Chapter-IIIB

**INTRODUCTION:**

The fused pyrimido benzothiazole and its derivatives display an extensive variety of biological activities like antibacterial activity\(^1\), antitumor activity\(^2\), antimicrobial activities\(^3\), anti-HIV\(^4\) and antiviral activity\(^5\). In considering the reported pharmacological activities of this fused pyrimido benzothiazole heterocycles has caught the consideration in recent time, which may be more biologically potent. Consequently, in present section pyrimidine and thiazole moiety are fused with pyrimido benzothiazoles to furnish the thiazolo pyrimido pyrimido benzothiazoles.

Kamlesh D. Niranjane et al.\(^6\) reported preparation, anti-inflammatory activity of new series of 2-amino-3-cyano-14-imino-10-methoxy-4-methylthiopyrimido[2,1-b]pyrazolo[4,5-d]pyrimido[2,1-b]benzothiazole (3B.3), the synthesis was carried out by reaction of 2-amino-6-methoxy benzothiazole (3B.1) and bis (methylthio) methylene malononitrile (3B.2) in presence of K\(_2\)CO\(_3\) and DMF.

![Reaction Scheme 1](image1.png)

S.V. Kuberkar et al.\(^7\) reported synthesis of 15-imnio benzothiazole [2,3-b]pyrimido[5,6-e]pyrimido[2,3-b]benzothiazol-14H-one (3B.6) by reaction of 2-thiomethyl-3-cyano pyrimido[2,1-b]benzothiazol-4H-one (3B.4) with 2-amino benzothiazole (3B.5) in DMF and K\(_2\)CO\(_3\). The prepared compounds exhibit significant antibacterial activity.

![Reaction Scheme 2](image2.png)

Elizaveta V. Resnyanskaya et al.\(^8\) reported by acylation of 5-amino-1-aryl-4-(2-benzothiazolyl)-2,3-dihydro-2-pyrrolones (3B.7) with excess of acid chlorides afford 1-acetyl-3-aryl-3H-pyrrolo[2’3’;4,5]pyrimido[6,1-b]benzothiazol-6-ium-2-olates (3B.8).
S.P. Vartale et al.\(^9\) reported by condensation reaction of pyrido[1,2-\(a\)]pyrimidine (3B.9) with substituted amino benzothiazoles (3B.10) to afford pyrido[1,2-\(a\)]pyrimido[5,6-\(e\)]pyrimido[2,3-\(b\)]benzothiazole derivatives (3B.11).

A.B. Chidrawar et al.\(^{10}\) reported by reaction of pyrazolo[3,4-\(e\)]pyrimido[2,3-\(b\)][1,3]benzothiazole (3B.12) with bis (methylthio) methylene malononitrile (3B.2) to afford pyrimido[2,3-\(b\)]pyrazolo[3,4-\(e\)]pyrimido[2,3-\(b\)][1,3]benzothiazole derivatives (3B.13).

**PRESENT WORK:**

In the here exploration, we report one pot preparation of 5,6-diimino thiazolo[2,3-\(b\)]pyrimido[5,6-\(e\)]pyrimido[2,3-\(b\)]benzothiazole and their 8/10/11 substituted derivatives (3B.15a-f), the reaction started with 6-cyano-5-imino-7-(methylthio)-5H-thiazolo[3,2-\(a\)]pyrimidine (3A.16) which was prepared by refluxing 2-amino thiazole with bis(methylthio)methylene malononitrile in presence of DMF and anhydrous K\(_2\)CO\(_3\) as catalyst. The compound (3A.16) was reacted with various 4/6/7-substituted-2-amino benzothiazoles (3B.14a-f) in DMF and K\(_2\)CO\(_3\) to obtain compounds (3B.15a-f) (Scheme IIIB-1).
The reactions begin with nucleophilic hit of amino group of 2-amino benzothiazoles on carbon flanked to SCH$_3$ group resulting in removal of best departing thiomethyl group in the form of CH$_3$SH. The resulted secondary amine on cyano carbon to gave cyclic product (3B.15a-f).

Plausible reaction mechanism for the structure of compounds (3B.15a-f) can be adduced as follows (Scheme IIIB-2).

