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Synthesis of Some 3,10-Disubstituted-6,13-dichloro-*bis*[s-triazolo (3,4-b)-1,3,4-thiadiazino-(5,6-b:5´,6´-e)-cyclohexa-1,4-diene]derivatives as Potential Bactericides

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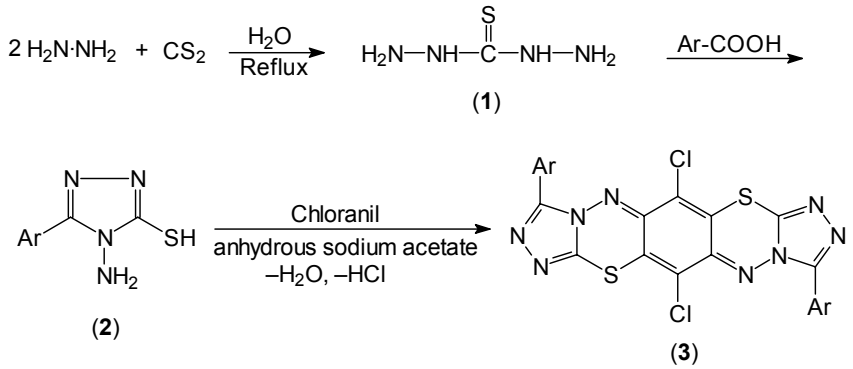
Reaction of hydrzine hydrate and CS_2 gives thiocarbohydrazide (**1**) which reacts with different aromatic acids in ethanol to give 3-substituted-4-amino-5-mercapto-s-triazoles (**2**). The condensation of **2** with chloranil in presence of anhydrous sodium acetate and absolute alcohol lead to the formation of 3,10-disubstituted-6,13-dichloro-*bis*[s-triazolo-(3,4-b)-1,3,4-thiadiazino-(5,6-b:5´,6´-e)-cyclohexa-1,4-diene]derivatives (**3**). The antibacterial activity of title compounds have been evaluated against *S. aureus* and *E. coli*.

Key Words: S-Triazole, Thiadiazine derivatives, Antibactierial activity.

INTRODUCTION

Heterocycles bearing symmetrical triazole ring have been reported to show a broad spectrum of biological activities[1,2]. In continuation of our studies on condensed heterocycles, some novel triazole derivatives have been synthesized and their antibacterial activities evaluated against *S. aureus* and *E. coli*. The fused triazolo-1,3,4-thiadiazine nucleous are associated with diverse biological activities[3-8]. The present communication deals with the synthesis and antibacterial activity of 3,10-disubstituted-6,13-dichloro-*bis*[s-triazolo-(3,4-b)-1,3,4-thiadiazino-(5,6-b:5´,6´-e)cyclohexa-1,4-diene]derivatives (**3**).

The required compound thiocarbohydrazide[9] (**1**) and 3-substituted-4-amino-5-mercapto-s-triazole[10] (**2**) were prepared by known method. The reaction of various s-triazoles with chloranil in presence of anhydrous sodium acetate yield the 3,10-disubstituted-6,13-dichloro-*bis*[s-triazolo-(3,4-b)-1,3,4-thiadiazino-(5,6-b:5´,6´-e)cyclohexa-1,4-diene]derivatives (**3**) (**Scheme-I**).



Ar = (a) 4-H_3CO-C_6H_4 (b) 2-H_3CO-C_6H_4 (c) 4-O_2N-C_6H_4 (d) 2-O_2N-C_6H_4 (e) 4-Cl-C_6H_4 (f) 3-Cl-C_6H_4 (g) 4-$(CH_3)_3C$-C_6H_4 (h) 4-HO-C_6H_4 (i) 2-HO-C_6H_4

Scheme-I

EXPERIMENTAL

All the melting points were taken in open capillary tubes and are uncorrected. IR (KBr, cm^{-1}) spectra were recorded on Jasco FT/IR-5300 and ^1H NMR (DMSO-d_6) were recorded on Perkin-Elmer spectrometer using TMS as reference compound (chemical shift in δ ppm).

3,10-Disubstituted-6,13-dichloro-*bis*[s-triazolo-(3,4-b)-1,3,4-thiadiazino-(5,6-b:5′,6′-e)cyclohexa-1,4-dienes (3a-i): Mixture of **2** (0.02 mol), chloranil (0.01 mol) and anhydrous sodium acetate (0.015 mol) in absolute ethanol (40 mL) was refluxed on steam bath for about 4 h. The reaction mixture was kept at room temperature and brownish-red coloured soild was separated. The solid was filtered, washed thoroughly with water and was recrystallized from DMF.

