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SYNTHESIS AND ANTIBACTERIAL ACTIVI TY OF 1-(2-AMINO-4-FLURO-6-METHYL)-3-CHLORO-4-ARYL AZETITIN-2-ONES

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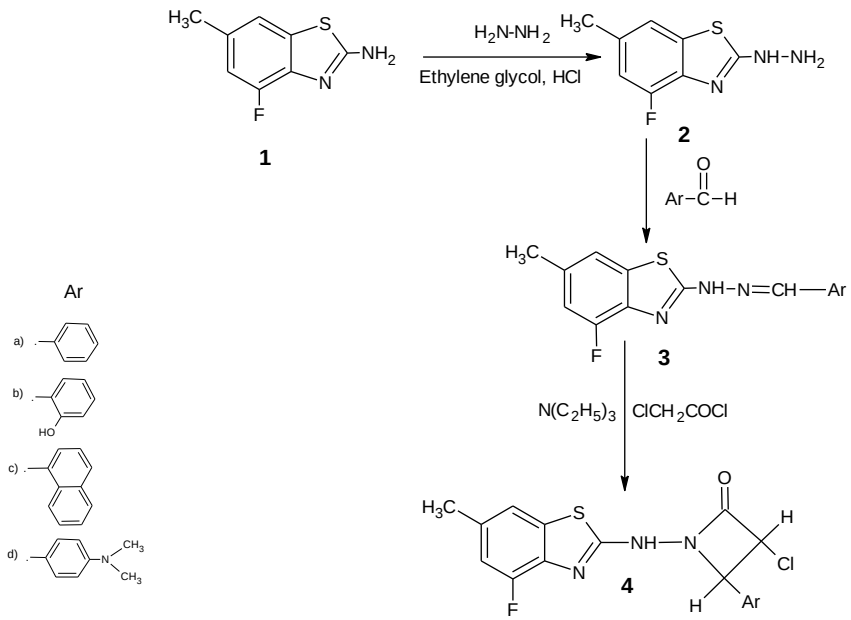
Abstract
4-Fluro-2-hydrazino-6-methyl **2** has been prepared by refluxing 2-amino-4-fluro-6-methyl benzothiazole **1** in ethanol with hydrazine hydrate. Compound **2** condensed independently with benzaldehyde, 2-hydroxy benzaldehyde, napthaldehyde and N, N-dimethylamino benzaldehyde to form corresponding hydrazones (**3a**- **3d**) which were treated with chloroacetyl chloride to afford correpondig azetidin-2-ones (**4a**-**4d**). The structure of the compounds has been confirmed by elemental and spectral analysis. All the newly synthesised compounds were evaluated for their antibacterial activity.

Keywords: Substituted benzothiazoles, Schiff bases, Azetidin-2-ones, Antibacterial activity.

Introduction:
A survey of literature reveals that heteryl hydrazines act as important precursors for the synthesis of various biologically active heterocyclic compounds. Benzothiazoles and azetidinones are reported to posses pharmacological properties[1-5]. The different methods[6-18] are reported in the literature for the synthesis of azetidin-2-one.
Hence it was considered worthwhile to prepare new azetidinones containing benzothiazolyl moiety. Therefore 4-bromo-2-hydrazino-6-methyl benzothiazole and 4-bromo-6-ethoxy-2-hydrazino benzothiazole were refluxed with different aryl aldehyde independently for three hours to obtain corresponding hydrazones (**3a**-**3d**). These hydrazones in dioxane were treated with chloroacetyl chloride in triethyl amine to obtain corresponding 1-(2'-amino-4'-fluro-6'-methyl benzothiazolyl) -3-chloro-4-aryl-azetidin-2-ones (**4a-g**)



Experimental:
All the melting points were determined in open capillary tube and may be uncorrected. The purity of compound was checked by TLC on silica gel coated glass plate. Infra-red spectra were monitored in Nujol / KBr palates on Bomen 104 FT infra-red spectrophotometer. [1]HNMR spectra were obtained on a Gemani 200 Mz spectrometer with tetra methyl silane

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as an internal standard. Mass spectra were recorded on FTVG-7070H mass spectrometer using the EI technique at 70ev. Elemental analysis was performed on a Heraeus CHN-O rapid analyser.

Synthesis of 4-fluro 2-aryl-6-methyl benzothiazolyl hydrazone. (3_{a-d})
The mixture of 2-hydrazino-4-fluro-6-methyl benzothiazole (0.01) was dissolved in ethanol (50ml) and aryl aldehyde (0.01M) was refluxed on water bath for two hours. The reaction mixture was cooled and solid obtained was filtered at pump, washed with ethanol and recrystalised from hot benzene.

1-(2'-amino-4'-bromo-6'-methyl benzothiazolyl)-3-chloro-4-aryl-azetidin-2-one.(4_{a-g})
4-bromo-2-aryl-6-methyl/6-ethoxy benzothiazolyl hydrazone(3_a-3_g) (0.0025 M) in 1,4-dioxane (10 ml) and triethyl amine (2 ml, 0.01 M) was taken in beaker. Chloroacetyl chloride (6 ml, 0.075 M) was added drop by drop maintaining temperature below 5 ^oC with stirring. The reaction mixture kept overnight. Seperated solid product was filtered, washed with water, dried and recrystallized from ethanol.

Result And Discusion :
Structures of the synthesized compounds have been confirmed by elemental analysis, Infrared, NMR and mass spectra. I.R. spectra of compound (4_a) shows absorption band at 3160 cm^{-1} due to N-H stretching and 1780 cm^{-1} due to four membered C=O stretching while NMR spectra shows peaks at δ 2.4(s, 3H, Ar-CH_3), δ 3.9 (d, 1H, CH), , δ 7.0 (d, 1H, -CH), δ 7.1-7.5 (m, Ar-H), δ 8.4 (s, 1H, NH).

Antibacterial activity:
The compounds 4_a-4_d were tested for their antimicrobial actrivity by cup plate agar diffusion method against *E. Coli*, *Erwinia carotovara*, *Bacillus subtilis* and *Xanthomonas citri* species using ampicilin, streptomycin, penicillin as a standard compound (positive control) for comparison. The antibacterial screening data of the compound are presented in table-1 From the results it is also clear that the compounds tested showed variable toxicity against different bacteria. This variation in toxicity can be attributed to different structures and functional groups attached to the basic nucleus. It is also clear from the results presented in table that phenolic –OH and aryl substituted amine groups in the basic nucleus, the antibacterial activity was increased. This was observed with bacteria that the subsequent addition of phenolic (-OH) and aryl substituted –OCH_3 groups antibacterial activity was enhanced.

Table 1:

Sr. No.	Comp.	Antimicrobial activity (zone of inhibition in mm)			
		E.coli	***Erwinia cartovara***	***Bacillus subtilis***	***Xanthom-onas citri***
1	4a	08	07	05	06
2	4b	12	13	12	10
3	4c	06	08	10	06
4	4d	10	12	14	12
Ampicillin		16	18	17	15
Streptomycin		20	18	22	18
Penicillin		15	20	18	17
Control		00	00	00	00

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