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SYNTHESIS OF SOME NEW 1, 3-DI METHYL SUBSTITUTED GUANIDINE WITH POSSIBLE ANTIBACTERIAL AND ANTIFUNGAL ACTIVITY

Bhupender Singh Rawat, S. C. Mehra
Department of Chemistry, Bareilly College, Bareilly U.P (India)
drbsrawat@gmail.com

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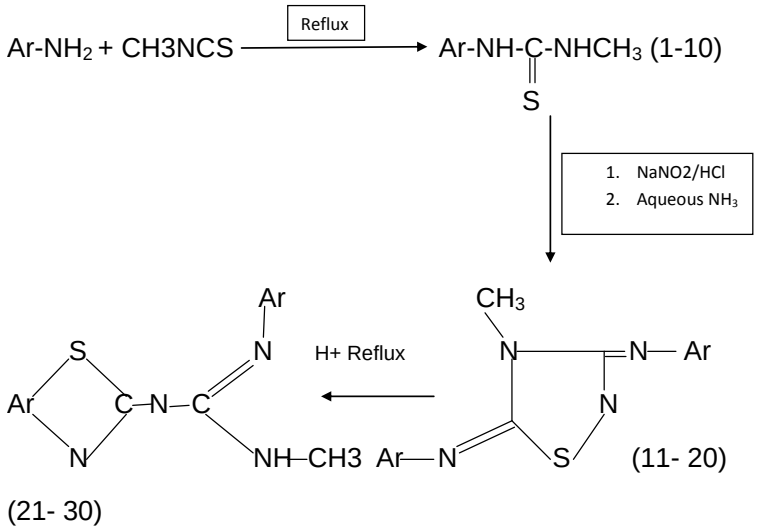
Abstract

The compounds containing thiazole, thiadiazole, oxazole, oxadiazole, imidazole, pyrimidine, pyridine & benzothiazole rings have been found to exhibit broad spectrum of biological activities.

Derivatives of 1, 2, 4-thiadiazole and 1, 2, 4-thiadiazolidines exhibit antibacterial and antifungal activity[1]. Thiazolyl guanidines2 and various substituted aryl guanidine's have been found to exhibit antibacterial & antifungal activities3.Keeping all these views in mind attempts were made to synthesized some new 1,3-di methyl Substituted Guanidine.

In the present work 2,4 Dimethyl -3,5-(di Aryl imino)-1,2,4-thiadiazolidines were prepared by nitrous acid oxidation of N-methyl –N Aryl thiourea4 & 2,4 dimethyl-3,5-(diaryl imino)-1,2,4-thiazolidines were converted to corresponding 1,3 di methyl substituted guanidine's by their acid catalyzed re-arrangment5.(Scheme-1)



(Scheme-1)

Antibacterial & Antifungal activity of the title compounds were evaluated against two bacteria, E.coli & lactobacillus & two fungi, A.Brassicicola & Aspergillus Niger. N=methyl-N`-Aryl thiourea (1-10) were prepared by refluxing a mixture of different 2-Amino Heterocyclic moieties with methyl iso thiocyanate in Ethanol.

A mixture of compound (1-100 and conc. HCl, ethanol was added drop wise & under stirring to a solution of NaNO2 in water afforded 2, 4-dimethyl-3, 5-(di Aryl imino)-1,2,4-thiadiazolidine (11-20) afforded 1,3 di methyl substituted guanidine's (21-30). Structures of the compounds were established by elemental analysis & spectral data.

EXPERIMENTAL

All the melting points are uncorrected.IR spectra were recorded in solid state using KBr pellet method. The spectra were recorded on Perkin Elmer FT-IR spectrophotometer (model RX-1). The PMR spectra were recorded in DMSO-d6 solvent at room temperature using TMS as reference compound. The spectra were recorded on Perkin Elmer Model 32 NMR spectrometer at 300MHz at CDRI Lucknow.

The reactions were monitored by TLC. The required methyl iso thiocyanate 6 & 2-Amino-4-[p-subst/unsubst] phenyl thiazoles7 were prepared by know method. Procedure for one compound of each step has been described in sequel.

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The physical Data of compounds are given in Table-1.

N-Methyl-N`-(2`-Pyridyl) thiourea: Methyl iso thiocyanate (0.1mol) was refluxed with 2-Amino Pyridine (0.1mol) in ethanol (25ml) for 1 hour. The solid so obtained was then washed with dil HCl & petroleum ether and crystallized from ethanol.

