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SYNTHESIS AND ANTIBACTERIAL ACTIVITY OF 3-[(4-BROMO-6-METHOXY-1,3-BENZOTHIAZOL-2-YL)AMINO]-2-SUBSTITUTED PHENYL-1,3-THIAZOLIDIN-4-ONE

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ABSTRACT

2-amino-4-bromo-6-methoxy benzothiazole were treated with 80% hydrazine hydrate to form 4-bromo-2-hydrazino-6-methoxy benzothiazole (2). Compound 2 condensed with O-vaniline, Anisaldehyde, P-vaniline, salicylialdehyde, p-hydroxy benzaldehyde and N,N-dimethlamino benzaldehyde to form corresonding hydrazones (3a-3f). These hydrazones were treated with mercapto acetic acid to afford 3-[(4-bromo-6-methoxy-1,3-benzothiazolyl)-amino]-2-substituted phenyl -1,3-thiazolidin-4-one(4a-4f). these newly synthesised 4-thiazolidinone were screened for their antibacterial activity against *Escherichia Coli*, *Bacillus subtilis*, *Erwinia Carotovora*, and *Xanthomonas Citri* species.

Key words: Benzothiazole, hydrazone, 4-Thiazolidinone, Antibacterial activity.

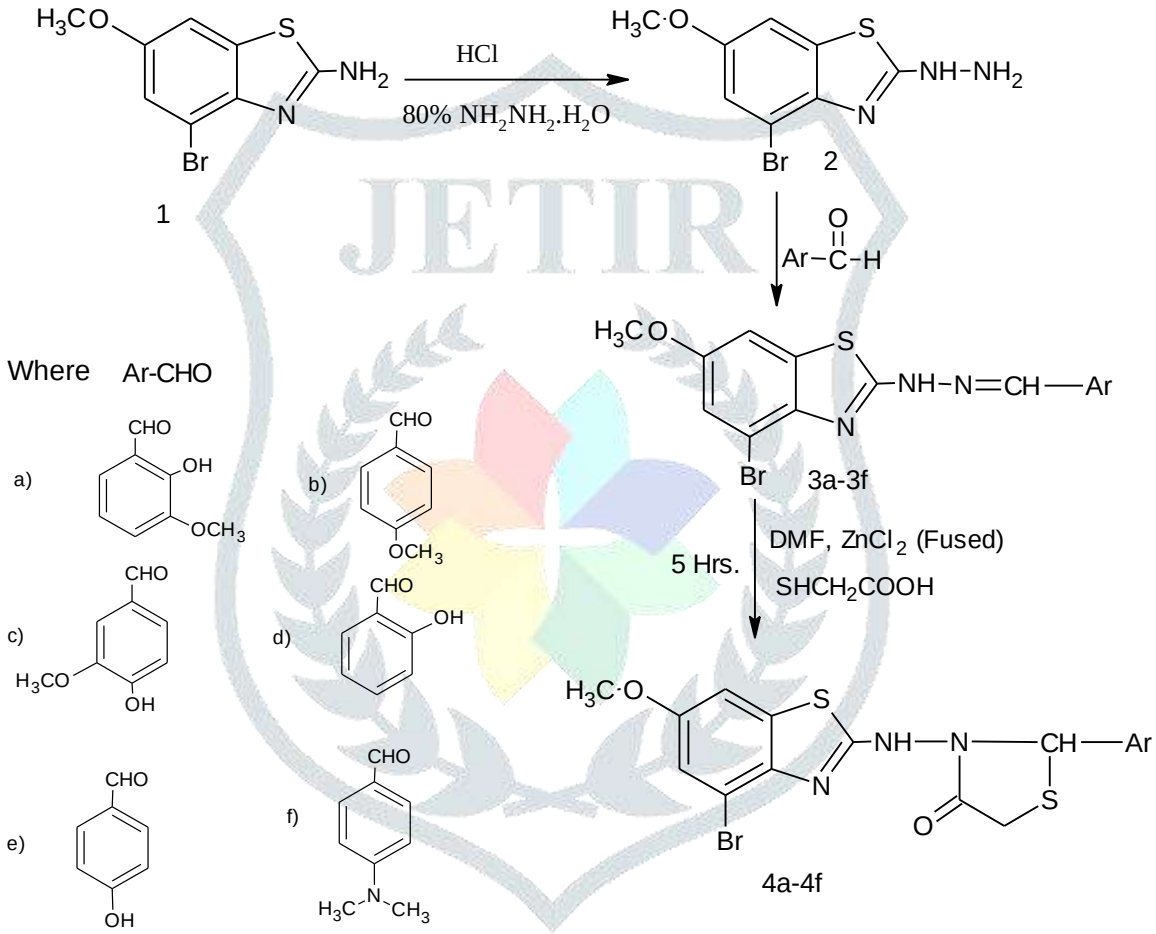
Introduction:

A survey of literature reveals that large work has been carried out on the synthesis of 4-thiazolidinone and known to exhibits various biological activities as antitubercular[1], antiallergic[2]. Schiff-bases give good antibacterial activity and pharmacological application[3]. 4-thiazolidinone ring are reported to possess various biological activities, as antimicrobial, anti-nflammatory, antiviral, antiparasitic and antituberculosis[4-10]. These Schiff-bases can be prepared by the acid catalysed reaction of amine and aldehyde or ketone which shows good fungicidal acivit[11].

4-thiazolidinone give good pharmacological properties[12] are known to exhibits antitubercular[13], antibacterial[14], anticonvulsant[15], antifungal activity[16]. Large work has been carried out on 4-thiazolidinone but very less information is available about 4-thiazolidinone bearing substituted benzothiazolyl moiety.

