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Synthesis of Some 2-Imino-N-(6′- Substituted Benzothiazo-2′-yl)-4-Thiazolidinones and Their Bis-Derivatives as Antibacterial Agents

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Several new 2-imino-N-(6′-substituted benzothiazolyl)-4-thiazolidinones Ia–f have been synthesised by the condensation of 6'-substituted benzothiazolyl thiourea with chloroacetic acid and fused sodium acetate and bis-2-imino-N-(6′-substituted benzothiazo-2′-yl)-5-chlorothiazolidine sulphide IIa–f from 4-thiazolidinones with thionyl chloride.

INTRODUCTION

A large number of compounds possessing benzothiazolyl moiety exhibit several pharmacological activities[1–3]. Thiazolidinones are known to possess diverse biological properties like hypnotic[4], anticonvulsant[5, 6], amoebicidal[7], antitubercular[8, 9], antifungal[10], antiradiation[11], nematocidal[12], antithyroid[13], anti-tumour and antiinflammatory[15]. In order to incorporate pharmacological properties of 4-thiazolidinones and their bis derivatives containing benzothiazolyl moiety therefore, we have prepared some 4-thiazolidinone derivatives and bis-thiazolidine derivatives.

The synthesis involves preparation of 6-substituted benzothiazolyl thiourea by heating 6-substituted-2-aminobenzothiazole with ammonium thiocyanide and hydrochloric acid which was treated with chloroacetic acid and fused sodium acetate in the presence of ethyl alcohol to obtain 4-thiazolidinone derivatives. These derivatives are treated with thionyl chloride in the presence of chloroform to give their bis derivatives (Scheme-1).

EXPERIMENTAL

All melting points were determined in open capillary in a liquid paraffin bath and are uncorrected. The purity of the compounds was checked by TLC. Then the structures were confirmed by spectral analysis.

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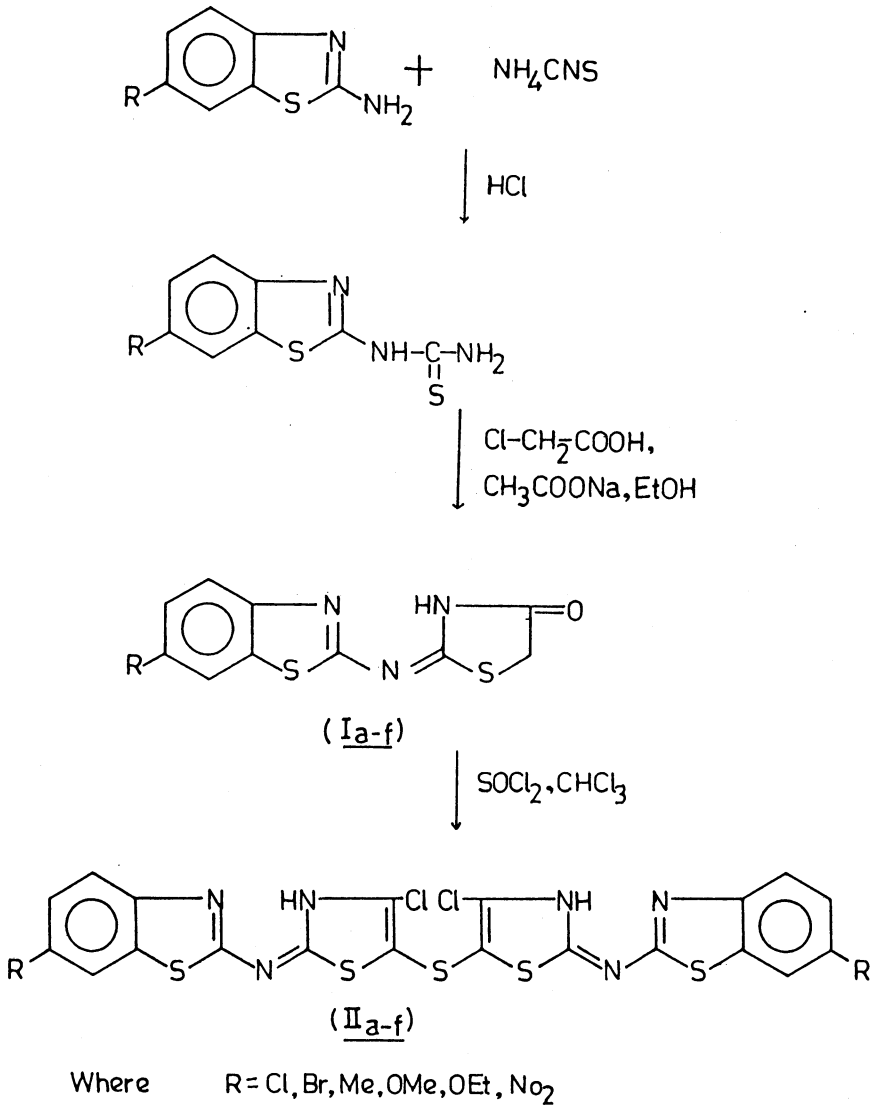

Scheme-1

Synthesis of 2-imino-N-(6′-chloro benzothiazo-2′-yl)-4-thiazolidinone Ia–f

A mixture of 6-chlorobenzothiazolyl thiourea (12.2 g, 0.05 mole), monochloroacetic acid (9.4 g, 0.1 mole), fused sodium acetate (8.2 g, 0.1 mole) in ethyl alcohol was refluxed on steam bath for 5 h. It was cooled and the solid obtained was filtered. The solid obtained was washed with water and crystallised from chloroform to get Ia, yield 54%, m.p. 264°C.