The structures of these newly synthesized compounds (3B.15a-f) were established on the basis of IR, $^1$H NMR and Mass spectral analysis. The IR spectra of compounds (3B.15a-f) showed the absence of CN stretching absorption band in the region 2206 cm$^{-1}$ which indicates that cyclization took place and showed the presence of absorption bands in the region 3420-3020 cm$^{-1}$ which can be assigned to (=NH). The $^1$H NMR spectra shows a singlet at 68.30-9.32, which can be assigned to imino (=NH) proton. Mass spectra shows that molecular ion peak which correlate to their molecular weights of compounds.
EXPERIMENTAL SECTION:


A mixture of 3A.16 (0.222 g, 0.001 mol) and independently with 2-amino benzothiazole (3B.14a), 2-amino-6-methyl benzothiazole (3B.14b), 2-amino-4,6-dimethyl benzothiazole (3B.14c), 2-amino-6-methoxy benzothiazole (3B.14d), 2-amino-6-chloro benzothiazole (3B.14e), 2-amino-6-nitro benzothiazole (3B.14f), (0.001 mol) in 15 ml of DMF and anhydrous K$_2$CO$_3$ (10 mg) was refluxed for 5-6 hours. The reaction mixture was cooled to room temperature and then poured into crushed ice containing cold water of 100 ml. The obtained solid mass of product was filtered, washed with cold as well as hot water and recrystallized using ethanol to give pure (3B.15a-f) respectively.

ANALYTICAL DATA:

1) 5,6-Diimino thiazolo[2,3-b]pyrimido[5,6-e]pyrimido[2,3-b]benzothiazole

(3B.15a).

- **Yield**: 65%
- **Appearance**: Yellow solid
- **Melting point**: 274°C
- **Molecular Formula**: C$_{14}$H$_8$N$_6$S$_2$
- **Mol. Weight**: 324
(2) **5,6-Diimino-10-methyl thiazolo[2,3-\(b\)]pyrimido[5,6-\(e\)]pyrimido[2,3-\(b\)] benzothiazole (3B.15b).**

- **Yield**: 78%
- **Appearance**: Brown solid
- **Melting point**: 295°C
- **Molecular Formula**: C_{15}H_{10}N_{6}S_{2}
- **Mol. Weight**: 338

(3) **5,6-Diimino-8,10-dimethyl thiazolo[2,3-\(b\)]pyrimido[5,6-\(e\)]pyrimido[2,3-\(b\)] benzothiazole (3B.15c).**

- **Yield**: 79%
- **Appearance**: Brown solid
- **Melting point**: >300°C
- **Molecular Formula**: C_{16}H_{12}N_{6}S_{2}
- **Mol. Weight**: 352
(4) 5,6-Diimino-10-methoxy thiazolo[2,3-b]pyrimido[5,6-e]pyrimido[2,3-b]benzothiazole (3B.15d).

Yield: 69%
Appearance: Grey solid
Melting point: 281°C
Molecular Formula: C_{15}H_{10}N_{6}OS_{2}
Mol. Weight: 354
IR (KBr) cm\(^{-1}\): 3417.63, 3340.48 (=NH stretch) (Spectrum IIIB-1)
\(^1\)H NMR: 3.750-3.826 (s, 3H, -OCH\(_3\)), 6.911-7.807 (m, 5H, Ar-H & thiazolic-H), 8.127-8.575 (s, 2H, two -NH) (Spectrum IIIB-2)
Mass (m/z): 355 (M +1) (Spectrum IIIB-3)


Yield: 74%
Appearance: Brown solid
Melting point: 222°C
Molecular Formula: C_{14}H_{7}ClN_{6}S_{2}
Mol. Weight: 358
(6) 5,6-Diimino-10-nitro thiazolo[2,3-b]pyrimido[5,6-e]pyrimido[2,3-b]
benzothiazole (3B.15f).

- **Yield**: 79%
- **Appearance**: Brown solid
- **Melting point**: 264°C
- **Molecular Formula**: C_{14}H_{7}N_{7}O_{2}S_{2}
- **Mol. Weight**: 369
- **IR (KBr) cm^{-1}**: 3394.48, 3271.05 (=NH stretch) (Spectrum IIIB-4)
- **^{1}H NMR**: 7.28-8.26 (m, 5H, Ar-H & thiazolic-H), 9.06 (DMSO\textsubscript{d6} \delta ppm) (s, 2H, two =NH) (Spectrum IIIB-5)
- **Mass (m/z)**: 370.3 (M+1) (Spectrum IIIB-6)
SPECTRA:
Chapter III-B

(Spectrum III-B-5)
REFERENCES: