SYNTHESIS AND ANTI-BACTERIAL, ANTI-FUNGAL ACTIVITY OF NOVEL ANALOGS OF FLUORO BENZOTHIAZOLE SCHIFF'S BASE

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ABSTRACT

4-Fluoro-3-chloroanilline treated with Potassium thiocyanate in presence of Glacial acetic acid and bromine was converted into 2-amino-6-fluoro-7-chlorobenzothiazole. The synthesized compound in presence of m-nitro benzaldehyde refluxed in ethanol to obtained 6-fluoro-7-chloro benzothiazole schiffs base. The above said compound was treated with ortho, meta and para nitroanillines, ortho, meta, para chloroanillines, morpholino, Piperazine, diphenylamine in the presence of DMF to obtain different analogs. Some analogs showed promising anti-bacterial and anti-fungal activity.

KEY WORDS: Benzothiazole, Schiff's base, Anti-bacterial, Anti-fungal activity.

1.INTRODUCTION

Fluorobenzothiazoles (Feller, 1995) exhibit the broad range of antibacterial (Sangai and Rastivona, 1986), antifungal (Gurupadiaiah, 1998), anthelmintic (Labendeno, 1980), anti-inflammatory (Areas, 1991) and antitubercular activity (Kapustyuk, 1963). In the present study we made an attempt to link fluorobenzothiazoles with m-nitro benzaldehyde for generating Schiffs base and various novel analogs were screened for antibacterial and antifungal activity (Lipathy, 1981; Eucast, 2000).

2.MATERIAL AND METHODS

Purity of compounds was checked by TLC. Melting points were determined by open capillaries method and are uncorrect. IR spectra (NaCl) are recorded on FTIR (Schimadzu-84005) spectrophotometer using nujol mull technique.

First Step

Synthesis of 2-amino-6-fluoro-7-chloro-(1,3)benzothiazole (1)

To the glacial acetic acid (20ml) which is cooled below room temperature, 8gm (0.08mol) of potassium thiocyanate and 1.45g (0.01 mol) of fluorochloroaniline was added. The mixture was placed in freezing mixture of ice and salt, mechanically stirred while 1.6ml of bromine in 6ml of glacial acetic acid was added, from a dropping funnel at such a rate that the temperature never raised beyond room temperature. After all the bromine was added (105min), the solution was stirred for 2 hours below room temperature and at room temperature for 10 hours, it was then allowed to stand over night, during which period an orange precipitate settle at the bottom, water (6ml) was added quickly and slurry was heated at 85^{0}c on a steam bath and filtered hot. The orange residue was placed in a reaction flask and treated with 10ml of glacial acetic acid heated again to 85^{0}c and filtered hot. The combined filtrate was cooled and neutralized with concentrated ammonia solution to p^H 6. A dark yellow precipitate was collected. Recrystalised from benzene, ethanol (1:1), after treatment with animal charcoal gave yellow plates of 2-amino-6-fluoro-7-chloro-(1,3) benzothiazole. After drying in a oven at 80^{0}c, the dry material (1gm 51.02%) melted at 210-212^{0}c. UV-307.4, 269nm, IR 1542cm^{-1}(aromatic C=C) and 3475cm^{-1} (NH_2); 1456 cm^{-1}(thiazole), 1215 cm^{-1}(aromatic-F), 712 cm^{-1}(aromatic-Cl).

Second Step

Synthesis of 2-[p-dimethylaminobenzylidine]-6-fluoro-7-chloro (1, 3) benzothiazole (2)

0.01 mol of 2-amino-6-fluoro-7-chloro (1, 3) benzothiazole with 0.015 mol solution of p-dimethylaminobenzaldehyde, added 20 ml ethanol and 3-4 drops of HCl and refluxed for 2-3 hrs. Solution cooled and poured into crushed ice. Recrystalised with benzene and ethanol.

Preparation of various derivatives (E_1-E_9)

Schiffs base treated with equimolar quantities of various aromatic amines, refluxed for 2 hours in presence of DMF, recrystalised from alcohol and benzene.

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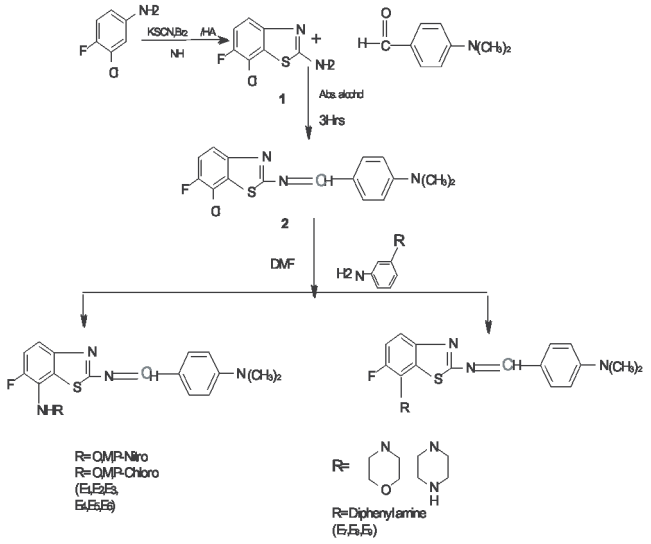