IR: ν_{max} 3300 cm^{-1}(N–H), 1690 cm^{-1}(>C=O), 1650 cm^{-1}(C=N), 1600 cm^{-1}(C=C).
PMR: δ 4.2 (s, 2H, —C(=O)—CH_2), 4.8 (s, 1H, NH), 6.8 to 7.3 (m, 4H aromatic).

All the compounds of this series were prepared by above procedure. Characterization data of these compounds are given in Table-1.

TABLE-1
CHARACTERISATION DATA OF 2-IMINO-N-(6′-SUBSTITUTED BENZOTHIAZO-2′-yl)-4-THIAZOLIDINONES (Ia-f).

Sr No.	R	Yield (%)	m.p. (°C)	Mol. formula	Elemental analysis % N	
					Found	Calcd.
Ia	Cl	54	264	$C_{10}H_6ON_3S_2Cl$	14.70	14.81
Ib	Br	62	195	$C_{10}H_6ON_3S_2Br$	12.95	12.80
Ic	CH_3	50	160	$C_{11}H_9ON_3S_2$	15.84	15.96
Id	OCH_3	58	135	$C_{11}H_9O_2N_3S_2$	15.20	15.05
Ie	OC_2H_5	52	187	$C_{12}H_{11}O_2N_3S_2$	14.27	14.33
If	NO_2	60	220(d)	$C_{10}H_6O_3N_4S_2$	19.17	19.04

All the compounds of this series were crystallised from chloroform

Synthesis of Bis-2-imino-N-(6′-chlorobenzothiazo-2′-yl)-5-chloro thiazolidine sulphide IIa–f

To the solution of 2-imino-N-(6′-chlorobenzothiazo-2′-yl)-4-thiazolidinone (2.73 g, 0.01 mole) in chloroform, thionyl chloride (1.8 mL, 0.015 mole) was added dropwise with continuous stirring. The reaction mixture was stirred for 9 h at room temperature and kept overnight. It was poured on crushed ice. The organic layer was separated from aqueous layer and concentrated to get IIa. It was crystallized from alcohol. Yield 42%, m.p. 176°C

IR: ν_{max} 3300–3200 cm^{-1} (N—H, broad), 1600 cm^{-1} (C=N).

PMR: δ 7.2 to 8.2 (m, 6H aromatic), 8.3 (bs, 2H, NH).

All the compounds of this series were prepared by above procedure. Characterization data of these compounds are given in Table 2.

TABLE-2
CHARACTERISATION DATA OF BIS-2-IMINO-N-(6′-SUBSTITUTED BENZOTHIAZO-2′-yl)-4-CHLOROTHIAZOLIDINE) SULPHIDES (IIa–f)

Sr No	R	Yield (%)	m.p. (°C)	Mol. formula	Elemental analysis % N	
					Found	Calcd.
IIa	Cl	42	176	$C_{20}H_8N_6S_5Cl_4$	13.15	13.24
IIb	Br	40	212	$C_{20}H_8N_6S_5Cl_2Br_2$	11.80	11.61
IIc	CH_3	44	184	$C_{22}H_{14}N_6S_5Cl_2$	14.26	14.16
IId	OCH_3	38	165	$C_{22}H_{14}O_2N_6S_5Cl_2$	13.33	13.44
IIe	OC_2H_5	46	202	$C_{24}H_{18}O_2N_6S_5Cl_2$	12.97	12.86
IIf	NO_2	45	195	$C_{20}H_8O_4N_8S_5Cl_2$	17.21	17.09

All the compounds of this series were crystallised from ethyl alcohol

Bactericidal Activities

Bactericidal activities of these compounds were screened[16] by using disc diffusion method against gram positive bacteria *S. aureus*, gram negative bacteria *E. coli* and *K. pneumoniae*. Out of 12 compounds seven were found to be against one or more strains of bacteria *in vivo*. Other compounds were found to be inactive. The antibacterial activities of these compounds are summarised in Table 3.

TABLE-3
ANTIBACTERIAL ACTIVITIES OF ISOLATED COMPOUNDS

Compd. No.	Antibacterial activity in millimetre against		
	Staphylococcus aureus	*Escherichia coli*	*Klebsiella pneumoniae*
Ia	20 mm	–	18 mm
Ib	11 mm	–	16 mm
Ic	07 mm	–	active
Id	–	09 mm	06 mm
Ie	–	–	–
If	–	–	–
IIa	–	17 mm	10 mm
IIb	–	–	08 mm
IIc	09 mm	07 mm	14 mm
IId	–	–	–
IIe	–	–	–
IIf	–	–	–

– = Inactive

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