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Synthesis of 2-[(1-Phenyl) (Aryl) Azo] Methyleneimino -6-Chloro/ Fluoro Benzothiazoles and their Antibacterial Activity

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ABSTRACT: 6-Chloro-2-aminobenzothiazole (1) on treatment with hydrazine hydrate and HCl gave 6-chloro-2-hydrazinobenzothiazole (2), which on condensation with substituted aromatic aldehydes affords aryl substituted (6-chloro-1, 3,-benzothiazole-2-yl) hydrazone (3). The latter on treatment with aryl diazonium chloride at 0-5 ^{o} c furnishes respective 2-[(1-phenyl/ aryl) azo] methyleneimino-6-chlorobenzothiazoles (4). The antibacterial activities of these compounds have been assayed against various Gram -ve, Gram +ve and fungal organisms. The constitutions of the products have been elucidated by IR, NMR spectral data and elemental analysis.
Key-words:- 2-Aminobenzothiazole, Hydrazone, Formazan, Antifungal and Antimicrobial.

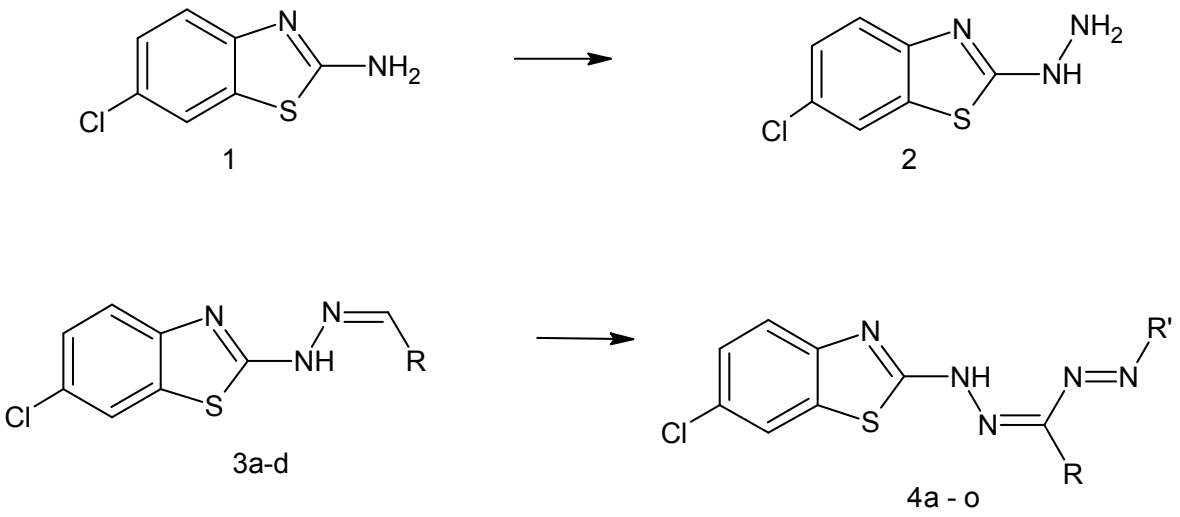
Introduction

2-Aminobenzothiazole and its derivatives have been reported to possess antimicrobial[1] and various other pharmacological activities like anticancer, antiulcer, antihistaminic, anti-inflammatory activity and analgesic activities.[2- 6] Furthermore the formazan nucleus is pharmacophoric in nature[7, 8]. It was envisaged that the compounds containing these moieties in their molecular frame work might show enhanced biological activity. Keeping this in view and in continuation of our search for pharmacologically potential benzothiazole derivatives, we now report the synthesis of 2-[(1-phenyl/aryl) azo] methyleneimino-6-chloro benzothiazoles and their antibacterial activity scheme-I.

The required starting material 6-chloro-2-amino benzothiazole (**1**) have been prepared by the routine procedure reported in the literature.[9] The compound (**1**) was then portion wise added to a mixture of cold solution of hydrazine hydrate, conc. HCl, followed by ethyleneglycol gave 6-chloro-2-hydrazino benzo thiazole**(2),** which on condensation with substituted aromatic aldehydes affords aryl substituted (6-chloro-1, 3,-benzothiazole-2-yl) hydrazone (**3**). This on treatment with aryl diazonium chloride at 0-5 ^{o} c gave2-[(1-phenyl) (aryl) azo] methyleneimino-6-chloro benzothiazoles (**4**).

Antimicrobial Activity

All the newly synthesized compounds were screened for their antimicrobial activity against *E.coli, pseudomanas, staphylococcus aereus, bacillus subtilis and* antifungal activity against *Aspergillus.Flavus, and candida albicans* using DMF as solvent at 50 and 100µg/ml concentration by using cup-plate method. After 24hrs of incubation at 37^{0} the zone of inhibition were measured in mm. The activities were compared with known reference drugs like procaine penicillin, streptomycin and griseofulvin. (Table-2)



scheme--1

Experimental

Melting points were determined in open capillaries and are uncorrected. The purity of all the synthesized compounds was checked by TLC, IR spectra were recorded on Shimadzu FTIR 8400S by using KBr disc method and the NMR spectra were recorded on AV-400 Instrument.

Synthesis of 6-chloro-2-hydrazino benzothiazole (2)
Concentrated. HCl (1ml) was added drop wise to hydrazine hydrate (0.2mol. 1ml 80%)at 5-10^0 followed by ethyleneglycol (40ml).To the above solution 2-aminobenzothiazole(0.01mol, 1.85g) was added in portions. It was then refluxed for 3-4 hrs, cooled and poured onto crushed ice. The separated solid was filtered, dried and recrystalized from ethanol.

