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Synthesis of benzothiazole derivatives and study of their antifungal activities

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ABSTRACT

Synthesis of new benzothiazole derivatives, derived from the condensation of 2-amino-7-chloro-6 fluro benzothiazole with different aroyl chloride and obtained compounds has been (substituted phenyl carboxamido) benothiazole and obtained compounds has been subjected to a substitution reaction with different amines to yield 7alkyl/aryl amino-6-fluro-2-phenyl carboxamido benzothiazoles and 7alkyl/aryl amino-6-fluro-2 (3-nitro phenyl carboxamido) benzothiazoles. The synthesized compounds were screened for antifungal activities.

Key words: Benzothiazole derivatives and antifungal activity.

INTRODUCTION

Benzothiazole are the important group of hetarcocylic compound, several derivatives of which have been marked as biologically and pharmacologically active product. Of these 2 substituted derivative[1-2] have been found to be most potent. The literature survey revealed that, fluro benzothiazole[3] also posses different activities like antibacterial[4], anti-inflammatory[5], anthelmintic activity[6]. In view of this observation and our continue interest in the synthesis of biologically active heterocyclic compounds, it also though of interest to synthesize some new substituted phenyl carboxamido benzothiazole for better activity.

EXPERIMENTAL

Melting point of all derivatives was determined by open capillary method and are uncorrected. IR spectra obtained by KBr disc method using Shimadzu FT-IR-8400S Spectrophotometer. NMR spectra obtained by AVANCN 300Mz spectrometer and purity of the synthesized compound was determined by TLC using silica gel-G. Physical and analytical data are given in (Table 1). All the compounds gave satisfactory elemental analysis for C, H and N.

MATERIAL AND METHODS

All the chemicals used for the experimental work are analytical grade. Solvent and reagents were also or AR grade and purified before use.

Preparation of 2-amino-6-fluro-7-chloro benzothjiazole

To glacial acetic acid, (20ml) cooled below room temperature, were added 8gm (0.08mol) of potassium thiocyanate and 1.45g (0.01mol) of fluoro chloro aniline. The mixture was placed in freezing mixture of ice and salt and 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 rose beyond room temperature. After all 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 settled at the bottom, water (6ml) was added quickly and slurry was heated at 85°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°c and filtered hot. The combined filtrate was cooled and neutralized with concentrated ammonia solution to pH 6. A dark yellow precipitate was collected.

Synthesis of 7-chloro-6-fluro-(substituted phenyl carboxamido) benothiazole

A sodium of triethylamine (0.101gm 0.001mole) and 2-amino-7-chloro-6-fluro-benothiazole (II) (0.203gm, 0.001 mole) in 10ml of 1,4-Dioxan was stirred on a magnetic at 50-60°C for 50-60 minutes. To this added dropwise, a solution of different aroyl chloride (0.001 mole) in the 10ml dry 1,4-Dioxan at the same temperature. After the addition, reaction mass was stirred for 3 hours. It was then poured in crushed ice. The solids separate out was flittered and washed with 1% potassium bicarbonate solution and water. Recrystalised with suitable solvent.

III: (R=H): MP: 230°C

IR (KBr) bands 3090cm^{-1} (-NH), 1680cm^{-1} (C=O), 1610 cm^{-1} (C=N), 1150cm^{-1} (C-F) 685cm^{-1} (C-CL). ^{1}NMR ($CDCl_3$): 6.9-8.0 (m, 7H Ar-H), 11.25 (S, CONH).

