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Synthesis and Characterizations of N^2,N^4-bis(5-nitro-1,3-benzothiazol-2-yl)-N^6-aryl-1,3,5-triazine-2,4,6-triamine,as Biological Agents

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ABSTRACT

Some novel N^2, N^4-bis (5-nitro-1,3-benzothiazol-2-yl) - N^6- aryl-1, 3, 5-triazine-2, 4, 6-triamine 1a-1l have been synthesized and characterized by elemental analyses IR and NMR spectra. The products tested for their antibacterial activity against gram (+)ve and gram (-)ve bacteria. Introduction of –OH, -NO_2, -Cl and –Br groups to the heterocyclic frame work enhanced antibacterial activities.

Keywords: 1, 3, 5-triazine-2, 4, 6-triamines; Antibacterial activity.

I. INTRODUCTION

Antibacterial and Antiviral diseases are very common in all over the world. The s-triazine based chalcones and their derivatives have been studied extensively because of their wide range of biological activity. The s-triazine[1-6] have been linked with a wide range of therapeutic activities[7-12] such as Antibacterial, Fungicidal, Anticancer, Antitubercular.

Among all heterocycles, nitrogen based heterocycles have specific and unique identity in the world. Pyrimidine, oxadiazole, coumarin, pyrimidine, s-triazine are some of the examples. The research work described here is humble effort to synthesis the nitrogen based novel heterocycles. And study of their pharmaceutical importance in medicinal chemistry.

The study of pyrazoline derivatives has been a developing field within the heterocyclic chemistrybroad spectrum of biological activity[13-20]. Pyrazoline derivatives have been found to be bactericidal[13,14], fungicidal[15,16], and insecticidal agents[17,18]. Asurveyof more recent literature reveals that some pyrazoline derivatives possess cerebroprotective properties[19] and antidepressant activity[20,21].

It is our project to produce new bioactive molecules. Currently used antibacterial agents are not effective due to the resistance developed by the bacterial. And therefore, it is an ongoing effort to synthesize new antibacterial agents.

In view of these observations we have synthesized s-triazine, 4a-m (scheme-1, Table -1) by the condensation of triazine with different aromatic amines. 6-chloro-N,N'-bis (5-nitro-1,3-benzothiazol-2-yl)-1,3,5-triazine-2,4-diamineafforded the title compounds 1a-1l respectively (scheme -1) the series of compounds were characterization by IR and NMR analysis.

II. METHODS AND MATERIAL

Biological Activity

Antibacterial Activity: Antibacterial activity was carried out by broth dilution method. Antibacterial activity was carried out by broth dilution method[22]. Concentrations of 1000, 200, 100, 50, µg/ml respectively (Table 2) of compound 1a-1l.

Antifungal Activity: Same compounds were tested for antifungal activity against *C. Albicans A.Niger and A. Clavatus* at concentrations of 1000, 500, 200, and 100 and 50 µg/ml respectively (Table 2) of compound 1a-1l. The results are recorded in the form of primary and secondary screening. Each synthesized drug was diluted to obtain 1000 µg/mL concentration, as a stock solution.

Experimental Section

Melting points were taken in paraffin bath and are uncorrected. IR spectra were recorded on FTIR-BRUKER spectrometer (V_{max} in cm^{-1}); Purity was checked by TLC using TLC aluminum sheets silica gel 60, supplied by E.Merck. The spots were located by keeping the plates in iodine vapor. 5-nitro-1,3-benzothiazol was prepared by methods as described in contain[23-25].

For 1a compound: IR (kbr): 3454 (-N-H str., sec.amine), 3083(-C-H str., aromatic), 1527 (> C = N- str., ter. Amine), 1350 (C-NO_2 STR.), 1122 (C-S-C str., thiazol), 952 (C-Cl str., aromatic), 808 (disubstituted aromatic),1431 (C = N str., sec.amine).
NMR Spectra: 1H NMR spectra, were recorded in CDCl3 solution on a Bruker Avance DPX 200 MHz spectrometer Chemical shifts are reported as δ (ppm) relative to TMS as internal standard.10.08δ (s, -NH, 2H), 9.29 δ (s, -NH, 1H), 9.44 δ (s, -NH, 2H), 6.54 δ (s, Ar-H, 8H).

