Synthesis and Antibacterial Activity Of 4-Aroyl-2-Amino-1,3-Thiazoles

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Abstract:

5-(2-Hydroxypheny1)-4-benzoy1-2-amino-1,3-thiazoles were synthesized froml-(2-hydroxypheny1)-2-bromo-3-pheny1-1,3propanediones and thiourea by refluxing the reaction mixture in ethanolic NaOH for three hours.
The semisolid products obtained on acidification with dil. HC1 were separated, washed with water and crystallised from ethanol to get colourless crystalline compounds. The structures of these compounds were confirmed on the basis of chemical properties and spectral analysis.
These compounds when assayed for their antibacterial activity against several organisms, it was found that halogen substituted compounds can act as bactericidal agents more effectively.

Keywords: 2-bromo -1,3-propanediones,thiourea,4-aroyl-2-amino -1,3-thiazoles.

Introduction:

Thiazoles are well known for their commerical importance particularly for their biological activity. Hofmann for the first time reported the synthesis of derivaties of benzothizole such as 2-chlorobenzothiazole and 2-phenyl benzothiazole.[1] Hantzsch and coworkers reported the compounds containing simple thiazole nucleus in series of papers since 1888[2].

In 1935 Williams and co-workers demonstrated the existance of the simple thiazole ring in vitamin B_1 (thiamine)[3]. Shortly thereafter, the development of the sulfa drugs led to the recognition of the usefullness of sulfa thiazole and several of its derivaties as chemotherapeutic agents for the treatment of bacterial infections[4]. 2-Aminothiazoles have been obtained when a mixture of ketone and thiourea was treated with any of several oxidizing agents including the halogens[5]. Interaction of several aminothioureas with phenacil bromide has been investigated as a new route to 5-ben-zoyl-2,4-di-(substitutedamino) thiazoles[6]. 5-ary1-4-aroy1-2-ammo-1. 3-thiazoles have been synthesised from a-bromo-p-diketones using DMSO as a solvent. 6-amino-2-alkylthiobenzothiazoles are found to possess bacteriostatic activity against. Mycobac-teriuin tuberculosis[8]. 2,3 Trifluoromethyl-5-[(2-thienyl) pyrozole-1-y11-4-p-chlorophenylthiazole was synthesised[9]. from the corresponding 3-diketones in ethanol containing few drops of acetic acid. Yokoyama et al [10] have synthesised several thiazoles by the reaction of N-(methyl thioalkylidene) glycine ethyl ester with diethyl oxalate, acid halides and thionesters in the presence of base.

The work presented here describes the synthesis of 5-aryl-4-aroy1-2-amino-1,3-thiazoles from 1-(2-hydroxypheny1)-2-bromo-3-phenyl-1,3, proponediones and thiourea in ethanol containing aq, sodium hydroxide and their antibacterial activity.

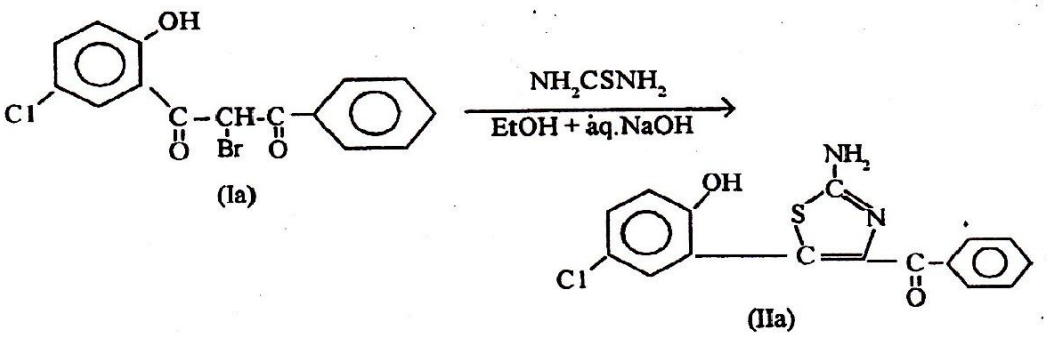
Materials and Method

Five 1-(2-hydroxypheny1)-2-bromo-3-phenyl-1,3-proponediones (la-e) were

prepared by bromination of 1-(2-hydroxyphenyl)-3-phenyl- 1 ,3-proponediones in 1 : 1 dioxane-DMSO mixture. The products formed on dilution with water were repeatedly washed with water and extracted with ether. The solvent when removed under reduced pressure gave colourless compounds the structures of which were established by chemical and physical methods.