M/S: m/2 306 (M^+) Peak. This happens to be agreement with mass number of assigned structure

Table 1: Physical and analytical data of compounds

S. No	Compound	R	R_1 and R_2	m.p. (°C)	mol formula	mol weight	yield (%)
1.	IVa	H	Dimethyl amino	181	$C_{16}H_{14}N_3OSF$	315	61
2.	IVb	H	Diethyl amino	218	$C_{18}H_{18}N_3OSF$	343	63
3.	IVc	H	N-methyl piperzino	210	$C_{19}H_{15}N_4OSF$	366	65
4.	IVd	H	p-toludino	215	$C_{21}H_{16}N_3OSF$	377	62
5.	IVe	NO_2	Dimethyl amino	178	$C_{16}H_{13}N_4O_3SF$	360	62
6.	IVf	NO_2	Diethyl amino	176	$C_{18}H_{17}N_4O_3SF$	388	63
7.	IVg	NO_2	N-methyl piperzino	178	$C_{19}H_{14}N_5O_3SF$	411	69
8.	IVh	NO_2	p-toludino	284	$C_{21}H_{15}N_4O_3SF$	422	64

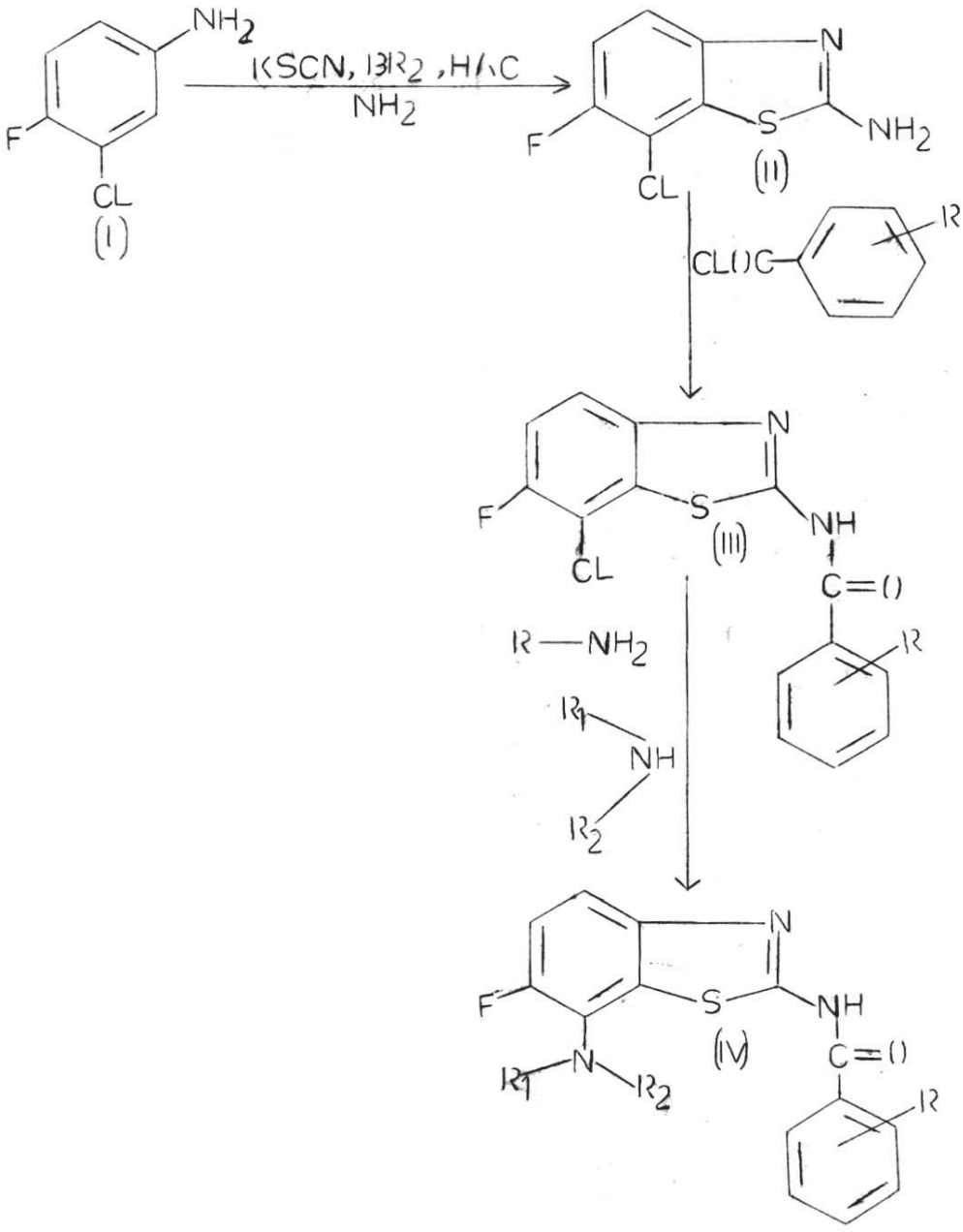
Table 2: Antifungal activity of compounds