RESULTS AND DISCUSSION

All the compounds gave satisfactorily elemental analysis. The physical and spectral data of the synthesized compounds are given in Table-1.

Antibacterial activity: The synthesized compounds **3a-i** were evaluated for their antibacterial activity at three different concentrations *viz.*, 1000, 100 and 10 ppm against *S. aureus* and *E. coli* by known method[11]. Results were compared with commercial bactericide ampicillin tested under similar conditions. All the compounds were found to have significant antibacterial activity at 1000 ppm against both the organism, but the antibacterial activity of all compounds decreases considerably upon dilution (Table-2).

The screening results clearly show that the compound **3c-f** are more active than all other compounds. Compound **3a** and **3h** are more active

TABLE-1
PHYSICAL AND SPECTRAL DATA OF THE SYNTHESIZED COMPOUNDS (**3a-i**)

Compd.	Ar	m.p. (ºC) / Yield (%)	IR (ν_{max}, KBr, cm^{-1})	^{1}H NMR (DMSO-d_6) δ (ppm)
3a	4-H_3CO-C_6H_4	250 / 68	1620 (C=N), 1525 (C–N), 1220 (N–N=C), 720 (C–S)	7.5-7.8 (8H, m, Ar–H)
3b	2-H_3CO-C_6H_4	244 / 65	1610 (C=N), 1520 (C–N), 1240 (N–N=C), 700 (C–S)	7.2-7.9 (8H, m, Ar–H)
3c	4-O_2N-C_6H_4	298 / 75	1616 (C=N), 1520 (C–N), 1225 (N–N=C), 710 (C–S)	7.4-8.3 (8H, m, Ar–H)
3d	2-O_2N-C_6H_4	283 / 70	1620 (C=N), 1530 (C–N), 1235 (N–N=C), 715 (C–S)	7.0-7.8 (8H, m, Ar–H)
3e	4-Cl-C_6H_4	265 / 68	1610 (C=N), 1515 (C–N), 1225 (N–N=C), 720 (C–S)	6.6-7.1 (8H, m, Ar–H)
3f	3-Cl-C_6H_4	257 / 64	1615 (C=N), 1510 (C–N), 1240 (N–N=C), 710 (C–S)	6.8-7.2 (8H, m, Ar–H)
3g	4-$(CH_3)_3C$-C_6H_4	270 / 71	1610 (C=N), 1525 (C–N), 1236 (N–N=C), 718 (C–S)	1.82-1.88 (9H, m, $C(CH_3)_3$); 7.2-7.8 (8H, m, Ar–H)
3h	4-HO-C_6H_4	281 / 62	1620 (C=N), 1515 (C–N), 1225 (N–N=C), 710 (C–S)	6.0 (1H, s, OH), 7.0-8.0 (8H, m, Ar–H)
3i	2-HO-C_6H_4	368 / 60	1625 (C=N), 1520 (C–N), 1230 (N–N=C), 715 (C–S)	6.1 (1H, s, OH), 7.4-8.2 (8H, m, Ar–H)

TABLE-2
ANTIBACTERIAL DATA OF COMPOUNDS (**3a-i**)

Compd.	Ar	Average % inhibition after 48 h					
		S. aureus			*E. coli*		
		1000 ppm	100 ppm	10 ppm	1000 ppm	100 ppm	10 ppm
3a	4-H_3CO-C_6H_4	58	47	34	56	44	33
3b	2-H_3CO-C_6H_4	52	42	33	50	40	32
3c	4-O_2N-C_6H_4	71	62	51	69	60	50
3d	2-O_2N-C_6H_4	69	60	48	66	57	47
3e	4-Cl-C_6H_4	75	63	52	77	61	51
3f	3-Cl-C_6H_4	70	61	50	68	58	50
3g	4-$(CH_3)_3C$-C_6H_4	48	36	25	44	35	23
3h	4-HO-C_6H_4	55	46	34	54	43	32
3i	2-HO-C_6H_4	52	44	32	49	42	31
	Ampicillin	99	86	72	99	85	70

than compound **3b**, **3g** and **3i**. It is probably due to methoxy, hydroxy and *t*-butyl group at appropriate position in the aryl moiety present in heterocyclic ring.

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