The starting compound substituted 2-hydrazino benzothizole (1) have been synthesise from substituted amine[17]. Substituted 2-hydrazino benzothiazole were condensed with various aldehyde to yield Schiff-bases (3a-3f). The Schiff-bases were further reacted with thioglycolic acid to yield 4-thiazolidinone derivatives (4a-4f).

Scheme 1



Experimental:

All the melting points were determined in open capillary tube and may be uncorrected. The purity of compound was checked by TLC on silicagel coated glass plate. Infra-red spectra were monitored in Nujol/KBr palates on Bomen 104 FT infra-red spectrophotometer. H1NMR spectra were obtained on a Gemani 200 Mz spectrometer with tetramethylsilane 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.

4-Bromo-2-hydrazino -6-methoxy-benzothiazole (2)

Hydrazine hydrate (80%, 9 ml) was taken in a round bottom flsk, cooled the solution to 5°C and added conc. HCl (6 ml) in dropwise fashion with constant stirring. The flask was kept at room temperature for half an hour. 2-amino-4-bromo-6-methoxy benzothiazole (6 gm) and ethylene glycol (24 ml) was added in portions. The contents of the flask were heated at 150 °C to 160 °C on an oil bath for three hours and then cooled. The obtained product, 4-bromo-6-methoxy-2-hydrazino benzothiazole was filtered, washed with cold water and crystallized from ethyl alcohol to give 3.6 gm (62%), M. P. 172°C, IR (KBr) : 3320 cm^{-1} (asymmetric N-H stretching of $–NH_2$), 3203 cm^{-1} (symmetric N-H stretching of $–NH_2$) m/z: 275 (M+2), 273 (M^+)

Hhydrazone of 4-bromo-2-hydrazino-6-methoxy benzothiazole and substituted aromatic aldehyde (3a-3f)

2-hydrazino-4-bromo-6-methoxy benzothiazole (0.01 M) and aromatic substituted aldehyde was suspended in ethanol seperatly. The mixtures of these suspended solution was refluxed on water bath for three hours. The reaction mixture was cooled and obtained solid filtered by using vaccume pump. The obtained product washed with ethyl alcohol and recrystallised from hot benzene.

3a. 2.5 gm , M. P. : 150 °C, IR(KBr) : 3160 (N-H) stretch), 3185 cm-1 (-OH Stretch),
1584 (C= N Stretch), 1290, (C-N Stretch),

3b. : Yield : 2.5 gm, M. P. : 130 °C. IR (KBr) : 3210 cm^{-1} (-OCH_3 Stretch), 3160 cm^{-1} (N-H Stretch), NMR shows 3.5 Singlet due to OCH_3 group.

3c. : Yield : 2.8 gm, M. P.: 115 °C. IR (KBr): 3175 cm^{-1} (-OH Stretch), 3170 cm^{-1} (N-H Stretch).

3d. : Yield : 2.6 gm, M. P. : 140 °C. I.R. (KBr) : 3389 (N-H stretching) 3060 (= C-H stretch in aromatic ring), 1541 (C=N stretch), 1290 (C-N stretch),

3e. Yield : 2.4 gm , M. P. 182 °C, IR (KBr):3420 cm-1 (O-H) stretching), 3205 cm-1 (N-H stretching),.

3f. Yield : 2.2 gm , M. P. : 138 °C, IR (KBr) :, 3200 cm-1 (N-H stretching),

Synthesis of 2-substituted phenyl 3-substituted benzothiazolyl amino 4-thiazolidinone.(4a-f)

A mixture of hydrazone (Schiff-bases, 3a-3f) (0.0025M), DMF (15ml) and thioglycolic acid (0.005) was taken in round bottom flask. Small amount of fused ZnCl2 (200mg) was added in reaction mixture. The contents of round bottom flask refluxed for five hours. Cooled and poured on crushed ice. Thus the product obtained was filtered, washed with water and recrystlised from DMF.

Result and Discusion:

Structures of the compounds synthesized have been confirmed by elemental analysis, IR, ^{1}HNMR and mass spectra.

I.R. Spectrum of compound (4a) in KBr shows absorption band 3163 cm^{-1} due N-H Stretching and at 1697 cm^{-1} to five membered cyclic amido C=O Stretching

PMR Spectrum of compound (4a) shows δ 2.4 due to $–COCH_2-$ δ 3.2 (s) due to Ar-OCH_3 δ 3.5 due to OCH_3, δ 6.7 due to –OH, δ 7.0 due to -CH-, δ 7.2-7.6 (m) due to Ar-H and δ 9.5 due to -NH. Mass spectrum of the same compound (4a) shows peak at 485 (M^+.) which corresponds to its molecular weight.

Similarly I.R. spectra of compounds (4b-4f) exhibit bands in the region 3100-3400 cm^{-1} and 1600-1800 cm^{-1} due to N-H stretching and C=O stretching respectively.

Antibacterial activity:

The compound 4a to fg 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 and penicillin as a standard compound (positive control) for comparison. The antibacterial screening data of the compound are presented in table---.

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 – OCH_3 groups in the basic nucleus, the antibacterial activity was increased.

Antibacterial activity of newly synthesized compounds.

Sr. No.	**Comp.**	**Antimicrobial activity (zone of inhibition in mm)**			
		E.coli	***Erwinia cartovara***	***Bacillus subtilis***	***Xanthom-onas citri***
1	4a	07	12	08	10
2	4b	07	10	06	06
3	4c	14	07	08	12
4	4d	13	10	09	14
5	4e	12	10	08	09
6	4f	08	06	08	07
Ampicillin		16	18	17	15
Streptomycin		20	18	22	18
Penicillin		15	20	18	17
Control		00	00	00	00

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