SYNTHESIS AND BIOLOGICAL EVALUATION OF 2-(N-SUBSTITUTED)-6-FLOURO-7-SUBSTITUTED BENZO (1, 3-B) THIAZOLES

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ABSTRACT

Sixteen new 2-(N-substituted)-6-flouro-7-substituted benzo (1,3-b)thiazoles have been prepared from 2-aminobenzothiazole. The prepared compounds were characterized by spectral (IR and NMR) data. Selected compounds were screened for antibacterial and antifungal at 50 ìg/ml and 100 ìg/ml concentrations. Some to the compounds showed weak to moderate biological activity against organisms tested.

1. INTRODUCTION

Benzothiazoles have been widely investigated due to their wide range of biological and pharmacological activities. Benzothiazole containing compounds are reported to possess antimicrobial (Trivedi, 1992) , antimycobacterial (Sidoova E, 1986), antifungal (Sreenivasa GM, 2004), anti-inflammatory (. Sangal S.K, 1986) and local anesthetic activity (Costakes E, 1979). Schiff's bases are known to possess bactericidal (Jag Mohan and Sangeeta Kataria, 1997), anthelmintic activity (Moharram HH, 1994). Our earlier interest to incorporate benzothiazole moiety into biologically potent heterocycles (Sreenivas GM, 2004) and multifarious application of benzothiazoles and schiff's bases have prompted us to undertake the synthesis of titled molecules.

2-amino-6-flouro-7-chloro benzothiazole (Singh SP. and Vaid PK, 1986) when reacted with benzaldehyde it gives 2 a. absence of peak at 3240 cm^{-1}, presence of band at 1550 cm^{-1} for C=N stretching confirms the reaction. Further 2a was refluxed with o-nitro aniline it gave 3a. Absence of peak at 800 cm^{-1} (for C-Cl) and presence for peak at 1350 cm^{-1} corresponding to Ar-No_2 and ^{1}H NMR spectrum data agreed well with this structure .

2. MATERIALS AND METHODS

Biological activity

Some of the synthesized compounds were screened for antibacterial and antifungal activity by paper disc diffusion method (IP, 1996). Antibacterial activity was carried out against *Staphylococcus aureus* (gram + ve) and *Escherichia coli* (gram – ve)using procaine penicillin streptomycin as standard drugs respectively. The result of the study is given in Table-2.

Antifungal activity was screened against *Aspergillus flavus* and *Candida albicans* using Griseofulvum as standard drug. The results are shown in Table-3.

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Experimental

Melting points of synthesized compounds were taken by open capillary method and are uncorrected. IR spectra was recorded on Shimadzu spectrophotometer and PMR spectra in ($CDCl_{3)}$ on Perkin-Elmer R-32 (90 MHz) spectrophotometer using TMS as internal standard (Chemical shift in " ppm). The purity of the compounds was checked by TLC and spots were visualized by iodine vapours. Physical data of the synthesized compounds is given in Table-1.

Preparation of 2-substituted-6-flouro-7-chlorobenzo(1,3-b)thiazole(2 a –d) :

Equimolar mixture of 2-amino-6-flouro-7-chlorobenzo(1,3-b)thiazole (1) and benzaldehyde (0.05 mol) in 50 ml of mixture of ethanol and glacial acetic acid (95: 5) were refluxed for 5 hr on steam bath. The mixture was allowed to cool , then poured into crushed ice. The solid thus separated out was collected by filtration, dried and recrystalised from benzene and ethanol.

Preparation of 2-substituted-6-flouro-7-substitutedbenzo(1,3-b)thiazole (3 a –d , 4 a – d, 5 a-d, 6 a-d):

Equimolar mixture of 2-substituted-6-flouro-7-chlorobenzo(1,3-b)thiazole and different aromatic anilines (0.01 mol) was refluxed in DMF for 6 hr on

steam bath. The reaction mixture was cooled to room temperature and poured into crushed ice. The compound thus obtained was filtered, dried and recrystalised from ethanol. 3a: IR (Nujol, Values in cm^{-1}) 3100 (Ar-CH), 1520 (C=N), 1200 (C-F), 850 (Ar-C = C), 1350 (Ar-No_2), 1600 (- NH bending) , 1450 (C-S); ^{1}H NMR (in " ppm): 6.25 (s , 1 H , -NH) 7.3-8.4 (m , 11 H , Ar H), 10.42 (s , 1H , -N = CH).

3. RESULTS AND DISCUSSION

In the present work series of schiff's base derivatives of benzothiazole were synthesized. Synthesized compounds were chartecterised by analytical and spectral studies. Some of the synthesized compounds were evaluated for antibacterial and antifungal activity by paper disc diffusion method.

Table-1
Physical data of titled compounds

Compound	R	R^1	Yield	M.P.(^{0}C)
2a	..	--	62	198
2b	2-OH	--	60	176
2c	2-NO_2	--	59	202
2d	4-N-(CH_3)$_2$	--	58	210
3a	..	..	52	179
3b	2-OH	2-OH	53	184
3c	2-NO_2	2-NO_2	53	176
3d	4-N-(CH_3)$_2$	4-N-(CH_3)$_2$	52	174
4a	..	..	63	175
4b	2-OH	2-OH	64	192
4c	2-NO_2	2-NO_2	61	188
4d	4-N-(CH_3)$_2$	4-N-(CH_3)$_2$	69	193
5a	..	..	76	169
5b	2-OH	2-OH	59	184
5c	2-NO_2	2-NO_2	72	168
5d	4-N-(CH_3)$_2$	4-N-(CH_3)$_2$	68	192
6a	..	..	48	143
6b	2-OH	2-OH	53	172
6c	2-NO_2	2-NO_2	49	155
6d	4-N-(CH_3)$_2$	4-N-(CH_3)$_2$	63	179

All the compounds gave satisfactory C, H N analysis.

Table-2
Antibacterial activity

Compound	Mean zone of inhibition			
	S .aureus		*E. coli*	
	50 µg/ml	100µ g / ml	50µ g /ml	100µg / ml
3a	10	19	08	14
3b	09	17	11	22
4a	11	22	13	25
4b	12	24	09	17
4d	09	19	12	23
5a	08	15	07	12
5b	07	14	10	19
6c	10	19	09	18
Std-1	18	28	--	--
Std-2	--	--	22	34

Std-1 : Procaine penicillin Std-2 : Streptomycin

Among the tested compounds 4a and 4b, 4a and 4b showed moderate antibacterial activity against gram + ve and gram – ve organisms respectively. In the antifungal study none of the tested compounds showed significant activity.

Acknowledgement:

The authors are thankful to Shri Sha.Bra. Chandramouleshwara swamiji, President, T.M.A.E.Society and Sri.T.M.Chandrahekariah, Manager, T.M.A.E.Society, Harapanahalli for providing necessary facilities through the principal, S.C.S.College of pharmacy, Harapanahalli to carry out this work.

Table-3
Antifungal activity

Compound	Mean zone of inhibition			
	C .albicans		*A. niger*	
	50 µg/ml	100µ g / ml	50µ g /ml	100µg / ml
3c	09	13	08	12
3d	08	11	--	--
4a	11	14	10	14
4d	07	16	09	10
5c	09	14	--	--
5d	10	15	11	15
6a	09	13	10	11
6b	12	17	11	16
6d	08	15	07	09
Std	15	23	17	26

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