Preparation of 6-chloro-N, N'-bis (5-nitro-1,3-benzothiazol-2-yl)-1,3,5-triazine-2,4-diamine:

In a conical flask, 1,3,5-triazine (1) (0.01 mol) was taken acetone (40 ml) and 5-nitro-1,3-benzothiazol-2-amine (2) (0.02 mol) was added to it. To this mixture, 4% NaOH was added drop wise at room temperature. Stirred the solution for 5 h. The reaction mixture was pour onto crushed ice with constant stirring. And it was neutralized with dil. HCl. The solid was filtered and washed with water. The product was recrystallized from acetone. M.p. 196ºc; yield 71.00%.

Preparation of N^2,N^4-bis(5-nitro-1,3-benzothiazol-2-yl)-N^6-aryl-1,3,5-triazine-2,4,6-triamine:

In a round bottom flask, 6-chloro-N, N'-bis (5-nitro-1, 3-benzothiazol-2-yl)-1, 3, 5-triazine-2, 4-diamine. (3) (0.01 mol) and 1,4-dioxane (10 ml) was taken. To this mixture, aniline (0.01 mol) was added. The pHwas adjusted to neutral by adding 8% NaOHin it . The reaction mixture was refluxed for 2.5 h. And was poured onto crushed ice with constant stirring. The mixture was then neutralized with dil. HCl. The product was filtered and washed with cold water. The product was dried and recrystallized from methanol. M.p. 286ºc; Yield 69%.

III. RESULTS AND DISCUSSION

Scheme 1:

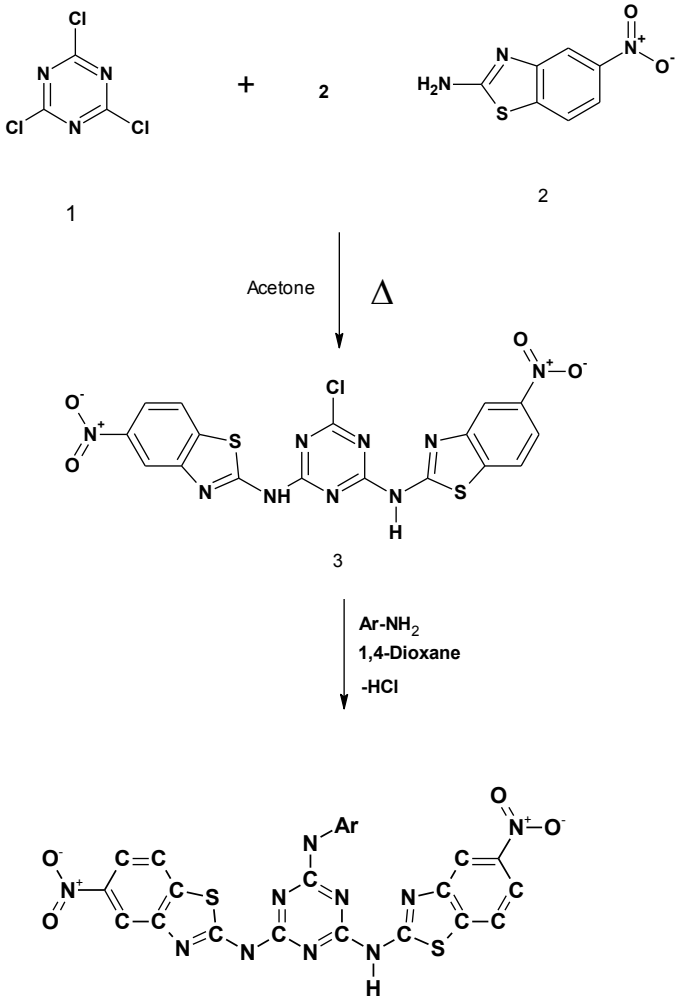

Figure 1. 1a-1l

Table 1 : Physical constant of the compounds (1a-1l):

