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Antimicrobial Activity of 1-substituted-2-thio- (1H)-4 (1-substituted thiocarbamido-3-yl)-6-substituted amino 1,2-dihydro-s-triazine.

M.E. Shelke

Department of Chemistry, H.V.P.M. College of Engineering and Technology, HVPM Campus, Amravati, India.

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Novel series of 1-substituted-2-thio-(1H)-4-(1-substitutedthiocarbamido-3-yl)-6-substitutedamino 1,2-dihydro-s-triazines[3a(I) to 3f(III)] have been obtained by the isomerisation of 2-substitutedamino-4-(1-substitutedthiocarbamido-3-yl)- 6-substitutedimino-1,3,5-thiadiazines[2a(I) to 2f(III)] in presence of ethanolic sodium bicarbonate solution, which have been obtained by basification of their hydrochlorides [1a(I) to 1f(III)] which are synthesized by the interaction of 1,3-Bis-(N- substitutedthioamido) guanidine and N-aryl/ alkylisocyanodichlorides. The latter were prepared initially by the condensation of guanidine carbonate and N-substitutedisothiocyanate. The structure of all these compounds was established on the basis of elemental analysis, IR and PMR spectral data. All the synthesized compounds have been screened for their antimicrobial activity against both gram-positive and gram-negative human pathogens.

Keywords: 1,3-Bis-(N- substitutedthioamido) guanidine, 1,3,5-thiadiazines, S-triazines, antimicrobial activity.

The literature survey reveals that the heterocyclic compounds containing nitrogen and sulphur have gain immense importance in human life due to their variety of applications in agricultural, medicinal, pharmacological and industrial value. It has also been found that the heterocyclic compounds containing S-triazine in the nucleus have been successfully tested against several pathogens and found that they possess insecticidal[1], medicinal, industrial, pharmaceutical, agricultural and bactericidal[2-4] properties. Some triazino compounds show remarkable biological activity[5-7] and help to find better alternative against drug.

All S-triazine compounds were screened for their antibacterial activity using cup plate diffusion method.[8 -9] The microorganisms used include both gram positive and gram negative bacteria like *S. aureus*, *S. typhi, A. aerogenes, E. coli* and *B. subtilis*.

The medium was prepared by dissolving 28 gm of ingredients in one liter of distilled water and was sterilized at 121°C temperature and 15 lbs/inch pressure in an autoclave for 15 minutes. After sterilization it was cooled down to 50°C and poured into sterile petriplates and allowed to solidify. The media plates were then seeded with 24 hrs old active nutrient growth culture of the test organism in order to obtain lawn culture. The compounds were dissolved in 50% dimethylformamide (DMF) solvent at fix concentration 100 mg/ml . To these added 2 drops of test solutions of synthesised compounds. Plane DMF solvent was used as control. The plates were then incubated at 37°C for 24 hrs. After

* To whom all correspondence should be addressed.
Mob.: +91-9421801166
E-mail: meshelke@rediffmail.com

incubation the zones of inhibition were recorded around the wells and results are cited in Table 1.

EXPERIMENTAL

All chemicals used were of analar grade. Aryl/alkylisothiocyanate, Aryl/alkylisocyanodichlorides were prepared according to literature method[10]. Melting points of all synthesized compounds were determine in open capillary. IR spectra were recorded on Perkin-Elmer spectrometer in the range 4000-400 cm^{-1} in KBr pellets. PMR spectra were recorded with TMS as internal standard using $CDCl_3$ and DMSO-d_6. TLC checked the purity of the compounds on silica gel-G plates with layer thickness of 0.3 mm.

Synthesis of 1-phenyl-2-thio-(1H)-4-(1-phenylthiocarbamido-3-yl)-6-phenylamino-1,2-dihydro-s-triazine [3a(i)]

2-phenylamino-4-(1-phenylthiocarbamido-3-yl)-6-phenylimino-1,3,5-thiadiazines [2a(i)] was suspended in 5% aqueous ethanolic sodium bicarbonate solution and refluxed for 2 hrs. during heating reactant went in to solvent. Then excess solvent was distilled off, a needle shape pale yellow crystals were separated out. It was crystallized from glacial acetic acid. Yield 71% m.p.227°C and identified as 1-phenyl-2-thio-(1H)-4-(1-phenylthiocarbamido-3-yl)-6-phenylamino-1,2-dihydro-s-triazine[3a(i)].

IR spectra of compound shows ν(NH) 3338.3 cm^{-1}, 3149.6 cm^{-1}, ν(C-H (Ar),

Table 1. Physical data and antimicrobial activity of the compounds [3a(ii) to 3f(iii)]

Compd.	R	R_1	Yield (%)	m.p. (°C)	*Gram Positive* *S. aureus*	*B. subtilis*	*Gram Negative* *A. aerogenes*	*E. coli*	*S. typhi*
[3a(i)]	Phenyl	Phenyl	71	227	+	-	+ +	+ + +	+ + +
[3a(ii)]	Phenyl	*p*-Chloro -pheny	71	207	+ + +	+ + +	+ +	+ + +	+ +
[3a(iii)]	Phenyl	Ethyl	79	189	+ +	+ +	+ +	-	+ + +
[3b(i)]	*p*-Chloro -phenyl	Phenyl	73	197	+ + +	+++	+ +	+ + +	+ +
[3b(ii)]	*p*-Chloro -phenyl	*p*-Chloro -phenyl	69	212	+ +	+ +	+ +	-	-
[3b(iii)]	*p*-Chloro -phenyl	Ethyl	72	205	-	-	+	+ +	+
[3c(i)]	*p*-Tolyl	Phenyl	64	213	+ +	+ + +	+ +	+ + +	+ + +
[3c(ii)]	*p*-Tolyl	*p*-Chloro -phenyl	69	221	-	++	+ + +	+ + +	++
[3c(iii)]	*p*-Tolyl	Ethyl	58	191	-	-	+	+ +	+
[3d(i)]	Ethyl	Phenyl	64	187	+ +	+ + +	+ +	+ + +	+ + +
[3d(ii)]	Ethyl	*p*-Chloro -phenyl	71	182	-	-	+	+ +	+ +
[3d(iii)]	Ethyl	Ethyl	69	179	+	-	-	+ + +	+
[3e(i)]	Methyl	Phenyl	72	167	+ + +	+ + +	+ +	+ + +	+ + +
[3e(ii)]	Methyl	*p*-Chloro -phenyl	76	171	++	++	+	+ + +	+ + +
[3e(iii)]	Methyl	Ethyl	68	168	-	-	+	+ +	+
[3f(i)]	*t*-Butyl	Phenyl	79	193	+ +	+ + +	+	+ + +	++
[3f(ii)]	*t*-Butyl	*p*-Chloro -phenyl	74	168	+ + +	+ +	+ +	+ + +	+ +
[3f(iii)]	*t*-Butyl	Ethyl	67	177	+ + +	-	-	++	++

* All the Compounds gave satisfactory C, H, N, and S analysis.
(-) - = Inactive (Less than 10 mm) (+) - = Weakly Active (10-14 mm)
(++) - = Moderately Active (15-18 mm) (+++)- = Highly Active (19-35 mm)

ν(C=N)1634.3 cm^{-1}, ν(C-N)1295.2 cm^{-1}, ν(C=S) 1198.6 cm^{-1}, ν(C-S) 777.9 cm^{-1}, ν(C=N) grouping 1634.3 cm^{-1}; The PMR spectra of compounds showed signals due to (Ar-NH) protons at δ 8.52 ppm, (Ar-H) protons at δ 6.87 ppm and NH protons at δ 8.08-8.16 ppm. and the signal at δ 3.31 ppm is due to moisture in DMSO-d_6. and the signal at d 2.55–2.56 ppm is due to moisture in DMSO. Similarly others compounds [3a(ii) to 3f(iii)] were synthesized by above mention method and enlisted in Table 1.

RESULTS AND DISCUSSION

All the bacterial strains studied are human pathogens. The activity is compared with standard drug ciprofloxacine at the same concentration. From the experimental data it has been observed that the compounds 3a(i), 3a(ii), 3c(i), 3d(i), 3e(i) and 4e(ii) shows high activity against *S. typhi* and compounds 3a(ii), 3b(i), 3c(i), 3d(ii), 3f(i), 3f(ii) and 3f(ii) shows moderate activity while remaining compounds are inactive against same pathogen. Similarly compound 3a(i), 3a(ii), 3b(i), 3c(i), 3c(ii), 3d(i), 3d(iii), 3e(i), 3e(ii), 3f(i) and 3f(ii) shows high activity while compound 3b(iii), 3c(iii), 3d(iii), 3e(iii), and 3f(iii), shows moderate activity and remaining compounds 3a(iii) and 3b(ii), shows inactivity against *E. coli*.

In case of Gram-positive bacteria like *S. aureus* the compound 3a(ii), 3b(ii), 3e(i), 3f(ii) and 3f(iii), shows highly activity while compound 3a(iii), 3c(i), 3d(i), 3e(ii), and 3f(i) shows moderately activity against the same bacteria. The compound 3a(ii), 3b(i), 3c(i), 3d(i), 3e(i) and 3f(i) were effective against *B. subtilis*. As newly s-triazines shows remarkable antimicrobial activity, these compounds can be easily used as alternative drugs for the treatment of diseases like typhoid and dysentery.

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