S. No.	Compounds	Diameter of zone inhibition in (mm) Candida albicans		Aspergillus niger	
		50µg	100µg	50µg	100µg
1.	IVa	11	14	12	17
2.	IVb	10	12	10	16
3.	IVc	11	15	10	12
4.	IVe	13	18	11	16
5.	IVf	10	15	13	15
6.	IVg	13	18	12	17
7.	IVh	12	14	13	15
8.	Giresoflavin	18	21	18	21

III: (R=3-NO_2): MP: 278°C
IR (KBr) bands 3099 cm^{-1}(-NH), 1650cm^{-1} (C=O), 1610 cm^{-1} (C=N), 1160cm^{-1} (C-F) 710cm^{-1} (C-CL), 1350 cm^{-1} (NO_2). ^{1}NMR ($CDCl_3$): 7.2-8.0 (m, 6H Ar-H), 11.25 (S,1H CONH).

General procedure for synthesis of new 7-alkyl/aryl-amino-6-fluro-2(substituted phenyl carboxamido) benothiazole)

A mixture of 7-chloro-6-fluro-(substituted phenyl carboxamido) benothiazole (0.01 mole) and different amines (0.002 mole) in equimolar in



Scheme 1

dimethyl formamide (20ml) and refluxed for 2-4hrs in oil bath. The reaction mixture was cooled and poured over crushe ice. The solid separaed out was filtered and recrystalised with suitabe solvent. (IVa) IR (KBr) bands 3095 cm^{-1}(-NH), 1690cm^{-1} (C=O), 1610 cm^{-1} (C=N), 1175cm^{-1} (C-F) ^{1}H NMR (DMSO) 1.6 (S, 6H, N $(CH_3)_2$), 7.0-8.1(m, 7H, Ar-H)11.0 (S,2H, CONH).

(IVd) IR (KBr) bands 1660 cm^{-1} (C=O), 3100 cm^{-1} (NH), 1608cm^{-1} (C=N), 1160 cm^1 (C-F). ^{1}H NMR (DMSO) 1.8 (S, 3H, CH_3), 6.8-8.0(m, 11H, Ar-H) 11.25 (S, 2H, NH).

(IV h) IR (KBr) bands 1675 cm^{-1} (C=O), 3196 cm^{-1} (NH), 1610cm^{-1} (C=N), 1220 cm^1 (C-F), 1310cm^{-1} (NO_2) ^{1}H NMR (DMSO) 1.7 (S, 3H, CH_3), 6.9-8.1(m, 10H, Ar-H) 11.25 (S, 2H, NH).

Fungicidal activity

The synthesized compounds have been screened for fungicidal activity two fungal species.

1. Candida albicans
2. Aspergillus flavus

Fungicidal activity was screened by employing cup-plate diffusion technique[6] and zone of inhibition is measured in mm. The Griseoflavin is used as standard durg.

RESULTS AND DISCUSSION

All the compounds have been found to exhibit moderate to good antifungal activity against the test fungi. They have been noted to exhibit a better zone of inhibition at 100 µg/ml concentration that at 50 µg/ml. From the experimental data given in the (Table 2). It has been found that compounds IVa, IVe, IVg, possess good activity against both two fungi in 100µg/ml concentration and IVb, IVf, possess poor activity against both fungi in 50µg/ml concentration.

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