Synthesis of aryl substituted (6-chloro-1, 3,-benzothiazole-2-yl) hydrazone (3)
6-chloro-2-hydrazinobenzothiazole(**2**), (0.1mole) and appropriate substituted aldehyde(0.1mol) were refluxed in ethanol in presence of acetic acid on a water bath for 4hrs.The resultant solution were cooled and poured on to crushed ice . The solid that separated was filtered and recrystalised from ethanol.

Synthesis of 2-[(1-phenyl) (aryl) azo] methyleneimino-6-chloro benzothiazoles (4a-o)
Aniline (0.02mole) in glacial acetic acid (2ml) and HCl (1.5ml) was diazotized with sodium nitrite (0.2g in 2ml water) at 0-5^0. The resultant benzenediazonium chloride solution was added with stirring to compound **3** (0.01mole) in pyridine (3ml) in ice-cold condition. The reaction mixture was left overnight at room temperature and poured into cold water (250ml) with continuous stirring when a dark coloured solid separated out. It was filtered, washed repeatedly with water and recrystalized from methanol to afford the title compounds (**4**a-o**)**

IR data 3150-3150 (N=H); 2880-2950 (-CH of aromatic and aliphatic); 1600-1620(C=N); 1520-1580cm-^{1}(N=N);
NMR data of 4f; 7.09-7.98 (m, 12 H, Ar -H); 8.16 (S, 1H,-NH); 10.40∂ (S, 1H, OH);
NMR data of 4n; 7.13-8.07 (m, 1H, Ar-H); 8.67-8.70∂ (S, 1H, NH);

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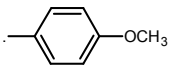
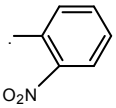
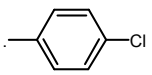
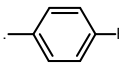
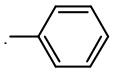
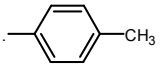
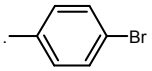
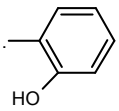
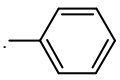
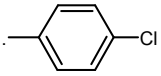
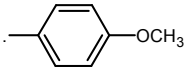
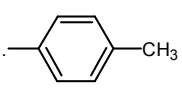
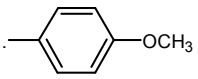
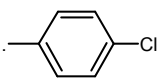
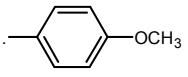
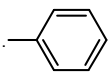
Table-1:Physical data of aryl substituted (6-chloro-1, 3,-benzothiazole-2-yl) hydrazone (3a-d) and 2-[(1-phenyl) (aryl) azo] methyleneimino-6-chloro benzothiazoles (4a-o)

Compound	R	R^1	MP (^{0}C)	Yield (%)
3a		------	205	80
3b		------	210	78
3c		-----	175	82
3d		-----	195-200	70
4a			174	75
4b			117-118	78
4c			215	80
4d			89-92	75
4e			185	80
4f			162-165	75
4g			145-148	80
4h			138-140	70
4i			128-130	70
4j			102-105	74
4k			78-80	75

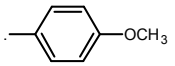
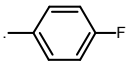
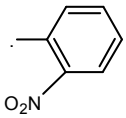
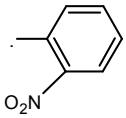
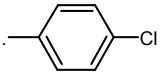
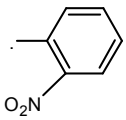
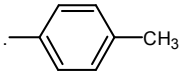
4l			88-90	80
4m			100-104	80
4n			98-100	75
4o			85-88	70

Table-2: Antimicrobial activity of 2-[(1-phenyl/aryl)azo]methyleneimino-6-chloro benzothiazoles

SL NO	NAME OF THE COMOUNDS	S. AEREUS		B. SUBTILIS		E.COLI		PSEUDO MONAS		CANDIDA ALBICANS		ASPERGIL LUS FLAVUS	
		50 µg	100µg	50 µg	100µg	50 µg	100µg	50 µg	100µg	50 µg	100µg	50 µg	100µg
1	**Procaine penicillin**	19	22	19	22	-	-	-	-	-	-	-	-
2	**Streptomycin**	-	-	-	-	18	21	18	21	-	-	-	-
3	**Griseofulvin**	-	-	-	-	-	-	-	-	19	20	20	21
4	**4a**	13	15	11	14	10	12	15	15	13	14	11	15
5	**4b**	12	15	12	12	15	17	13	15	12	16	14	16
6	**4c**	14	14	11	14	15	16	10	15	14	16	13	17
7	**4d**	11	13	14	16	14	12	11	16	11	17	16	16
8	**4e**	13	14	11	17	15	01	12	16	11	13	12	14
9	**4f**	08	10	13	15	15	16	14	17	12	18	14	16
10	**4g**	12	13	15	14	06	07	13	18	13	15	15	17
11	**4h**	07	09	17	15	07	07	11	13	14	17	11	14
12	**4i**	14	12	13	16	11	12	10	14	10	16	09	12
13	**4j**	11	11	16	17	16	18	10	13	09	14	12	12
14	**4k**	06	08	13	13	12	15	11	13	11	13	10	11
15	**4l**	16	17	15	11	07	09	12	17	14	15	12	14
16	**4m**	15	16	11	11	12	13	15	15	12	13	13	15
17	**4n**	15	17	11	10	16	17	13	13	14	19	16	18
18	**4o**	10	12	15	15	11	10	10	14	12	18	11	19

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