INTRODUCTION:

The pyrimido benzothiazole fused heterocyclic compounds and their derivatives impart wide variety of biological actions like antifungal\(^1\)-\(^2\), antibacterial\(^3\), anticonvulsant\(^4\), antiinflammatory\(^5\), anthelmintic\(^6\), antimicrobial activity\(^7\). In view of the reported biological activities of this fused pyrimido benzothiazole heterocycles has fixed the consideration in current era, which may be more effective. Therefore in this section pyrimido pyrazine and benzothiazole moiety are fused to give the pyrazino pyrimido pyrimido benzothiazoles.

Sambhaji P. Vartale et al.\(^8\) reported reaction of 4-cyano-(3-methylthio)-5-oxo-2\(H\)-pyrazole-1(5\(H\))-carbothioamide (5B.1) and 2-amino benzothiazole (5B.2) in DMF and K\(_2\)CO\(_3\) afford benzo[4,5]thiazolo[3,2-a]pyrazolo[3,4-d]pyrimidine derivatives (5B.3), these newly synthesized compounds shows good zone of inhibition against antimicrobial strain as compared to standard streptomycin and penicillin.

Shiksha Gupta et al.\(^9\) reported synthesis of pyrimido[2,1-b]benzothiazol-2-ones (5B.5) by refluxing mixture of 2-amino benzothiazole (5B.4) and alkynic acid in 1-butanol for 48 hrs, these prepared compounds exhibit significant antimicrobial activity against \(E.\) coli, \(S.\) aureus, \(Entero\) bacteria and antifungal activity against \(C.\) albicans.

V.P. Vaidya et al.\(^{10}\) reported synthesis of 2-methyl-4\(H\)-pyrimido[2,1-b][1,3]benzothiazole derivative (5B.7a-b) by refluxing mixture of 2-amino benzothiazole (5B.6) with ethyl aceto acetate and pheynlidine acetoacetate, the pyrimido benzothiazole compounds were evaluated for antibacterial, antifungal and anti-inflammatory activities.
S.V. Kuberkar et al.\textsuperscript{11} reported reaction of 8-methoxy-3-cyano-2-methylthio-4-imino-4H-pyrimido[2,1-b][1,3]benzothiazole (5B.8) with aryl/heteryl hydrazine in presence of DMF and K\textsubscript{2}CO\textsubscript{3} to obtain 3-amino-8-methoxy-4-imino-2H-pyrazolo[3’,4’:5]pyrimido[2,1-b][1,3]benzothiazole (5B.9).

Vinayak K. Deshmukh et al.\textsuperscript{12} reported synthesis of pyrimido[2,1-b]benzothiazole derivative (5B.13) by three component reaction of 2-amino benzothiazole (5B.10), aromatic aldehyde (5B.12) and active methylene compound (5B.11) in triethyl amine by microwave irradiation, these synthesized compounds were screened for anticancer activity using non small cell lung cancer (NCI-H522) cell line with chloro and methoxy substituent.
Hemendra Pratap Singh et al.\textsuperscript{13} reported synthesis of 3-cyano-9-chloro-8-fluoro-2-(methylthio)pyrimido[2,1-\textit{b}]benzothiazole-4\textit{H}-one (5B.16) by condensation of 2-amino-7-chloro-6-fluoro benzothiazole (5B.14) with ethyl-2-cyano-3,3-bis methylthio acrylate (5B.15) in presence of DMF and K$_2$CO$_3$, all the synthesized 2-substituted derivatives of pyrimido benzothiazole were screened for their \textit{in-vitro} & \textit{in-vivo} anti-inflammatory activity.

![Chemical Structure Image]

**PRESENT WORK:**

In the present investigation, we report synthesis of 7,8-diimino pyrazino[1,2-\textit{a}]pyrimido[4,5-\textit{d}]pyrimido[2,1-\textit{b}]benzothiazole and its 2/3/5 substituted derivatives (5B.19a-f). The reaction begin with 3-cyano-4-imino-2-(methylthio)-4\textit{H}-pyrimido[1,2-\textit{a}]pyrazine (5B.17) and its synthesis was discussed in IV chapter. The compound (5B.17) was reacted independently with substituted benzothiazoles (5B.18a-f) in DMF and K$_2$CO$_3$ to afford compounds (5B.19a-f) (Scheme VB-1).

![Chemical Structure Image (Scheme VB-1)]

The formation of compounds (5B.19a-f) begin with nucleophilic attack of amino group of benzothiazoles at thiomethyl flanked carbon of 3-cyano-4-imino-2-(methylthio)-4\textit{H}-pyrimido[1,2-\textit{a}]pyrazine (5B.17) resulting in loss of thiomethyl group in the form of thiomethyl alcohol. The obtained secondary amine on intramolecular cyclization with cyano carbon to obtain cyclic product (5B.19a-f).