Yield: 38%, M.P 141°C (Found: N, 25.1; S, 19.1. C7H9N3S requires: N, 25.14; S, 19.16%). IR (KBr): 1185cm-1 (due to C=S), 3305 cm-1 (due to –NH).1605 cm-1 & 1250 cm-1 (due to C=N & C-N).

2, 4-di methyl-3, 5-(di pyridyl imino)-1, 2, 4-Thiadiazolidine (17): A mixture of thiourea (7) (0.05 ml) and conc. HCl (36%, 12.9 ml), ethanol (50 ml) was added drop wise and under stirring to a solution of NaNO2 (0.1 mol) in water (25ml).

After one hour of stirring at room temperature, the precipated sulphur was removed. The filtrate was basified with ammonia solution and the resulting solid was crystallized from ethanol. Yield: 32%, M.P 153°C (Found: N, 28.13; S, 10.67. C14H14N6S requires: N, 28.18; S, 10.73%). IR (KBr):1605 cm-1 & 1250 cm-1 (due to C=N & C-N).

1-[2`(Pyrido-thiazolyl)]-1,3-dimethyl-4-(2`pyridyl)Guanidine,(27): A mixture of 1, 2, 4-Thiadiazolidine (17) (0.01 mol) was refluxed with conc. HCl (1 mol) for 2.5 hrs. The contents were then basified with NaOH (1mol) at 0°C and the resulting crude product was crystallized from ethanol. Yield: 30%, M.P 162°C (Found: N, 28.11; S, 10.67. $C_{14}H_{14}N_6S$ requires: N, 28.18; S, 10.73%). IR (KBr): 3210 cm^{-1} (due to –NH).1605 cm^{-1} & 1250 cm^{-1} (due to C=N & C-N). PMR: δ 5.25-5.75(1H, bs,-NH, D2O exchangeable). δ 2.95-3.24(6H, 2s, 2xN-CH_3), δ 7.18-8.56 (7H,m,Ar-H).

ANTIBACTERIAL AND ANTIFUNGAL SCREENING

All the synthesized compounds were screened for their Antibacterial properties against E.coli, Lactobacillus & Antifungal Properties against A. Brassicicola & Aspergillus Niger. The activity of the synthesized compounds was tested using filter paper disc method[8] at 500 ppm concentration using 5mm filter paper disc. The activity of the compounds was compared with antibacterial streptomycin & commercial fungicide Carbendazim.

From the activity Data (Table 2), we concluded that compound No 21 & 25 showed maximum inhibition & compound No 24, 26 & 28 showed moderate activity against E.Coli. Compound No 21 & 25 showed maximum inhibition & compound No 26, 28 & 30 showed moderate activity against lactobacillus. Compound No. 22, 25, 26 & 28 showed maximum inhibition & Compound No 21, 27 & 29 showed moderate against A.Brassicicola. Compound No 22, 25 & 28 showed maximum inhibition & Compound No 21 & 26 showed moderate inhibition against A. Niger.

Table1: Physical Data of Compounds

Compound number	Nature of Ar-NH2	Yield	M.P (°C)	Molecular Formula
1	2-Amino-4-phenyl thiazole	51	141	$C_{11}H_{11}N_3S_2$
2	2-Amino-4-(p-chloro) phenyl thiazole	42	172	$C_{11}H_{10}N_3S_2Cl$
3	2-Amino-4-(p-fluoro) phenyl thiazole	44	179	$C_{11}H_{10}N_3S_2F$
4	2-Amino-4-(p-nitro) phenyl thiazole	33	164	$C_{11}H_{10}N_4S_2O_2$
5	2-Amino-4-(p-methoxy) phenyl thiazole	26	170	$C_{12}H_{13}N_3S_2O$
6	2-Amino-4-(p-Hydroxy) phenyl thiazole	29	168	$C_{11}H_{11}N_3S_2O$
7	2-Amino-Pyridine	38	141	$C_7H_9N_3S$
8	2-Amino-Pyrimidine	39	187	$C_6H_8N_4S$
9	α- Naphthyl Amine	36	175	$C_{12}H_{12}N_2S$
10	β- Naphthyl Amine	35	188	$C_{12}H_{12}N_2S$
11	2-Amino-4-phenyl thiazole	43	153	$C_{22}H_{18}N_6S_3$
12	2-Amino-4-(p-chloro) phenyl thiazole	35	190	$C_{22}H_{17}N_6S_3Cl$
13	2-Amino-4-(p-fluoro) phenyl thiazole	33	189	$C_{22}H_{17}N_6S_3F$
14	2-Amino-4-(p-nitro) phenyl thiazole	27	179	$C_{22}H_{17}N_7S_3O_2$
15	2-Amino-4-(p-methoxy) phenyl thiazole	20	197	$C_{23}H_{20}N_6S_3O$
16	2-Amino-4-(p-Hydroxy) phenyl thiazole	25	182	$C_{22}H_{18}N_6S_3O$
17	2-Amino-Pyridine	32	153	$C_{14}H_{14}N_6S$
18	2-Amino-Pyrimidine	30	191	$C_{12}H_{12}N_8S$

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Compound number	Nature of Ar-NH2	Yield	M.P (°C)	Molecular Formula
19	α- Naphthyl Amine	31	180	$C_{24}H_{20}N_4S$
20	β- Naphthyl Amine	33	195	$C_{24}H_{20}N_4S$
21	2-Amino-4-phenyl thiazole	35	166	$C_{22}H_{20}N_6S_3$
22	2-Amino-4-(p-chloro) phenyl thiazole	30	197	$C_{22}H_{18}N_6S_3Cl_2$
23	2-Amino-4-(p-fluoro) phenyl thiazole	28	193	$C_{22}H_{18}N_6S_3F_2$
24	2-Amino-4-(p-nitro) phenyl thiazole	23	189	$C_{22}H_{18}N_8S_3O_4$
25	2-Amino-4-(p-methoxy) phenyl thiazole	17	210	$C_{24}H_{24}N_6S_3O_2$
26	2-Amino-4-(p-Hydroxy) phenyl thiazole	20	188	$C_{22}H_{18}N_6S_3O_2$
27	2-Amino-Pyridine	30	162	$C_{14}H_{14}N_6S$
28	2-Amino-Pyrimidine	25	197	$C_{12}H_{14}N_8S$
29	α- Naphthyl Amine	24	186	$C_{24}H_{20}N_4S$
30	β- Naphthyl Amine	26	199	$C_{24}H_{20}N_4S$

Table 2: Screening Results of the newly synthesized Compounds Antibacterial & Antifungal Activity

Comp[d]No	A. Brassicicola	A. Niger	E.Coli	Lactobacillus
21	+8	+7	-	+6
22	+10	+9	+9	+10
23	+6	-	+8	+6
24	+6	-	+8	-
25	+12	+10	+10	+9
26	+9	+7	+8	+7
27	+7	-	+6	-
28	+10	+9	+7	+8
29	+7	-	-	+6
30	+6	-	-	+8
Control	Carbendazim	Carbendazim	Streptomycin	Streptomycin
	+14	+13	+13	+11
(5mm, filter paper disc was used)				

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REFERENCES

1. G. Brekel hammer and G. Asato, Science 1968; 162, 1146. I. B. Simon and I. Kovlunovskaya, L. Evshina: Chem abstr.19, 60, 54, 24760. C. K. Bradsher, F. C. Brown, E. F. Sinclair & S.T. Webster: J. Am Chem Soc., 1958, 80, 414.
2. T.Noguchi, A.Kaji, S.Kosak & T. Muraina: Jap. Pat. 17997/1962 (Chem. Abstr. 1963; 59, 11540).
3. H. Schroeder & J. H. Reinhart: Belg.Pat. 624, 636/1963 (Chem. Abstr. 1963, 59, 11508).
4. R.E. Alleno, R.S. Shelton and M.G. Vanampen: J.Am. Chem. Soc., 1954, 1158. G.D. Thorn: Can.J. Chem. 1960, 38, 2349.
5. P.N. Bhargawa and Shree Prakash, J. Ind. Chem. Soc. 1980 56 (9), 937.
6. S. N. Pandey and P.R. Naik: J. Ind. Chem. Soc., Vol.73 July 1996, 363-365.
7. D.C. Schroeder: Chem. Rev., 1955, 55, 181.
8. C. Christopheresen, T. Ottersen, K. Seff and S. Treppendahi: J.Am. Chem.Soc, 1975, 97, 5237. Horning: Collective Volume III, 599.
9. R.M. Dodson and L.C. King: J.Am. Chem. Soc., 1945, 2242, 67.
10. Y.L.Nene & P.N. Thapliyal: Fungicides in Plant Diseases Control 1982 (Oxford and IBH Publ., New Delhi) P.192.