The above compounds (la-e) were then reacted with thiourea in presence of aqueous NaOH in ethanol for three hours. The reaction mixture on cooling and acidification with dil. HC1 gave semisolid products. They were separated, washed with water and crystallised from ethanol to get colourless crystalline compound ,5-(2-hydroxyphenyl)-4-benzoy1-2-amino-1,3-thiazoles (Ila-e). The structures of these compounds were confirmed on the basis of chemical properties and spectral analysis.

Reaction -



Antibacterial Activity of the Compounds:

These compounds were tested for their antibacterial activities[11] against six test organisms namely Klebsiella pneumoniae, Escherichia coli; Proteus mirabilis, Stahylococcus aureus, Shigella dysenteiy and Salmonella typhi[12]. 'T'heir MIC values against these organisms were determined by 'Serial dilution method' using DMF as a solvent. The results are given in the following table 2.

Results:

The above compounds when tested for their antibacterial activity against *Kpneumoniae, E. coli, P. mirabilis, S. aureus. S. dysentery and S. typhi* [at a temperatureof 37°C (+ 1°C)], a large number of them showed positive results. 90% of the total samples tested showed antibacterial activity. All the compounds are found to be active against K. pneumoniae, P. mirabilis, and S. Dysentery and The compounds Il_a and II_d are found to be active gainst all the aganisms. Hence it may be concluded that halogen substituted compounds can act as bactericidal agents more effectively.

Table. 1- Spectral data -

1)	IR (KBr)		3440 (phenolic OH), 1610 (C=0),
			1571 (C=C), 1188 (C-0), 776 (C-C1),
			700 (C-Br)
	PMR ($CDC1_3$)		4.62 (S,1H-CH), 6.95-7.97 (m,8H,Ar-H),
			12.03 (S,1H,Ar-OH)

	I (2-Hydroxy-5-Chloro Pheny1)-2-Bromo-3-phenyl -1,3 -propanedione (Ia)		
2)	IR (KBr)	-	3231 (NH2), 3085 (Phenolic OH), 1671 (C=Oof
			aroyl group), 1610 (C=N), 1443
			(N-C=N), 787 (C-Cl).
	PMR ($CDCl_3$)		6.82 (S, 2H, NH2), 7.24 (S, 1H, Ar-OH),
			7.5-8.2. (m, 8H, Ar-H) Anal.Calculated for $C_{16}H_{11}O_2N_2SCl$:C,58.09;H,3.32;N,8.47;S,9.68 Found:C,58.05;H,3.30;N,8.32;S,9.56

5(2-hydroxy-5 -chlorophenyl)-4-benzoy1-2-amino-1,3-thiazole(II_a)

Table. 2- Antibacterial Activity of compounds

Sr. No.	Compund (MP in ˚C)	MIC value (in'Jfg/ml) against test organism						
			K	*E.*	*P.*	*S.*	*S.*	*S.*
		Pneumoniae		*coli*	*mirabilis*	*aureus*	*dysentery*	*typhi*
1.	5-(24iydroxy-5-chlorophenyl)-4-	125		500	250	500	1000	500
	-benzoy1-2-aniino-1,3-thiazole (Ila) (175)							
2.	5-(2-hydroxyphenyl)-4-benzoyl -	250		1000	250	-	500	1000
	2-amino-1,3-thiazole (IIb) (128)							
3.	5-(24iydroxy-5-niethylphenyl)-	500		-	500	1000	500	500
	4-bcnzoy1-2-amino-1,3							
	thiazole(IIc) (126)							
4.	5-(2-hydroxy-3-bromo-5-	125		250	250	500	250	500
	methyl-phenyl)-4-benzoyl-2-							
	amino-1,3-thiazole (lid) (140)							
5.	5-(2-hvdroxy-4-	250		500	125	500	500	D
	methylpheny1)--4-(4-methoxy							
	benzoy1)-2-amino-1,3-							
	thiazole(Ile) (106)							

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