Compd.	-Ar	Molecular Formula	m.p. (ºC)	Yield (%)	C (%) Found	C (%) Reqd.	N (%) Found	N (%) Reqd.
1a	$-C_6H_5$	$C_{23}H_{14}N_{10}O_4S_2$	220	65	49.44	49.46	25.06	25.08
1b	$-3-Cl-C_6H_4$	$C_{23}H_{13}ClN_{10}O_4S_2$	160	59	46.52	46.58	23.60	23.62
1c	$-4-Cl-C_6H_4$	$C_{23}H_{13}ClN_{10}O_4S_2$	226	54	46.54	46.58	23.59	23.62
1d	$-3-NO_2-C_6H_4$	$C_{23}H_{13}N_{11}O_6S_2$	210	65	45.70	45.77	25.51	25.53
1e	$-4-NO_2-C_6H_4$	$C_{23}H_{13}N_{11}O_6S_2$	245	62	45.71	45.77	25.49	25.53
1f	$-4-Br-C_6H_4$	$C_{23}H_{13}BrN_{10}O_4S_2$	170	57	43.30	43.34	21.95	21.97
1g	$-4-F-C_6H_4$	$C_{23}H_{13}FN_{10}O_4S_2$	184	64	47.85	47.91	24.20	24.29
1h	$-2-C_5H_4N_2$	$C_{22}H_{13}N_{11}O_4S_2$	196	65	47.19	47.22	27.50	27.54
1i	$-4-C_5H_4N_2$	$C_{22}H_{13}N_{11}O_4S_2$	223	68	47.20	47.22	27.49	27.54
1j	$-N-CH_3-C_6H_4$	$C_{24}H_{16}N_{10}O_4S_2$	290	59	50.30	50.34	24.40	24.46
1k	$-4-CH_3-C_6H_4$	$C_{24}H_{16}N_{10}O_4S_2$	288	56	50.29	50.34	24.41	24.46
1l	$-2-NO_2-C_6H_4$	$C_{23}H_{13}N_{11}O_6S_2$	256	55	45.74	45.77	25.50	25.53

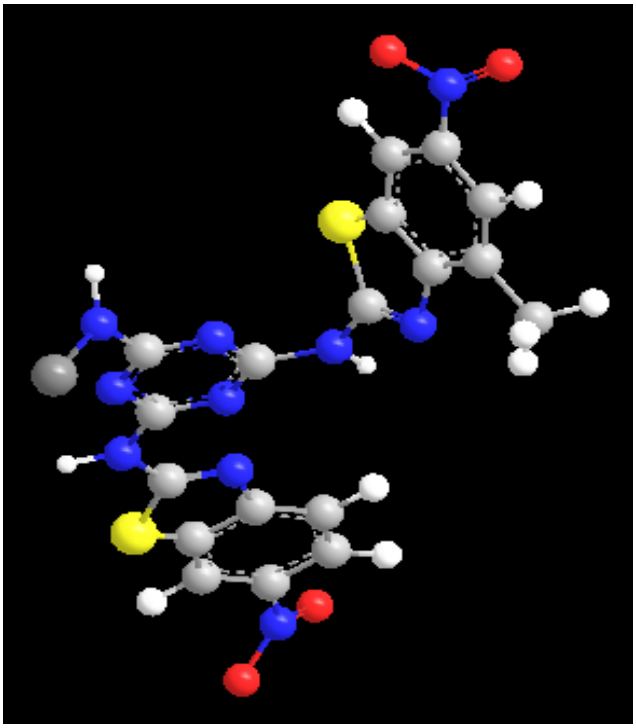

Figure 2. 3d-structure of : 1a

Table 2 : Antibacterial and Antifungal Activities:

SR NO.	Minimal bactericidal concentration (MBC) in µg/ml				Minimal fungicidal concentration (MFC) in µg/ml		
	E.coli	*P.aeruginosa*	*S.aureus*	*S.pyogenus*	*C.albicans*	*A.nigar*	*A.clavatus*
	MTCC	MTCC	MTCC	MTCC	MTCC	MTCC	MTCC
	- 443	-1688	-96	- 442	-227	-282	-1323
1a	100	50	100	200	500	500	500
1b	100	100	500	500	100	100	500
1c	100	250	25	500	100	100	100
1d	50	500	500	500	50	50	50
1e	500	500	100	250	50	50	100
1f	100	250	250	500	100	100	100
1g	500	250	250	500	500	1000	1000
1h	50	500	500	500	500	500	500
1i	50	500	1000	1000	50	50	50
1j	100	500	100	100	200	200	200
1k	250	250	100	250	50	100	100
1l	500	250	100	200	100	100	500

IV.CONCLUSION

In this work, a series of compounds comprising of S-triazine based chalcone were successfully synthesized using this method. s-triazine provided a versatile synthetic approach for the synthesis of differently bioactive substituted triazine. The synthetic yields of the generated products are ranged from 50 to 70 % and their structures were established by spectral data (IR and NMR). Finally, all of synthesized compounds have been tested by elemental and spectral analysis.

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