Table No. 1 Analytical Data of the Compounds (E_1-E_9)

Compds	R	M.P (°C)	Yield (%)	Molecular Formula	Molecular Wt.	Elemental Analysis Data (Calculated in %)		
						C	H	N
E_1		172	63	$C_{22}H_{18}N_5O_2SF$	435	60.68	4.13	16.09
E_2		190	69	$C_{22}H_{18}N_5O_2SF$	435	60.68	4.13	16.09
E_3		180	77	$C_{22}H_{18}N_5O_2SF$	435	60.68	4.13	16.09
E_4		172	57	$C_{22}H_{18}N_4SFCl$	425	62.11	4.23	13.17
E_5		162	76	$C_{22}H_{18}N_4SFCl$	425	62.11	4.23	13.17
E_6		168	69	$C_{22}H_{18}N_4SFCl$	425	62.11	4.23	13.17
E_7		170	52	$C_{20}H_{17}N_4OSF$	380	63.15	4.47	14.17
E_8		167	58	$C_{20}H_{18}N_5SF$	379	63.32	4.74	18.46
E_9	$-N(C_6H_5)_2$	132	77	$C_{28}H_{23}N_4SF$	466	72.10	4.93	12.01

Table2. IR spectral assignments of synthesized compounds (E_1-E_9)

Compounds	Characteristic absorption bonds (in cm^{-1})						
	C=N Str.	Aro.C=C Str.	C-F Str.	NO_2	C-Cl	3°-Nitrogen	C-H
E_1	1630	1688	1232	1396	---	3088	3477
E_2	1570	1677	1243	1399	---	3084	3433
E_3	1600	1667	1244	1409	---	3066	3409
E_4	1630	1610	1228	---	1197	3080	3435
E_5	1667	1600	1300	---	1198	3100	3400
E_6	1700	1656	1345	---	1127	3090	3434
E_7	1625	1693	1244	---	---	3074	3456
E_8	1630	1606	1247	---	---	3095	3479
E_9	1620	1780	1271	---	---	3074	3477

Anti-bacterial and Anti-fungal Screening (Elias and Rao,1988)

The anti-bacterial activity was tested against Gram positive and Gram negative bacteria and antifungal activity against various fungal strains. Synthesized compounds were screened for their in vitro antibacterial activity against the standard strains *S. aureus, B. subtilis, E. coli,* and the yeasts *C. albicans, A.flavus and A.niger.* To evaluate the activity of synthesized compounds against bacteria minimum inhibitory concentrations (MICs) were determined. Procaine penicillin and Streptomycin (the reference antibacterial drug) and Griseofulvin (the reference antifungal drug) were used as positive control. The results are described in the table no. 3.

Table3. Anti-bacterial and Anti-fungal of synthesized compounds (E_1-E_9)

Compounds	Mean Zone of Inhibition (in mm)					
	Bacteria			Fungie		
	S.aureus	*B.subtillis*	*E.coli*	*C.albicans*	*A.flavus*	*A.niger*
Procaine penicillin	20	24	25	---	---	---
Streptomycin	17	23	23	---	---	---
Griseofulvin	---	---	---	20	18	24
E_1	10	14	11	13	10	09
E_2	09	12	11	08	06	13
E_3	10	14	06	11	13	14
E_4	08	14	10	12	15	12
E_5	09	13	11	14	16	15
E_6	14	16	05	09	11	13
E_7	07	11	13	11	12	15
E_8	13	14	12	16	13	14
E_9	17	16	15	12	16	18

3.RESULTS AND DISCUSSION

An attempt is made to synthesize the novel analogs of the fluorobenzothiazole schiffs base using p-dimethylamino benzaldehyde and screened for anti-bacterial and anti-fungal activity using various bacterial and fungal strains and some of the analogs showed significant activity.

REFERENCES

Areas J.J, Chem.Abst.., 14, 1991, 71453d.

Elias G and Rao M.N.A, Indian J.Exp.Bio., 26, 1988, 540.

Eucast, definitive documents, E.Def.3.1, 2000.

Feller R J, Fluorine Chem., 33, 1995, 366.

Gurupadiaiah B.M, Jayachandran E, Nargund L.V.G, Shivkumar B, Indian J.Heterocycl., 7, 1998, 213-216.

Kapustyuk S.M, Nauk Z.B, Prats, Med.Inst., 24(78), 1963, 1077f.

Labendeno N.Yu., Chem.Abstr., 92, 1980, 922882.

Lipathy T, Foltinova P, Chem.Abstr., 94, 1981, 10322u.

Sangai S.K, Rastivona P.K, Chem.Abstr., 104, 1986, 34029.