Mechanism for the synthesis of compounds (5B.19a-f) can be given as follows (Scheme VB-2).
The structures of newly prepared compounds (5B.19a-f) were confirmed on the basis of spectral analysis like IR, $^1$H NMR and Mass spectral technique. The compounds (5B.19a-f) showed the absence of CN stretching absorption band in the region 2220-2204 cm$^{-1}$ of IR spectrum which confirm that cyclization took place and exhibit strong absorption bands in the functional group region 3480-3220 cm$^{-1}$ which can be assigned to imino (=NH) stretching. The $^1$H NMR spectra impart singlet peak at δ8.960-8.256, which can be assigned to imino (=NH) proton. Mass spectra exhibit that molecular ion peak which corresponds to its molecular weights of compounds.

**EXPERIMENTAL SECTION:**

**Synthesis of 7,8-diimino pyrazino [1,2-a] pyrimido [4,5-d] pyrimido [2,1-b] benzothiazole and their 2/3/5 substituted derivatives (5B.19a-f).**

A mixture of 3-cyano-4-imino-2-(methylthio)-4H-pyrimido[1,2-a]pyrazine (5B.17) (0.217 g, 0.001 mol) and independently with 2-aminobenzothiazole (5B.18a), 2-amino-6-methyl benzothiazole (5B.18b), 2-amino-4,6-dimethylbenzothiazole (5B.18c), 2-amino-6-methoxy benzothiazole (5B.18d), 2-amino-6-chloro benzothiazole (5B.18e), 2-amino-6-nitro benzothiazole (5B.18f), (0.001 mol) in 15 ml of DMF and anhydrous K$_2$CO$_3$ (10 mg) was refluxed for 5-6 hours. The reaction mass was cooled to room temperature and then poured into ice cold water crushed ice (100 ml). The separated solid mass of product was filtered, washed with cold water and recrystallized using absolute ethanol to give pure (5B.19a-f) respectively.
ANALYTICAL DATA:

(1) 7,8-Diimino pyrazino[1,2-a]pyrimido[4,5-d]pyrimido[2,1-b]benzothiazole
(5B.19a).

- Yield : 72%
- Appearance : Brown solid
- Melting point : 272°C
- Molecular Formula : C_{15}H_{9}N_{7}S
- Mol. Weight : 319
- IR (KBr) cm^{-1} : 3421.48, 3348.19, 3220.90 (=NH stretch) (Spectrum VB-1)
- \(^1\)H NMR (DMSO\(_d_6\) \(\delta\)ppm) : 7.436-7.563 (m, 7H, Ar-H), 8.356-8.372 (s, 2H, =NH) (Spectrum VB-2)
- Mass (m/z) : 320.2 (M+1) (Spectrum VB-3)

(2) 7,8-Diimino-3-methyl pyrazino[1,2-a]pyrimido[4,5-d]pyrimido[2,1-b]
benzothiazole (5B.19b).

- Yield : 62%
- Appearance : Pale Yellow solid
- Melting point : 248-250°C
- Molecular Formula : C_{16}H_{11}N_{7}S
- Mol. Weight : 333

- Yield: 69%
- Appearance: Brown solid
- Melting point: 222-224°C
- Molecular Formula: C_{17}H_{13}N_{7}S
- Mol. Weight: 347


- Yield: 71%
- Appearance: Brown solid
- Melting point: 262-264°C
- Molecular Formula: C_{16}H_{11}N_{7}OS
- Mol. Weight: 349
(5) 3-Chloro-7,8-diimino pyrazino[1,2-a]pyrimido[4,5-d]pyrimido[2,1-b]
benzothiazole (5B.19e).

- Yield: 61%
- Appearance: Brown solid
- Melting point: 278-280°C
- Molecular Formula: C_{15}H_8ClN_7S
- Mol. Weight: 353

(6) 7,8-Diimino-3-nitro pyrazino[1,2-a]pyrimido[4,5-d]pyrimido[2,1-b]
benzothiazole (5B.19f).

- Yield: 75%
- Appearance: Brown solid
- Melting point: 240°C
- Molecular Formula: C_{15}H_8N_8O_2S
- Mol. Weight: 364
- IR (KBr) cm\(^{-1}\): 3479.34, 3359.77, 3220.90 (=NH stretch) (Spectrum VB-4)
- \(^1\)H NMR: 7.424-7.667 (m, 6H, Ar-H), 8.354-8.370 (DMSO \(d_6\) \(\delta\)ppm) (s, 2H, =NH) (Spectrum VB-5)
- Mass (m/z): 364 (M\(^+\)) (Spectrum VB-6)
SPECTRA:
REFERENCES: