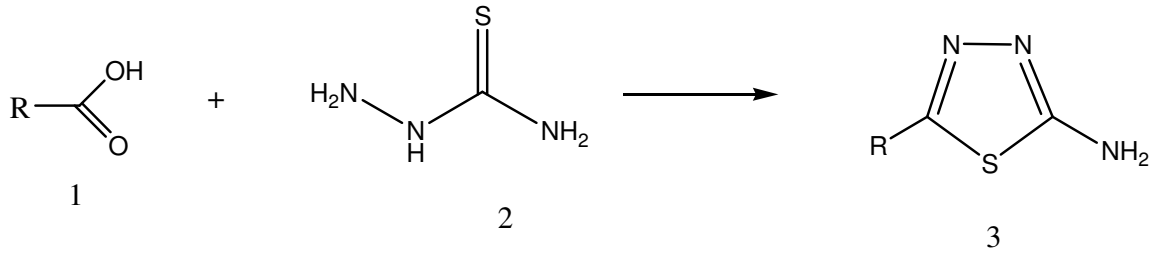
INTRODUCTION

A recent literature survey revealed that the 1, 3, 4- thiadiazole[1] moiety have been widely used by the medicinal chemist in the past to explore its biological activities. Different classes of thiadiazoles were known to possess various biological and pharmacological properties[2-5]. Hence, this field has-ever-growing importance resulting in the development scores of thiadiazoles. Therefore, it has been considered worthwhile to synthesize some new series of 1,3,4-thiadiazole, to characterize the new thiadiazoles by their analytical and spectral (IR, ^{1}H NMR and Mass) data. (Scheme-I)



1 2 3

Scheme-I

Physical data of new 1,3,4-thiadiazoles are presented in Table-1.

EXPERIMENTAL

Experimental procedures are given as general methods.Melting points of the synthesized compounds were determind in open capillaries by using Toshnwal melting point apparatus. Functional group analysis was done by using Shimadzu FTIR-8700 spectrometer in KBr pellet method. Proton NMR were recorded using TMS as internal standard by omega-500 MHz spectrometer chemical shifts were expressed in δ ppm,. molecular weight of the compounds determined by using VG micro mass 7070 H spectrometer

Synthesis of 2-Amino-5-alkyl/aryl/heteryl-1,3,4-thiadiazoles

General Procedure

Appropriate aliphatic or aromatic carboxylic acid (0.05 M) and thiosemicarbazide (0.05M) were taken into a RB flask and dissolved in alcohol (25 ml) by shaking. To this, concentrated sulphuric acid (10 drops) was added while shaking and the reaction mixture was heated under reflux for 1-2 hrs, on a hot water bath. The progress of the reaction was monitored by using thin layer chromatography. After completing the reaction time the solvent was removed by distillation process and triturated with little amount of crushed ice. The product was filtered, washed with small portion of cold water and dried. It was purified by recrystallization from hot alcohol.

Spectral characterization data of compound 3d

Infrared spectrum of the compound (KBr): has exhibited absorption characteristics of: 3214 (-NH_2), 3036 (C-H, aromatic), 1478 (C=C, aromatic)Cm^{-1}, respectively

^{1}HNMR spectrum of the compound ($CDCl_3$): showed proton signals at: 7.22 (s, 2H, -NH_2 of thiadiazole), 7.55 to 8.02 (m, 4H, -Ar-H) δ, ppm, respectively.

Mass spectrum of the compound exhibited its molecular ion (M^+) at m/z 211.

Thus, based on the specified spectral data the compound has been characterized as 2-amino-5-(4-chloro phenyl)-1,3,4-thiadiazole (3d; R = C_6H_4.Cl-4).

Adopting the above procedure six different 2-amino-5-alkyl/aryl/heteryl-1,3,4-thiadiazoles have been synthesized and characterized.

ANTIMICROBIAL ACTIVITY

All the synthesized compounds have been screened for their antimicrobial activity by cup-plate[6] agar diffusion method by measuring inhibition of zone in mm. Norfloxacin (50µg/ml) was used as a standard drug for antibacterial activity. The compounds were screened for their antibacterial activity against *Staphylococcus aureus. Escherichia coli,* in nutrient agar medium. The test compounds were kept in the cavities with micropipette and allowed to diffusion for one hour.

Dimethyl sulfoxide (DMSO) was used as a solvent for all compounds and as a control. These plates were incubated at 37^{o}C for 34 hrs. The zone of inhibitionwas observed around the cups and calculated. The results are presented in Table2.

RESULTS AND DISCUSSION

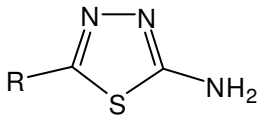
2-Amino-5-alkyl/aryl/heteryl-1,3,4-thiadiazoles could be successfully synthesized by using appropriate aliphatic or aromatic carboxylic acid and thiosemicarbazide. All the six compounds (3a-3f) have been screened for their antimicrobial activity by cup-plate agar diffusion method by measuring the zone of inhibitionin mm. Norfloxacin was used as a standard drug for antibacterial activity. The thiadiazole derivative 3f having a 4-pyridyl group showed potent antibacterial activity against *s. aureus*, where as compound 3d having 4-chloro group showed maximum inhibition against *E.Coli* and remaining compound showed mild to moderate antibacterial activity.

CONCLUSION

The newly synthesized compounds are characterized by spectral data (IR, ^{1}HNMR & Mass) and screened for antimicrobial activity. Among the synthesized compounds **3f** and **3d** exhibited significant antimicrobial activity. These derivatives have been given a key to more modifications in pharmacophore replacements.

Table-1

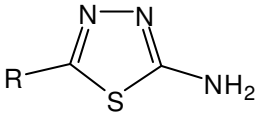
Physical data of 2-amino-5-alkyl/aryl/heteryl-1,3,4-thiadiazoles (3a-f)



Compound	R	m.p^{0}C	%Yield	Mol. Formula	Mol.Wt.
3a	-*n*-Pr	200-202	48	$C_5H_9N_2S$	101
3b	-*n*-Bu	186-188	56	$C_6H_{11}N_2S$	115
3c	-C_6H_5	222-224	64	$C_8H_7N_2S$	177
3d	-C_6H_4, Cl-4	230-232	70	$C_8H_9N_2SCl$	211
3e	-C_6H_4, CH_3 -4	218-220	68	$C_9H9_7N_2S$	191
3f	4-pyridyl	242-244	54	$C_6H_6N_3S$	178

Table2

Antimicrobial Activity of 2-amino-5-alkyl/aryl/heteryl-1,3,4-thiadiazoles (3a-f)



Sl.No	Sample Code	*Staphylococus aureus*	*Escherichia coli*
1	3a	14	15
2	3b	16	14
3	3c	16	16
4	3d	19	20
5	3e	17	18
6	3f	20	18
7	Norfloxacin	**24**	**22**

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